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ETHICS AND HUMAN RIGHTS IN HIV-RELATED CLINICAL TRIALS IN AFRICA WITH SPECIFIC REFERENCE TO INFORMED CONSENT IN PREVENTIVE HIV VACCINE EFFICACY TRIALS IN SOUTH AFRICA

BY

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Thesis submitted in partial fulfilment of the requirements for the degree

DOCTOR LEGUM

in the

FACULTY OF LAW

UNIVERSITY OF PRETORIA

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PRETORIA 2007

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I declare that the thesis, which I hereby submit for the degree Doctor Legum (LLD) at the University of Pretoria, is my own work and has not previously been submitted for a degree at another university.

Signed at Pretoria on this the 26th day of June 2007.

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SUMMARY

This thesis examines the regulation of HIV-related clinical research in Africa, with special emphasis on preventive HIV vaccine efficacy trails in South Africa. The discussion centres on aspects of the South African economic, social and political context, which increase not only certain communities' vulnerability to HIV infection, thereby accelerating the spread of the disease, but also those communities' vulnerability to exploitation and abuse during clinical research.

Human rights law is suggested as a viable alternate model to bioethical regulation to protect participants in HIV-related clinical trials. It is demonstrated that, in certain instances, human rights law has important advantages over bioethics, not only because it has the force of law, but also because it positions the research participant within a specific social context. It is proposed that a normative model derived from human rights' principles adds value to the bioethical debate in the context of clinical research in South Africa and the rest of the world.

The thesis concludes that in order to make clinical research more responsive to circumstance, bioethics should be inspired by a broader social, economic and political perspective, such as is provided by a human rights-based analysis.

The thesis recommends that bioethics and human rights law, rather than being seen as different systems, should be unified into a single system of protection under the Constitution and the Bill of Rights. In order to do this, legislation that integrates ethical guidelines and human rights law needs to be drafted to give effect to the constitutional guarantee in section 12(2)(c). At the international level, the adoption of a convention which integrates human rights law and ethical guidelines is proposed.

OPSOMMING

Die proefskrif ondersoek die regulering van MIV-verwante kliniese navorsing in Afrika, met spesifieke verwysing na kliniese proefnemings in Suid-Afrika om die doeltreffendheid van voorkomende MIV-entstowwe te bepaal. Die bespreking gee aspekte van die Suid-Afrikaanse ekonomiese, sosiale en politisie konteks weer, wat nie net sekere gemeenskappe se kwesbaarheid vir MIV-infeksie bevorder nie, en dus die verspreiding van die siekte aahelp nie, maar wat ook daardie gemeenskappe meer kwesbaar maak om uitgebuit en misbruik te word gedurende kliniese navorsing.

Menseregte word voorgestel as 'n lewensvatbare alternatiewe model teenoor bio-etiese regulering om die belange van deelnemers aan MIV-verwante kliniese proefnemings te beskerm. Die proefskrif wys daarop dat, onder sekere omstandighede, menseregte belangrike voordele bo die bio-etiek het, nie net omdat dit regskrag het nie, maar ook omdat dit die deelnemer aan navorsing posisioneer binne 'n spesifike sosiale konteks. Daar word aan die hand gedoen dat 'n normatiewe model, afgelei vanaf menseregte-beginsels, waarde sal toevoeg tot die bio-etiek-debat in die konteks van kliniese navorsing in Suid-Afrika en die res van die wêreld.

Die proefskrif bevind dat, om kliniese navorsing meer responsief tot omstandighede te maak, die bio-etiek geïnspireer moet word deur 'n breër sosiale, ekonomiese and politiese perspektief, soos wat voorsien word deur 'n menseregte-gebaseerde analise.

Die proefskrif maak die aanbeveling dat die bio-etiek en menseregte, eerder as om as twee verskillende stelsels gesien te word, saamgevoeg moet word in 'n enkele stelsel van beskerming ondergeskik aan die Grondwet en die Menseregtehandves. Ten einde hierdie doel te bereik, moet wetgewing aangeneem word wat effek gee aan die grondwetlike waarborg in artikel 12(2)(c) en sodoende etiese riglyne en menseregte integreer. Op die internasionale vlak word aan die hand gedoen dat 'n internasionale konvensie aangeneem moet word wat menseregte en etiese riglyne integreer.

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for

E, who cooked a roast
W, who was patient
and
my parents, who would have been so proud

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ACKNOWLEDGEMENTS

I have been given great intellectual, moral and practical support.

The International Clinical, Operational, and Health Services Award (ICOHRTA) and the NIH sponsored my Post-Doctoral Fellowship at CIRA, Yale University, in 2003 where I did research and wrote the first chapters of the thesis.

The supervisor, Professor Frans Viljoen, and co-supervisor, Professor Pieter Carstens, provided valuable guidance. Professor Viljoen, especially, has been unstinting in his advice, support and humour.

I thank Walter, for inspiring me with his quest for knowledge and ideas, his practical support in editing the thesis, and his effort to create the right conditions for the completion of the thesis.

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ABBREVIATIONS AND ACRONYMS

ACHPR	African Charter on Human and Peoples' Rights
ADCC	antibody-dependent cellular cytotoxicity
AIDS	Acquired Immune Deficiency Syndrome
ART	anti-retroviral therapy
ARV	antiretroviral
AU	African Union
AZT	Zidovudine
CAT	Convention Against Torture
CEDAW	Convention on the Elimination of All Forms of Discrimination Against Women
CIOMS	Council for International Organizations of Medical Sciences
CMI	cell-mediated immunity
CRC	Convention on the Rights of the Child
CSA	Centre for the Study of AIDS, University of Pretoria
DNA	deoxyribonucleic acid
DH	Department of Health (South Africa)
DWB	Doctors Without Borders
FDA	Federal Drug Administration (United States of America)
GC	General Comment
GDP	Gross Domestic Product
HAART	Highly Active Anti-retroviral Therapy
HAVEG	HIV Vaccine Ethics Group
HCP	health care providers
HIV	Human Immunodeficiency Virus
HSRC	Human Sciences Research Council
ICCPR	International Covenant on Civil and Political Rights
ICESCR	International Covenant on Economic, Social and Cultural Rights
IDU	injection drug user
IRB	Institutional Review Board
IUD	intra-uterine device
MCC	Medicines Control Council (South Africa)
MDG	Millennium Development Goals
MP	Member of Parliament
MRC	Medical Research Council (South Africa)

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MSM	men who have sex with men
MTCT	mother-to-child transmission
NEPAD	New Partnership for Africa's Development
NGO	non-governmental organisation
NIH	National Institutes of Health
OAU	Organisation of African Unity
OHCHR	UN Office of the High Commissioner for Human Rights
PI	principal investigator
PIL	patient / participant information leaflet
PLWHA	people living with HIV/AIDS
PLWV	people living with the virus (HIV)
PMTCT	prevention of mother-to-child transmission
REC	research ethics committee
RCCT	randomised controlled clinical trial
RNA	ribonucleic acid
SADC	Southern African Development Community
SAAVI	South African AIDS Vaccine Initiative
SIV	Simian Immunodeficiency Virus
STI	sexually transmitted infection
STD	sexually transmitted disease
TB	Tuberculosis
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNDP	United Nations Development Programme
UNESCO	United Nations Educational, Scientific and Cultural Organization
UNGASS	United Nations General Assembly Special Session on HIV/AIDS
USA	United States of America
VCT	voluntary counselling and testing
WHO	World Health Organisation
WHA	World Health Assembly
WMA	World Medical Association
WSW	women who have sex with women

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CHAPTER 1

INTRODUCTION

Outline

1 Contextual background

2 Significance of the topic

3 Research question

4 Aims of study

5 Research methodology
5.1 Literature review
5.2 Interviews

6 Scope of study

7 Difficulties and limitations of study
7.1 Difficulties
7.2 Limitations

8 Work already done in the field

9 Outline and overview of chapter content

1 CONTEXTUAL BACKGROUND

> It was the best of times, it was the worst of times, it was the age of wisdom, it was the age of foolishness, it was the epoch of belief, it was the epoch of incredulity, it was the season of Light, it was the season of Darkness, it was the spring of hope, it was the winter of despair ...[1]

Charles Dickens' depiction of the human condition as it was in 1775 may, in equal measure, be applied to humanity's state in 2007 as the HIV and AIDS pandemic rages. Although therapeutic agents, able to slow down the progress of the disease significantly,[2] have been developed, the side effects, the exacting administration regimens and, most importantly, the cost of these agents, suggest their inadequacy as a long-term solution to combat the epidemic, especially in the developing world. Because of these drawbacks, for many in Africa, antiretrovirals offer a 'winter of

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1 Dickens (1964) 1.
2 See para 3.4 of ch 2 below.

despair' - it is as though they cannot afford to pay for 'life itself'[3] – even if elsewhere it is the 'spring of hope'.

Sub-Saharan Africa is, by far, the region that is the worst affected by the HIV and AIDS epidemic. Two thirds or 66.6 per cent of all adults and children with HIV globally live in sub-Saharan Africa, amounting to almost 25 million people.[4] Also, 2.1 million Africans died of AIDS in 2006, totalling almost three quarters or 72 per cent of all AIDS deaths globally.[5] Within sub-Saharan Africa, southern Africa is the worst off - one third or 32 per cent of all people living with the virus (PLWV) are in southern Africa and 34 per cent of all AIDS deaths in 2006 occurred in southern Africa.[6]

Within southern Africa, South Africa is experiencing one of the most devastating epidemics. A total of 5.5 million people in South Africa were living with the virus by the end of 2005 – the highest number of individuals infected by HIV in any single country in the world.[7] The level of HIV among women attending antenatal clinics in South Africa is at its highest yet – 30.2 per cent.[8]

Even though the Human Sciences Research Council's (HSRC) *South African national HIV prevalence, HIV incidence, behaviour and communication survey 2005*[9] puts South Africa's overall HIV prevalence rate lower than that estimated by UNAIDS, these percentages are still alarming.[10] In three provinces (the Eastern Cape, Free State and KwaZulu-Natal) the average life expectancy has fallen below 50 years.[11]

Despite their initial optimism and hope, scientists admit that the possibility of developing a cure for AIDS within the next decade remains remote. Furthermore,

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3 Cameron (2000) First Jonathan Mann Memorial lecture: 'The deafening silence of AIDS' XIII International AIDS Conference, Durban, 7 - 14 July. Also see para 2.3.2 of ch 5 below.

4 UNAIDS (2006) *AIDS epidemic update* 6. Also see para 3.3.4 of ch 2 below.

5 As above.

6 n 4 above, 3.

7 As above, 11.

8 As above; based on statistics supplied by the Department of Health, South Africa, 2006.

9 HSRC (2005) 'South African national HIV prevalence, HIV incidence, behaviour and communication survey 2005'.

10 HSRC 21 - 41. Different HIV prevalence studies yield different results. In 2004, the Department of Health published the 2004 National HIV and Syphilis antenatal sero-prevalence survey, which, based on a sample of 16 061 women at antenatal clinics across the country. This survey estimated that in 2004, 29.5% of pregnant women in South Africa were HIV positive and that a total of 6.29 million South Africans were living with HIV. The HSRC's survey, however, estimates that a lower total, 24.4%, were living with HIV. This lower estimate may be due to the different methodologies used by the two surveys - in this regard, see n 225 of ch 5.

11 n 4 above, 11.

although education and information programmes aimed at reducing the HIV infection rate are in place, these have had only limited success.[12] Experience teaches us that greater knowledge of the risk of HIV infection does not necessarily lead to individual behavioural change. If education and information programmes are to succeed, the individual must realise, first, that she is at risk and, second, she must be in a position to avoid the risk. Often, neither of these two preconditions required for the success of information and education programmes is present. Hence, as with many viral diseases, such as smallpox and poliomyelitis, the development of an effective vaccine offers the only hope of halting or slowing the HIV and AIDS epidemic.

Phase II clinical trials which have the purpose of establishing the efficacy of various candidate vaccines against HIV are underway in South Africa, and Phase III trials will start in the near future.[13] By definition, these trials involve human subjects. Thus, it is crucial that the existing ethical and human rights frameworks for the protection of research subjects be examined critically. As Charles McCarthy observes: 'We must develop ethical and legal answers that are as sophisticated as the science that develop the vaccine itself'.[14]

Although much attention has been paid to ethical guidelines governing clinical trials involving human subjects, generally, until very recently only limited work had been done on HIV vaccine trials, specifically. Similarly, scant attention has been given to issues relating to the human rights of HIV vaccine trial participants.

In the past, violations of the rights of participants in HIV-related clinical research by trial administrators were seen as violations of universal (medical) ethical principles and not as violations of the human rights of trial participants.[15] It is to be expected that this view should dominate, as clinical research is the domain of science and the medical profession: medical professionals, although well-versed in medical ethics, are relatively unfamiliar with human rights discourse.

In contrast to the traditional approach, this study places HIV-related human subject research within the context of the human rights discourse. The focus of the study is on preventive HIV vaccine efficacy trials in South Africa, seen within the context of HIV-related clinical research in Africa.

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12 Such as the ABC campaign in Uganda. See ch 2 below.

13 See para 4 of ch 2 and para 2.3.1 of ch 5 below.

14 McCarthy, quoted in Weisburd (1987) 131 *Science News* 329.

15 See for example, the debate regarding the supposed unethical nature of the short-duration AZT trials in Africa, discussed in ch 3 below.

The systems for protecting the interests of clinical research participants are analysed in terms of *concepts*: the study investigates norms related to human rights and bioethical discourse, and the implementation of each system.

2 SIGNIFICANCE OF THE TOPIC

Groups such as the HIV/AIDS Vaccine Ethics Group (HAVEG) have done valuable work in the delineation and scrutiny of ethical guidelines relating to HIV vaccine research, as well as building the capacity of non-governmental organisations (NGOs) working in the field. Because their focus is ethics, these groups concentrate on issues relating to the ethics of informed consent; the decision-making processes of trial participants; and cultural differences in the perceived voluntariness of trial participation. They rely on ethical guidelines expressed, for example, in the World Medical Association's Helsinki Declaration which governs biomedical research involving human subjects.

This study, by way of contrast, focuses on those aspects which relate to the human rights of trial participants. It investigates the protection afforded preventive HIV vaccine trial participants in South Africa by global, regional and domestic human rights instruments. As well, it surveys one of the major ethical concerns associated with HIV-related clinical trials in Africa – informed consent to participation. No similar study has been undertaken to date.

The value of the application of human rights discourse to the fields of medicine and clinical research has been advocated by various persons.[16] However, human rights discourse has not been used extensively to frame the rights of research subjects. In South Africa individual human rights are entrenched in a supreme constitution,[17] rendering the utility of such an approach self-evident.

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16 Such as the efforts of Jonathan Mann. See Mann *et al* 'Health and human rights' in Mann *et al* (eds) (1999) 7 - 20. Also see Macklin (2004) *Double standards in medical research in developing countries*. Macklin deals with the ethical controversies that surround research conducted in the developing world, and sponsored by the developed world. In ch 7, entitled 'Respecting, protecting and fulfilling human rights', Macklin advocates the utility of a rights-based approach to clinical research in the developing world, but sees human rights law as limited by its lack of realisation (she writes: 'As is true of the gap between the enunciation of ethical principles and their full realisation, a gulf exists between the human rights stipulated in or derived from these instruments and their full realisation. In developing countries generally, ... this gulf is the widest' (222)). On the whole, Macklin's study deals with the ethical concept of justice and the human rights norm of access to health care, and not with autonomy or informed consent (informed consent is touched upon in ch 5 of her work). Aspects of Macklin's work are discussed in chs 3 and 5 below.

17 Constitution of the Republic of South Africa 1996. See chs 4 and 5 below.

3 RESEARCH QUESTION

The thesis investigates the following research question:

> Do human rights afford more adequate protection to participants in preventive HIV vaccine efficacy trials in South Africa than that which is afforded by ethical guidelines, and what is the relationship between human rights and ethical guidelines in the protection of participants?

In order to answer the research question, it first must be established if it is more appropriate to rely upon human rights law rather than ethical guidelines to protect the interests of participants in HIV-related clinical research in Africa.

4 AIMS OF STUDY

The study centres on clinical trials to test the efficacy of a preventive HIV vaccine in South Africa. Preventive HIV vaccine testing is likely to take place in communities in which economic, medical, educational and other resources are stretched and where there is a high risk of HIV infection.[18] Because of the stigma attached to HIV infection and the victimisation of people who are (or are perceived to be) HIV positive, the rights of the participants in the various trials must be held sacrosanct, as must those of the community in which HIV vaccine trials are conducted.

The study has three primary aims.

- An investigation into the protection that ethical guidelines laid down by international and national bodies and adhered to by international and local ethical review committees, research institutions and researchers, afford HIV vaccine efficacy trial participants, in order to arrive at a comprehensive understanding of the extent of the protection afforded;

- An investigation into the protection international human rights instruments and the South African Constitution, 1996, afford to preventive HIV vaccine efficacy trial participants, in order to arrive at a comprehensive understanding of the extent of the protection afforded; and

- An investigation into the relationship between the different layers of protection afforded by human rights law and ethical guidelines to preventive

HIV vaccine efficacy trial participants in South Africa, in order to establish whether they are complementary or adversarial.

In addition, the study considers the following broader issues relating to **HIV clinical research in Africa**.

- The implications for clinical research in Africa of 'principlism' in bioethics and research ethics, embodied by Beauchamp and Childress' four principles-approach[19] and represented in international and national ethical guidelines and discourse;

- The limits of classical ethical discourse and the potential gains of employing human rights discourse in the protection of clinical research participants in Africa;

- The implementation of international human rights law in Africa;

- The clinical research endeavour as a means of accessing health care in the African context;

- The role of 'cultural relativism' in the application of 'universal' international ethical and human rights norms to research in developing countries. The issue is raised in the context of the debate over the use of placebo-controlled trials in Africa when an efficacious (but unsuitable) form of treatment has already been developed; and

- International collaborative research in the developing world and the potential for exploitation in this context.

These are the issues which are anticipated to be particularly contentious in relation to **preventive HIV vaccine efficacy trials in South Africa**.

- Informed consent - as an ethical guideline and as a human right embodied in international instruments, and in section 12(2)(c) of the South African

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18 See paras 5.4.1 and 5.4.2 of ch 2 and para 2 of ch 5 below.
19 See ch 3 below.

Constitution. In particular, the role of context in ensuring informed consent and the peculiar position of rural women as vaccine trial participants with regard to their economic and social vulnerability need to be taken into consideration in terms of whether their agreement is in compliance with ethical guidelines and human rights norms on informed consent;

- The nature and level of the risks which attach to the preventive HIV vaccine trial. These risks are scientific and social in nature, for example, the discrimination experienced by the participant consequent upon testing HIV positive on standard laboratory Elisa assays[20] according to the presence of vaccine-induced HIV antibodies in the trial subjects' blood, and stigmatisation because of perceptions that trial participants are at high risk for HIV infection;

- Whether preventive HIV vaccine efficacy trials should be classified as 'therapeutic' or 'non-therapeutic' research, and the implications of such a classification;

- The capacity of members of ethics committees to assess HIV vaccine efficacy trial protocols;

- Autochthonous collectivist notions with reference to ethical issues, such as voluntary consent in clinical trials; and

- Participation in HIV vaccine efficacy trials as a means of accessing health care in a setting where resources are stretched. This is problematic, especially in the case of the development of a therapeutic vaccine where such a programme represents the only chance of survival for HIV positive participants.

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20 See ch 2 below.

5 RESEARCH METHODOLOGY

The thesis is a theoretical study based on a literature review of the following:[21]

- A literature survey of the HIV virus, scientific progress in developing a HIV vaccine and the dangers inherent in participating in HIV vaccine research;
- A literature survey of relevant ethical principles - embodied in ethical rules and guidelines on clinical research;
- An analysis of the human rights which relate to clinical research, especially informed consent to participation in research, as well as instances in which these rights have been litigated nationally and internationally;
- A comparative literature study of relevant sections of selected African constitutions in order to arrive at an understanding of the scope of the protection provided to research participants in individual countries' constitutional frameworks;
- An analysis of the legal position regarding informed consent to research participation in South Africa, which includes an analysis of the common law, case law, legislation, ethical guidelines and human rights law;
- A brief analysis of a report on an empirical study of an informed consent process in a HIV vaccine efficacy trial in South Africa; and
- A critical scrutiny of the readability and comprehensibility of an informed consent document utilised in a HIV drug trial in South Africa.

In examining the protection afforded by bioethics and human rights to participants in clinical research, the thesis focuses on:

- the origins and normative framework of each system;
- the applications of each system as contained in their principles and norms;
- the implementation mechanisms of each system; and

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21 Additionally, while doing research at Yale University in the United States of America, I was able to interview members of NGOs and government, AIDS activists, academics, vaccine scientists and ethicists about some of the issues discussed in this study. On the whole, these interviews relate to the scientific background of the study.

- sanctions for non-compliance.

6 SCOPE OF STUDY

The aim of the study is to examine the protection afforded by ethical guidelines and human rights instruments to participants in HIV vaccine efficacy trials in South Africa. These are the steps taken in the study to achieve this goal:

- Positioning the study within a scientific context; in which the HIV virus is discussed, the course of the epidemic is delineated and the importance of clinical research aimed at providing an effective preventive vaccine is posited;

- Analysing the nature of ethical principles and the various enforcement mechanisms that exist internationally and locally, as well as presenting an overview of how these principles and mechanisms have served participants in HIV-related clinical research in Africa in the past;

- Analysing the nature of human rights and the various enforcement mechanisms that exist internationally and locally, as well as presenting an overview of the way in which these principles may be employed to serve participants in HIV-related clinical research in Africa;

- Scrutinising the scientific, political, economic and social contexts in which preventive HIV vaccine efficacy trials are likely to take place in South Africa and the risks that may be anticipated by trial participants; and

- Examining informed consent as an ethical and human rights imperative and analysing the manner in which the discourses of ethics and human rights ensure the informed consent of HIV vaccine efficacy trial participants in South Africa.

7 DIFFICULTIES AND LIMITATIONS OF STUDY

7.1 Difficulties

An evident difficulty for a layperson in the course of doing the scientific research for this study is coming to terms with the medico-scientific terminology. Vaccine science is a highly specialised field and, understandably, scientific journals do not make concessions to the lay reader. Because of the difficulty in comprehending scientific

texts, it has been a problem to read these texts critically. I have relied heavily on scientific colleagues for advice and information.

Further to this problem, HIV vaccine science is still developing, with the consequence that previously-held convictions and theories are being continually discarded. Scientific thought on suitable HIV-vaccine strategies, for example, is changing as more knowledge is gained about the human immune response to the virus.

A significant conceptual difficulty arises in attempting to impose a rights-based discourse on an ethical model. Rights and principles differ greatly in their origin and nature and are not easily interchangeable. The wariness of members of the medical profession in relation to a rights-based approach is symptomatic of this difficulty.

Related to this difficulty is the lack of a body of jurisprudence which utilises international human rights law to remedy abuses in clinical research in Africa.[22] The abuse of research participants is seen as a violation of ethical guidelines and not as an infringement of their human rights. Victims of abuse in Africa have attempted to take their case to court, but have not used human rights law as the basis for such litigation.[23]

7.2 Limitations

The study does not provide a number of things:

- An exhaustive epidemiological or public health-related analysis of HIV;
- Anything other than a representation of the science of HIV and vaccine research at the most basic (undergraduate) level – the aim is merely to introduce the reader to the scientific discourse on HIV in the context of its relevance to the thesis;
- A detailed examination of ethical guidelines and human rights instruments relevant to participants in *therapeutic* HIV vaccine efficacy trials;
- An investigation of issues related to the access of trial participants and their community to an effective vaccine once it has been developed – in terms of

22 See ch 5 below.

23 One exception to this is the case of the participants in the recent Trovan trials in Nigeria. See para 4.2.2 of ch 3 below.

the ethical value of justice and the human rights value entrenched in section 27 of the South African Constitution. This limitation is due to the focus of the thesis on informed consent in terms of the ethical value of respect for persons or autonomy, and the human rights value entrenched in section 12(2)(c) of the South African Constitution;

- A philosophical analysis of ethical theory, or an exhaustive account of modern ethical theory. It briefly investigates the traditional ethical theories that are the foundation of bioethical discourse. The challenges posed by the ethics of feminism and multiculturalism will be mentioned in passing, and particularly in chapter 5 below;

- A thorough-going philosophical analysis of ethics and human rights discourses within the context of post-modern philosophical thought;[24] and

- Finally, as no Phase III preventive HIV vaccine efficacy trials have yet been concluded in South Africa, chapter 5 of the thesis can present only an estimate of the problems likely to be encountered in these trials. For the same reason it was not possible to include a linguistic analysis of a consent document used in such a trial.

8 WORK ALREADY DONE IN THE FIELD

Until recently surprisingly little has been written on the role of ethics in HIV vaccine efficacy trials. Although ethical issues in clinical research have been dealt with extensively, to the extent of devoting entire journals to the issue,[25] vaccine efficacy trials have received little attention. This lack may be due in part to the fact that only a single candidate HIV vaccine has progressed to large-scale phase III clinical trials.[26] As was indicated above, the human rights of trial participants have not been attended to in the literature.

Scientific journals with articles on the science of HIV vaccine research are abundant. Vaccine strategies are examined and positive as well as negative research

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24 A number of post-modern philosophers, such as Alain Badiou, argue that human rights and ethical discourses merely serve to reinforce the individual's powerlessness. This contention falls outside of the scope of this study. See ch 6 below.

25 eg *Journal of Medical Ethics, Bioethics, Journal of Medicine and Philosophy, Kennedy Institute of Ethics Journal, Developing World Bioethics*, etc.

26 The VaxGen trial, see para 4.6 of ch 2 below.

results have been reported. However, these studies do not comment on the ethics of HIV vaccine research. An important analysis of current HIV vaccine science, (edited by Flossie Wong-Staal and Robert Gallo) is provided in a compilation of essays indicating current directions in HIV vaccine research. The first essay deals with the problems that have been encountered in HIV vaccine research.[27]

The pioneering work on ethical issues relating to HIV vaccine efficacy trials is that by Christine Grady, published in 1995, entitled *The search for an AIDS vaccine*. Grady's emphasis is on local[28] and international ethical guidelines relating to HIV vaccine research. By her own admission, she pays scant attention to issues specific to international vaccine efficacy trials.[29] Less thorough, is the work of Thomas Kerns, *Ethical issues in HIV vaccine trials*, published in 1997.

Specific to the African context, is a preliminary study by Nicholas A Christakis, entitled 'The ethical design of an AIDS vaccine trial in Africa', published as a Hastings Center Report in 1988.[30] Christakis touches on issues such as the design of a HIV vaccine trial, the selection of suitable subjects, risks and consent issues, the beneficent treatment of participants, ethical standards in cross-cultural perspective and maintaining research ethics in the face of such a devastating epidemic.

In 2000, UNAIDS published a guidance document, entitled *Ethical considerations in HIV preventive vaccine research*. Professor Robert Levine, a highly respected academic and ethicist, is one of the authors. Although the document provides a sound preliminary understanding of relevant issues, again, it focuses exclusively on ethics.

In South Africa, various preliminary explorations of ethical issues relating to HIV vaccine efficacy trials have been published, such as by Cathy Slack *et al*;[31] Lindegger and Richter[32] and Abdool Karim.[33]

The most thorough study of ethical issues relating to HIV vaccine efficacy trials in a South African context to date is that by Keymanthri Moodley - entitled 'HIV vaccine trial participation in South Africa – an ethical assessment', published in

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27 Nabel in Wong-Staal and Gallo (eds) (2002) 1 – 7.
28 Local to the United States of America.
29 Grady (1995) 10.
30 Christakis (1988) 18 *The Hastings Center Report* 31-37.
31 Slack *et al* (2000) 96 *SA J Science* 291.
32 Lindegger and Richter (2000) 96 *SA J Science* 313.
33 Abdool Karim (2002) 20 *CME* 588.

2002.[34] Moodley's study has a strong philosophical emphasis. She examines tensions which arise when developed countries sponsor research in the developing world. Specifically, she argues that in many societies in Africa, especially in rural regions, a moderate form of communitarianism exists in contrast to western liberal individualism. She explores concepts such as ethical relativism within the context of HIV vaccine efficacy trials in South Africa. However, although well-reasoned, Moodley's study focuses on ethics rather than on human rights.

A number of articles published recently deal with adolescent preventive HIV vaccine trial participation in South Africa in the light of new statistics[35] showing the increasing incidence of HIV infection in that age group.[36] The articles investigate the implications of the new National Health Act,[37] the Constitution and local and international ethical guidelines upon adolescents' vaccine trial participation and the notion of informed consent. By contrast, this thesis focuses on informed consent with respect to adults; the problems presented by adolescent participation are referred to in passing.

9 OUTLINE AND OVERVIEW OF CHAPTER CONTENT

The study consists of six chapters which are structured as follows:

In this chapter **(Chapter 1)** a general introduction is presented. The HIV/AIDS epidemic is examined as a public health issue and the argument for the importance of developing an effective vaccine is presented. Furthermore, the study is located within the South African context, so as to explore the peculiarities, if any, of the South African and African situation. It then will be possible to articulate the research question the study proposes and provide an outline of subsequent chapters.

Chapter 2: The Human Immunodeficiency Virus and the mechanics for developing an effective vaccine are dealt with here. The nature and functioning of retroviruses are discussed. The Human Immunodeficiency Virus is described as a sub-type of this group of viruses. The way in which a vaccine functions is traced and a distinction is

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34 Moodley (2002) 27 *J Med and Philosophy* 197. Also reprinted in Van Niekerk and Kopelman (eds) (2005) 160 – 178.

35 See HRC (n 10 above) 37.

36 See eg Van Wyk (2005) 68 *J Contemporary Roman Dutch L* 35; Strode *et al* (2005) 101 *SA J Science* 225; Slack and Kruger (2005) 96 *SA Med J* 269; Jaspan *et al* (2005) 95 *SA Med J* 685; Slack *et al* (2005) 95 *SA Med J* 682. On the scientific justification for adolescent participation, see Jaspan *et al* (2005) 95 *SA Med J* 785.

37 Act 61 of 2003.

made between preventive and therapeutic vaccines. Different research methodologies are outlined and possible strategies for the development of an effective HIV vaccine are explored.

Chapter 3: The origin and nature of ethical principles are examined. An analysis of the protection afforded by fundamental ethical principles, such as autonomy, informed consent, beneficence (including nonmaleficence), and justice, as they are embodied in various international and domestic documents, is presented. The protection afforded by international documents, such as the Nuremberg code, the International Ethical Guidelines for Biomedical Research involving Human Subjects, the Belmont Report and the Declaration of Helsinki will be scrutinised. Domestic documents, such as the Medical Research Council's Guidelines on Ethics for Medical Research of 1993 and the practices of Institutional Ethics Review Committees at different universities will be investigated. Examples of the abuse of research participants in Africa and elsewhere are discussed. The purview in this chapter is not limited to preventive vaccine efficacy trials in South Africa, but looks at clinical trials in Africa relating to HIV in general.

Chapter 4: In this chapter justiciable human rights are offered as an alternative means to protect the rights of participants in contrast to non-binding ethical guidelines. The origin and nature of human rights are explored. A critical examination of the protection international and domestic human rights documents and instruments offer is extended. The chapter additionally examines the implementation of international human rights law in Africa and South Africa. Again, the discussion in the chapter is not limited to preventive HIV vaccine efficacy trials in South Africa, but looks at clinical trials in Africa relating to HIV in general.

Chapter 5: The focus here is on informed consent in HIV vaccine efficacy trials in South Africa. The effectiveness of the ethical guidelines and human rights standards in South Africa for the protection of participants in HIV vaccine efficacy trials is considered. The chapter outlines the epidemiologic, scientific, political and socio-economic contexts in which HIV vaccine efficacy trials are taking place and are likely to take place in South Africa. In the first instance, the chapter highlights difficulties arising out of the use of non-binding ethical guidelines and the implications in a

South African context. In the second instance, the chapter debates the advantages of deploying human rights law in a South African context.

Chapter 6: Conclusion – a summary of the research findings. The research question that has been asked is revisited. A synthesis between the two systems is arrived at, rejecting the notion that either ethical guidelines or human rights on their own are able to function effectively to protect the interests of clinical research participants. Recommendations as to a discourse which will offer trial participants the maximum protection are offered with regard to the proposal in the thesis that the discussion with reference to an ethical discourse should be positioned more broadly than the limits of classical principlism allow.

Chapter 2, which follows, presents an examination of the scientific background to the discussion in subsequent chapters of ethical and human rights issues in relation to HIV-related clinical research and the search for an effective preventive vaccine against HIV infection.

CHAPTER 2

SCIENTIFIC FRAMEWORK: HIV/AIDS AND THE SEARCH FOR A PREVENTIVE VACCINE

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2.3 Resistance to infection: The human immune system

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6 Conclusion

1 INTRODUCTION

This chapter presents the scientific background to the discussion in subsequent chapters of ethical and human rights issues in relation to HIV-related clinical research and the search for an effective preventive vaccine against HIV infection.

The Human Immunodeficiency Virus (HIV) is characterised in the context of a general discussion of viruses as infective agents. The peculiarities of the HIV and AIDS syndrome, as well as the progress that has been made in its treatment, are investigated. The extent of the epidemic is outlined and it is argued that a vaccine offers the only chance of halting the spread of the epidemic.

Next a short history of the development of successful vaccines against pathogenic infections is given, and the focus is on challenges facing the development of a preventive HIV vaccine. In this section various options for candidate preventive HIV vaccines are explored.

Finally, clinical research, generally, and vaccine efficacy trials, specifically, are discussed. The discussion aims to provide the scientific setting for the third and fourth chapters that examine ethical issues associated with HIV-related research in Africa, as well as the setting for the fifth chapter which focuses on preventive HIV vaccine efficacy trials in South Africa. Throughout, the terms which relate to the HIV, vaccine development and clinical research are introduced and explained.

2 VIRUSES AND DISEASES

2.1 Viruses

A virus is the smallest form of life that is able to replicate – it is smaller than a bacterium and its measurement is taken in nanometres.[1] Viruses are totally dependent on living cells for their replication and existence. They can only replicate

inside cells, using the host cell's machinery for this process.[2] Viruses possess only one species of nucleic acid, either DNA or RNA.[3] The hereditary information of the virus is contained here.[4] Viral genomes commonly consist of ten to fifteen genes, but they may have as few as 3 or as many as 100 genes.[5] Viruses attach to cells by means of a receptor-binding protein; they exist in human, animal, plant, insect or bacterium cells and depend upon these cells for protein production.[6]

Viruses are classified into families according to whether their nucleic acid is RNA or DNA,[7] the number of strands they possess, and their polarity.[8] They may be divided further into sub-families[9] and genera.[10]

A virus is structured as follows:[11]

- a genome (sum total of genes);
- a capsid, which is the protein shell that surrounds and protects the DNA or RNA genome, and which acts as a vehicle to convey the virus from cell to cell and organism to organism; and
- an envelope, which is a loose, fragile lipoprotein membrane that covers the capsid. This envelope is acquired mainly from the host cell and in some cases viral proteins are added to the envelope.[12]

The replication cycle of a virus typically consists of the following elements:[13]

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1 Collier and Oxford (2000) 7. One nm is 1/100 000 of a cm. The smallest virus is more or less the size of haemoglobin molecules of red blood cells. The word virus is derived from Latin where it means 'poison' and 'slimy material'.

2 Collier and Oxford (n 1 above) 7; Cloete and Atlas (eds) (2006) 11; Nicklin *et al* (1999) 269. Because of this, some microbiologists view viruses as parasites of the host cells within which they replicate. Viral replication results in changes within the host cell, often causing its death (see Cloete and Atlas 11 – 12).

3 As above. DNA is **d**eoxyribo**n**ucleic **a**cid – the nucleic acid type where the linker molcule is deoxyribose sugar. RNA is **r**ibo**n**ucleic **a**cid – the nucleic acid type where the linker molecule is ribose.

4 Collier and Oxford 11; Cloete and Atlas 11.

5 Collier and Oxford 15; Nicklin *et al* (n 2 above) 279.

6 Collier and Oxford 7; Nicklin *et al* 282.

7 Nicklin *et al* 269; 285. Higher organisms consist of DNA.

8 Collier and Oxford 16. They may be either positive or negative stranded.

9 Depending on their gene structure; Nicklin *et al* 270.

10 Depending on antigenic and other biological properties (Cloete and Atlas 57; Nicklin *et al* 270).

11 Schoub (1994) 44; Nicklin *et al* 268; Cloete and Atlas 11 – 12. Because of their simplicity, viruses have no capacity to generate the energy that they need for processes such as replication. To carry out these processes, viruses make use of the host cell's machinery and biochemical facilities, sometimes, but not always, to the detriment of the host cell.

12 Not all viruses have such an envelope (Cloete and Atlas (n 2 above) 11); Nicklin *et al* (n 2 above) 270.

- attachment to the host cell surface;
- penetration into the cytoplasm;
- release of the viral genome within the infected cell;
- replication of viral nucleic acid and proteins;
- assembly of new virus particles; and
- their release from infected cells which may be accompanied by the acquisition of an envelope.

2.2 Viral disease

Viruses are classified as well according to their pathogenicity and virulence in causing disease.[14] Viruses vary in terms of the number of hosts they can infect, the tissues they infect,[15] and the mechanisms by which they are able to cause disease in the host.[16]

The typical spread of a virus in a host takes this route:[17]

- The virus enters the host (for example, via the respiratory tract, the gastrointestinal tract, conjunctiva, or via the genital tract).
- The virus then replicates in susceptible cells at the site of entry (called the site of inoculation).
- The virus manages to overcome the defence of local cells (at the site of inoculation), such as lymphocytes, macrophages[18] and interferon.
- The virus now spreads to other areas of the host via the bloodstream.
- The virus replicates further in a target area (localised or generalised).[19]

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13 Mackett and Williamson (1995) 15.

14 Schoub (n 11 above) 48. Pathogenicity is a comparison of the severity of disease caused by various viruses, while virulence is a comparison of the severity of disease caused by different strains of the same virus – eg HIV is more pathogenic than measles; HIV I is more virulent than HIV II.

15 Schoub 48. Tissue tropism. Possible target organs include the skin (herpes simplex virus), the lungs, the liver (hepatitis virus) and the central nervous system.

16 Pathogenesis.

17 Collier and Oxford (n 1 above) 30; Schoub 51 – 55; Cloete and Atlas 12; 18 – 20; Nicklin *et al* 307 – 309.

18 A macrophage, a type of helper-T cell, is a large immune system cell in the tissues that 'eats up' invading pathogens. The word 'macrophages' literally means 'big eaters' (Rick (2004) 85). Macrophages stimulate other immune cells by presenting them with small pieces of the invaders.

19 An example of a virus that attacks a localised target area is adenovirus conjunctivitis which causes eye infections, and a virus that attacks a generalised target area is measles.

- Finally, the virus leaves the host (sometimes called 'shedding' or 'budding') in sufficient quantities so that it may spread to another host (and so ensure its continued existence).

In humans, viral infections follow one of three basic patterns of disease (some, but by no means all, fatal):[20]

- Acute, non-persistent infections (influenza).
- Persistent infections with acute onset (HIV; herpes simplex).
- Insidious infections (sub-acute sclerosing panencepehalitis).

2.3 Resistance to infection: The human immune system

Over time humans have developed a complicated and efficient system of fighting infections caused by viruses and other organisms which is known as the human immune system.[21] The immune system is a complex system of cells, tissues and organs that protects the body against infectious agents and cancer[22] by means of different processes.[23] Scientists talk about 'non-specific' and 'specific' resistance to infection by the human immune system.[24] Before the discussion turns to a detailed description of the components and functioning of the specific and non-specific immune system, it is important to remember that certain general factors play a role in a person's resistance to infection.[25] These are:[26]

- mechanical or chemical barriers (such as the skin or a low PH balance in the stomach);
- fever (viruses find it difficult to replicate in temperatures above 37°C);
- age (for example, a younger person may not have acquired immunity to a certain disease because she has not yet been exposed to that disease; an older person may have a weakened immune system due to chronic illnesses and so on);

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20 Collier and Oxford (n 1 above) 34 – 36; Schoub (n 11 above) 53; Nicklin *et al* (n 2 above) 310 - 312.

21 Delves and Roitt (2000) 343 *New Engl J Med* 37; Nicklin *et al* 314.

22 Certain cancers are caused by viruses, such as cervical cancer, which is caused by the human papilloma virus. Viruses that transform cells and cause cancerous cells are called oncogenic viruses (Cloete and Atlas (n 2 above) 25.

23 Collier and Oxford (n 1 above) 38; Delves and Riott (n 21 above) 37.

24 As above.

25 Burton and Engelkirk (2000) 310 – 323; Collier and Oxford (n 1 above) 38; Schoub (n 11 above) 71 – 81.

26 As above.

- nutritional status (poor nutrition may exacerbate the severity of some infections);
- hormones (certain cancers 'feed off' hormones, for example oestrogen-positive breast cancers);
- genetic factors (some people are genetically predisposed to certain infections, while others may have a stronger immune system); and
- species resistance (for example, some viruses are able to infect humans only, others are able to infect all mammals).

As its name indicates, a non-specific immune response is a response by immune system cells that attack *any* infectious agent.[27] Non-specific immune system cells include:[28]

- phagocytes (that engulf and destroy infectious agents) consisting of:
  - macrophages[29] that generally engulf cells infected with viruses, such as monocytes,[30] tissue macrophages, and microglial cells;[31] and
  - neutrophils that generally attack foreign bacteria.
- mast cells, basophils and eosinophils that attack protozoa and large parasites such as worms.
- natural killer (cytotoxic) cells that attack virus-infected cells and tumour or cancer cells.

'Specific' immunity is characterised by:[32]

- the ability to launch an enhanced response against a specific antigen[33] (viruses or other micro-organisms) that has been encountered before; and
- the ability of the immune system to distinguish between its own molecules and 'non-self' molecules.

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27 As above.

28 Mackett and Williamson (n 13 above) 41; Burton and Engelkirk (n 25 above) 311 – 313; Nicklin *et al* (n 2 above) 314 - 315.

29 See n 18 above.

30 macrophages in blood.

31 macrophages in the brain.

32 Collier and Oxford (n 1 above) 39 – 47; Mackett and Williamson (n 13 above) 41 - 46.

33 An 'antigen' is any substance that is able to stimulate the immune system to produce antibodies, usually viruses and bacteria.

This system is considered 'specific' in that it consists of immune system cells that respond only to very specific foreign agents (molecular components of an infectious agent, such as a viral protein).[34] These are the two main components of specific immunity to viral infections.[35]

- Humoral (antibody-mediated, or resulting from the activity of antibodies) immunity which is produced by B-cells[36] (B-lymphocytes), which release masses of antibodies[37] into the bloodstream, in co-operation with antigen-presenting cells and T-lymphocytes.[38]
- Cell-mediated immunity (CMI) established by a variety of T-cells (T-lymphocytes), including particular helper, suppressor, and killer (cytotoxic) cells.

Antibodies act in protecting the body against viral attack in a number of ways. An antibody:[39]

- neutralises the virus by agglutinating (a process of glueing or clumping) the virions[40] and thus stops them from attaching to susceptible cells;
- acts as an opsonin, whereby it combines with virions and increases the ability of macrophages to destroy them;
- coats macrophages with specific antibody so that these macrophages are 'armed' to destroy those viral antigens that express that specific viral antigen;

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34 Burton and Engelkirk (n 25 above) 352.

35 Klein and Ho (2000) 22 *Clinical Therapeutics* 300; Rick (n 18 above) 78.

36 A B-cell (or B-lymphocyte) is one of the major classes of lymphocytes. They are white blood cells that are derived from the bone marrow and spleen. B-cells develop into plasma cells, which produce antibodies.

37 An antibody that is an infection-fighting protein molecule in blood and secretions, that tags, neutralises and destroys pathogenic microorganisms or toxins. Antibodies, also known as immunoglobulins, are made and secreted by B-lymphocytes in response to stimulation by the antigen. An antibody produced by a particular B-cell specifically recognises and binds to a particular foreign antigen (eg p24 protein of HIV).

38 A T-cell is a white blood cell that is critical to the body's immune response and can destroy cancer cells and cells infected with viruses, fungi and bacteria. These cells are also known as killer or helper T-cells or lymphocytes, and kill virus-infected cells, whereas antibodies target free-floating viruses in the blood. Killer (cytotoxic) T-lymphocyte (CTL) responses are suspected to be a correlate of HIV immunity.

39 Collier and Oxford (n 1 above) 43 – 44; Burton and Engelkirk (n 25 above) 336 – 339; Mackett and Williamson (n 13 above) 41.

40 The whole virus particle (nucleocapsid and outer envelope) is called a virion; Nicklin *et al* (n 2 above) 270.

- exerts antibody-dependent cellular cytotoxicity (ADCC), whereby it combines with the viral antigen expressed on the surface of the infected cell which it then kills; and
- interferes with the uncoating sequence[41] of the virus after the virus has entered a cell.

The body's B-cell (antibody) response acts to prevent the infiltration of cells by circulating virus. Once the virus is inside the cell, circulating antibodies specific to the virus cannot get at them and it is here that T-cells perform their function.[42]

T-cell response differs from the methods of B-cells. Whereas B-cells secrete antibodies into the general circulation, T-cells recognise virally infected cells and eliminate them.[43] Two types of T-cells exist.[44]

- CD4 cells (or helper T-cells), which are the regulators of the immune function, recruiting non-specific immune cells and stimulating the production of antibodies by B-cells.
- CD8 cells (or cytotoxic T-cells), which both kill virus-infected cells and release anti-viral cytokines in the blood.

The killer (cytotoxic) T-lymphocyte[45] (CTL) or CD8 cell binds directly to - and kills - cells carrying a foreign antigen that its receptor recognises, such as virus-infected cells and tumour cells.

Helper T-lymphocytes or CD4[46] (T4) cells are equally important. They play a central role in both humoral and cell-mediated immunity. They do not kill infected cells, but are necessary for the functioning of both B-lymphocytes and killer (or cytotoxic) T-lymphocytes.[47] They 'help' these cells to perform their function.

Immune responses to virus infections are sometimes complicated by the ability of some viruses to infect and damage the very cells that mediate this

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41 The virus literally takes off its coat, or envelope, in order to integrate itself with the host cell and replicate.

42 Klein and Ho (n 35 above) 300; Rick (n 18 above) 86; Mackett and Williamson (n 13 above) 41.

43 As above.

44 Klein and Ho (n 35 above) 300 – 301; Rick (n 18 above) 86.

45 See n 38 above.

46 CD4 is an abbreviation for 'cluster of differentiation 4', which refers to cell surface molecules that are used to identify stages of maturity of immune cells, for example CD4 cells.

47 Burton and Engelkirk (n 25 above) 335; Schoub (n 11 above) 71 – 81.

response. Finally, it is important to note that the mechanisms of the immune system's response vary according to the type of virus it is defending against.[48]

We now turn to the virus of interest to this study, the Human Immunodeficiency Virus.

3 THE HUMAN IMMUNODEFICIENCY VIRUS (HIV)

3.1 Classification

HIV is the virus that causes AIDS.[49] It is a lentivirus[50] and belongs to the family of viruses known as retroviruses.[51]

HIV consists of a RNA genome.[52] Inside the infected cell, reverse transcriptase[53] produces a DNA copy of HIV's RNA genome.[54] The virus then uses this DNA copy to replicate inside the invaded cell, producing a haploid double-stranded DNA provirus that gets inserted into the chromosomal DNA of the host cell.[55]

Once inside the host cell, the provirus may remain latent, especially in resting lymphocytes.[56] However, the moment these cells are activated, transcription and translation occur, and viral proteins assemble to form new virions.[57] Finally, the infected cell releases hundreds of new virions,[58] or viruses, which in turn are able to infect other cells.[59]

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48 Schoub (n 11 above) 81; Klein and Ho (n 35 above) 298; Cloete and Atlas (n 2 above) 22.

49 This scientific fact is questioned by only a few non-mainstream scientists and by misguided politicians. See Weiss and Weiss in Smith *et al* (eds) (2001) 147.

50 From the Greek *lenti* which means 'slow'. All lentiviruses produce slow viral diseases, and many affect the cells of the immune system (Schoub (n 11 above) 54).

51 Burton and Engelkirk (n 25 above) 424; Schoub 55; Klein and Ho 299. The scientific name is Retroviridae. Up until the mid-1970s, no member of the retrovirus family was known to occur in humans.

52 Weiss and Weiss in Smith *et al* (n 49 above) 127.

53 An enzyme unique to retroviruses. Nicklin *et al* (n 2 above) 303.

54 Schoub 81; Cloete and Atlas 22; Nicklin *et al* 303; Weiss and Weiss in Smith *et al* 127. Reverse transcriptase, as its name suggests it, causes the reverse of the normal transcription process (that involves the synthesis of RNA from a DNA template) in that it causes the synthesis of DNA from an RNA template.

55 Graham in Nelson *et al* (eds) (2000) 521 - 522; Nicklin *et al* 303. When incorporated into the host cell's DNA the virus can be transferred to each daughter cell when the host's cell divides.

56 Graham in Nelson *et al* 522.

57 As above.

58 a complete, infectious viral particle. Virions are released from host cell by means of 'budding' (Cloete and Atlas (n 2 above) 22.

59 Graham in Nelson *et al* (n 55 above) 522.

HIV is of medium size, more or less 100 – 150 nm in diameter.[60] It is roughly circular in shape, but may become oval or irregular because of the elasticity of the viral envelope.[61]

HIV's genome is composed of nine genes[62] which carry the code for the inner proteins, the envelope proteins and the enzymes.[63] Three of these genes carry the information needed to make key structural proteins for the new virions.[64] These three genes are called the *gag*,[65] *env*[66] and *pol*.[67] The six regulatory genes of HIV are *tat*, *rev*, *vif*, *nef*, *vpu* and *vpr*.[68]

HIV's replication rate is considered to be extremely high as it produces more or less 10 billion particles every day.[69] This replication rate may be compared with that of Hepatitis B which also replicates by means of reverse transcriptase, but which undergoes many fewer replications per unit of time.[70] This high replication rate and the fact that there is no proofreading mechanism during reverse transcription are responsible for HIV's high mutation rate[71] which has implications for anti-retroviral treatment and the development of a future vaccine.[72]

Upon infection HIV invades the dendritic cells[73] in the genital or oral mucosa of the infected person. These cells then fuse with CD4-lymphocytes (helper T-cells) and spread to deeper tissues.[74]

Helper T-lymphocytes are the ultimate target of the virus,[75] but HIV also infects the following cells:[76]

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60 Schoub (n 11 above) 56; Graham in Nelson *et al* 522.

61 As above.

62 Klein and Ho (n 35 above) 300.

63 As above. An enzyme is a protein produced by cells to accelerate a specific chemical reaction without itself being altered. Enzymes are generally named by adding '-ase' to the name of the substance on which the enzyme reacts, eg protease is an enzyme that acts on proteins.

64 Schoub 58; Graham in Nelson *et al* 522.

65 stands for group antigen.

66 stands for envelope.

67 short for polymerase (Schoub (n 11 above) 59 – 60).

68 Klein and Ho 300.

69 Perelson *et al* (1997) *Nature* 188; Klein and Ho 299. RNA viruses lack the 'proofreading' abilities of DNA viruses that enable them to correct mistakes.

70 Holmes (2003) 77 *J Virology* 3893; see also eg Coffin (1995) 267 *Science* 483.

71 Wodarz and Nowak in Domingo *et al* (eds) (1999) 199; Schoub (n 11 above) 65.

72 See para 4.5 below. Also see Meyerhans and Vartanian in Domingo *et al* (n 71 above) 87 – 88; Wodarz and Nowak in Domingo *et al* 199 – 200.

73 Dendritic cells are immune system cells with threadlike tentacles called dendrites used to enmesh antigens, which they present to T-cells. Langerhans cells, found in the skin, and follicular dendritic cells, found in lymphoid tissues, are both types of dendritic cells.

74 Burton and Engelkirk (n 25 above) 424.

- helper T-lymphocytes (they are in fact killed);[77]
- macrophages (the virus merely replicates inside macrophages without harming them);[78]
- dendritic cells; and
- nervous system cells.[79]

On looking at the types of cells that are infected, it becomes evident that HIV infects two systems in the body – the immune system and the nervous system.[80] Sources of HIV in a HIV-infected person are (amongst others):[81]

- semen (contains helper T-cells, macrophages);
- blood (contains T-cells, macrophages, dendritic cells);
- vaginal/cervical secretions (contain helper T-cells, macrophages);
- menstrual fluid (contents the same as blood); and
- breast milk (macrophages).[82]

The incubation period of the virus varies in accordance with various factors, such as the infected person's general state of health and nutrition.[83] If left untreated, about 90 per cent of all infected adults will develop AIDS within ten years to twelve years of infection.[84]

At present, two laboratory tests are used to establish the presence of HIV in the body:[85]

- An ELISA[86] HIV-antibody test.[87]
- Western Blot.[88]

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75 Klein and Ho (n 35 above) 299.
76 Schoub (n 11 above) 81 – 86.
77 which causes a failure of humoral immunity and cell-mediated immunity.
78 Also see Wodarz and Nowak in Domingo *et al* (n 71 above) 198.
79 The specific cells are still unclear.
80 Schoub 82 - 83.
81 Schoub 83; Lecture notes, Prof Robert Dubrow, Yale University School of Medicine.
82 Body fluids that are not sources of HIV include saliva, urine, tears, faeces and perspiration. These contain little or no live cells which makes it virtually impossible for HIV to be transmitted along these routes (Schoub 83).
83 Graham in Nelson *et al* (n 55 above) 524.
84 As above. Antiretrovirals seem to be able to (perhaps indefinitely) delay the onset of AIDS. See para 3.4 below.
85 Graham in Nelson *et al* 524. There are also so-called 'quick-tests' which are often used by public testing centres.
86 ELISA stands for enzyme-linked immunoabsorbent assay. This test detects antibodies based on a reaction that leads to a detectable colour change in the test tube.

An ELISA HIV-antibody test indicates the presence of HIV antibodies in the blood. The ELISA assay is 99.9 per cent accurate, but may at times give a false positive reading.[89]

A Western Blot test is used to confirm a positive ELISA. This test is more specific (as it detects antibodies to specific viral proteins), but also more complicated and therefore more expensive.[90] Tests that estimate the viral RNA load and CD4-count are important measures of the progression of the disease and of the effectiveness of anti-retroviral therapy.[91]

3.2 The natural history of HIV

There are different ways in which to categorise the progression of HIV infection.[92] Graham and Schoub categorise HIV's progress as follows:[93]

- primary infection (acute HIV syndrome);
- asymptomatic silent phase;
- initial symptoms;
- early immune failure; and, finally,
- AIDS or end-stage HIV infection.

3.2.1 Primary infection and acute HIV syndrome

Symptoms of acute HIV syndrome following infection usually appear within a few days to weeks after exposure to the virus, mostly two to four weeks after infection.[94] The symptoms of acute HIV infection last from a few days to a few weeks.[95] These

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87 used routinely.

88 a test detecting antibodies to specific viral components. This test is often used to confirm a positive ELISA, and is more expensive.

89 As it may react to other viral proteins than those belonging to HIV (Graham in Nelson *et al* 524; Schoub (n 11 above) 88 – 89.

90 A positive result on a HIV-antibody ELISA test may also be confirmed by doing two further ELISAs that use different HIV proteins (called a 'triple' ELISA).

91 The test which estimates viral RNA-load is also known as a polymerase chain reaction (PCR) test and measures the amount of HIV in the blood. The CD4-count measures the number of CD4-cells in the blood, which also indicates the progression of the disease.

92 The World Health Organization, for example, categorises the progression of HIV differently from that which is preferred by Graham and Schoub.

93 Graham in Nelson *et al* (n 55 above) 524; Schoub (n 11 above) 88 – 89. Also see Wodarz and Nowak in Domingo *et al* (n 71 above) 179 – 180 and Rouzine and Coffin in Domingo *et al* 225 – 226.

94 Weiss and Weiss in Smith *et al* (n 49 above) 137; Graham in Nelson *et al* 525.

95 As above. Also see Wodarz and Nowak in Domingo *et al* 197 – 198.

symptoms are flu-like[96] (also called 'viremia'), such as fever, rash, headache, generalised lymphadenopathy,[97] pharyngitis,[98] joint pain, weight loss, fatigue, lethargy, depression, night sweats, and various other symptoms.[99] Not everyone experiences all these symptoms, and the intensity of the symptoms varies from person to person.

Acute HIV syndrome occurs in 50 to 70 per cent of infected persons; during this stage of infection, laboratory findings show large quantities of HIV in the blood of the infected person, and also a suppression of helper T-lymphocytes.[100] Most important, seroconversion takes place during this stage: seroconversion is the point in time where a person 'converts' from a situation in which there is no production of HIV antibodies (HIV negative) to the production of HIV antibodies (HIV positive).

3.2.2 Asymptomatic 'silent' phase

During this phase of infection the body's immune system fights off the initial HIV onslaught and the person recovers from acute HIV syndrome.[101] There are now no overt symptoms of disease present and the person feels and appears healthy. There is a very low level of HIV in the blood at this stage (viral RNA load)[102] and this level remains relatively constant. The person's helper T-lymphocytes (CD4 cell) count returns to normal or near normal (600 – 1500 cells per ml of blood).[103]

Although this phase is often referred to as the 'silent' phase, an enormous struggle is being waged between HIV and the immune system.[104] Each day, approximately 100 million HIV particles are produced and are then destroyed by the immune system. Also, approximately two billion helper T-cells are destroyed and replaced.[105] Graham remarks that the main site is in the lymphoid tissue and not in the bloodstream as many lay people suppose.[106]

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96 Rouzine and Coffin in Domingo *et al* 226.
97 swollen lymph glands.
98 a sore throat.
99 Graham in Nelson *et al* 525; Rouzine and Coffin in Domingo *et al* 226; Weiss and Weiss in Smith *et al* 129.
100 Wodarz and Nowak in Domingo *et al* 197.
101 As above.
102 Viral RNA load is an important predictor of the progression of the disease.
103 Graham in Nelson *et al* (n 55 above) 525; Weiss and Weiss in Smith *et al* (n 49 above) 129; Wodarz and Nowak in Domingo *et al* (n 71 above) 198. Rouzine and Coffin in Domingo *et al* are of the opinion that the CD4-count returns only partially to its pre-infection level (226).
104 Weiss and Weiss in Smith *et al* 137.
105 This is 5% of the total helper T-cell population.
106 Graham in Nelson *et al* 525; Wodarz and Nowak in Domingo *et al* 198.

Eventually the immune system becomes exhausted and the viral load increases because HIV infects and damages the very cells that mediate the body's immune response.[107] It attacks and destroys CD4 or helper T-lymphocytes, which play a significant role in both humoral and cell-mediated immunity.[108] As a consequence, the CD4-count decreases.[109]

This phase may last from anything between one to fifteen years, but may be prolonged (perhaps even indefinitely) when triple-antiretroviral therapy is taken.[110]

3.2.3 Initial symptoms

The initial symptoms that an infected person shows during this stage are those of a lymphadenopathy syndrome.[111] Lymph glands in the neck, armpits and groin are enlarged. Wasting syndrome also sets in, and a person experiences weight loss, fever and night sweats. Some instances of neurological disease may also occur during this phase.[112]

3.2.4 Early immune failure

During this phase, because of the virus's gradual destruction of the body's immune system, the infected person suffers from relatively minor opportunistic infections caused by minor microorganisms.[113] These include candidiasis,[114] shingles[115] and hairy leukoplakia.[116]

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107 HIV infects and replicates in lymphocytes and macrophages and so destroys these cells which are crucial to the body's immune response.

108 See para 2.3 above.

109 Graham in Nelson *et al* 525; Wodarz and Nowak in Domingo *et al* 198; Rouzine and Coffin in Domingo *et al* 226.

110 As above. See para 3.4 below.

111 persistently enlarged lymph glands.

112 Graham in Nelson *et al* (n 55 above) 525.

113 As above. Opportunistic infections are infections that do not cause serious disease in persons who have a normal immune system.

114 Graham in Nelson *et al* 525. This is an infection by the *candida* fungus - a harmless infection that is kept in check by a healthy immune system. In HIV positive persons, the fungus causes thrush, esophagitis (it spreads down the esophagus) and vaginal candidiasis. It is treated with Mycostatin which controls the infection but does not eliminate it.

115 Graham in Nelson *et al* 525. This is caused by a reactivation of the varicella zoster virus (which causes chicken pox), which is dormant in the nerve cells. It causes a painful rash on the trunk of the person and can recur.

116 Graham in Nelson *et al* 525; Weiss and Weiss in Smith *et al* (n 49 above) 1138. Hairy leukoplakia is an infection caused by the Epstein Barr virus (mononucleosis

3.2.5 AIDS

Without anti-retroviral therapy, about 90 per cent of HIV infected persons will develop AIDS within ten to twelve years.[117] There is an upsurge in the viral load during this phase.[118] AIDS is a severe, life-threatening syndrome,[119] which represents the late clinical stages of HIV infection.[120] A medical definition of AIDS is that there is a helper T-lymphocyte-count of less than 200 cells per millilitre of blood.[121] This is because HIV has destroyed the HIV-infected person's helper T-cells (immunosuppression).[122] An infected person's immune system can no longer produce antibodies in response to T cell-dependent antigens and, thus, cannot cope with challenges from viruses, bacteria and fungi. People with AIDS die because of a variety of opportunistic infections which are able to take advantage of the weakened immune system. AIDS syndrome includes lymphadenopathy syndrome, wasting syndrome, neurological disease, opportunistic infections and various types of cancers. Major opportunistic infections include pneumocystis carinii pneumonia (PCP),[123] systemic mycosis,[124] cryptosporidium gastro-enteritis[125] and toxoplasmosis.[126] Opportunistic bacterial infections include mycobacterium tuberculosis[127] and mycobacterium avium-intracellulare.[128] Viral diseases include

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virus). It causes white plaques on the surface of the tongue and is not really seen in people other than those infected with HIV.

117 Weiss and Weiss in Smith *et al* 138.

118 Wodarz and Nowak in Domingo *et al* (n 71 above) 198; Rouzine and Coffin in Domingo *et al* 226.

119 AIDS is referred to as a 'syndrome' as it produces a group of symptoms.

120 Graham in Nelson *et al* (n 55 above) 525. Also see Wodarz and Nowak in Domingo *et al* 198 – 216 for a possible explanation of the evolutionary dynamics which are responsible for the transition from the asymptomatic period of the infection to AIDS.

121 As above; Wodarz and Nowak in Domingo *et al* (n 71 above) 198. A healthy, uninfected person has about 1000 CD4 cells per millilitre of blood (Wodarz and Nowak in Domingo *et al* 198).

122 Graham in Nelson *et al* 525.

123 As above. This infection was first identified in 1981 amongst men who have sex with men (MSM).

124 As above. This is caused by common soil fungi and results in devastating systemic infections.

125 Graham in Nelson *et al* 525. This is an infection of the gastro-intestinal tract that is caused by a protozoa. There is no cure for this disease. It causes prolonged, severe diarrhoea and weight loss. It occurs in 5% of AIDS patients.

126 Yet another protozoan disease, and although it can affect many organs, it often affects the brain and causes convulsions, disorientation and dementia. It is effectively treated by antibiotics.

127 Graham in Nelson *et al* 525. This is the most important infection amongst AIDS patients in Africa. It reactivates latent tuberculosis and is often multiple-drug resistant.

128 Causes a tuberculosis-like disease in the lungs.

cytomegalovirus (CVM)[129] and herpes simplex virus.[130] Cancers include Kaposi's sarcoma,[131] B-cell lymphoma[132] and cervical cancer.[133]

Other opportunistic diseases that sometimes are found in AIDS patients are: neurological disease,[134] HIV infection of the nervous system, which causes encephalopathy,[135] myelopathy[136] and peripheral neuropathy.[137] Previously, the diagnosis of HIV infection and AIDS was considered a death sentence,[138] but advances in anti-retroviral therapy have (indefinitely) extended the lives of many people living with HIV.[139]

3.3 An overview of the epidemiology of HIV and AIDS

3.3.1 Introduction

The purpose of this section is to describe the epidemiology of HIV/AIDS. Modes of transmission and risk factors are outlined. Finally, global trends in the epidemiology of HIV and AIDS are discussed, and emphasis is placed on the epidemic in sub-Saharan Africa.

3.3.2 Subtypes

Two subtypes of HIV have been identified, namely HIV I[140] and HIV II.[141] On the whole, the two subtypes have the same modes of transmission.[142] However,

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129 This is caused by a virus of the herpes family and causes severe pneumonia, blindness and gastro-enteritis. Antiviral drugs are used to control this infection.

130 Whereas this virus causes cold sores in persons who have a normal immune system, it causes very severe infections of the skin, mucus membranes and internal organs of AIDS patients.

131 This is the most common cancer associated with AIDS and is a cancer of the blood vessels that is very rare in persons with a normal immune system. It causes pink, purple or brown skin lesions. It is treated quite effectively with chemotherapy.

132 This is, as its name indicates, a cancer of the B-lymphocytes. Although it is treatable, there is no cure. It seems to be caused by the Epstein Barr virus.

133 Graham in Nelson *et al* (n 55 above) 525. This type of cancer is increasing in incidence and is caused by the human papilloma virus.

134 Graham in Nelson *et al* 525. This is caused by direct damage by the HIV virus which infects the nervous system and may cause a tumour in the brain.

135 of the brain – AIDS dementia.

136 of the spinal cord - weakness and paralysis of the lower limbs.

137 of peripheral nerves – loss of sensation and paralysis.

138 Without anti-retroviral treatment, death occurs between eighteen months and two years after onset of AIDS.

139 Graham in Nelson *et al* 525. These are the so-called 'long-term survivors'. See paras 3.4 and 3.5 below for some of the problems encountered in the long-term use of anti-retroviral therapy.

140 Weiss and Weiss in Smith *et al* (n 49 above) 129; Graham in Nelson *et al* 527; identified in 1983 and the more virulent of the two.

whereas HIV I-infection occurs worldwide, HIV II-infection is limited to West Africa and India.[143]

HIV I is subdivided into three groups or 'clades' - group M (major group), group O (outlier group) and N (non-M, non-O) - consisting of at least ten genetic subtypes or clades.[144] The three groups or clades each have a distinct genetic composition, making it possible to distinguish between the different groups. Some clades are found more frequently in certain parts of the world.[145] Recombination between different clades has also been documented.[146] Clade B predominates in industrialised Western countries, whereas clades A, C, D and E predominate in Africa and Asia.[147] In southern Africa, clade C predominates.

3.3.3 Modes of transmission

HIV is regarded as one of the less efficient viruses in its ability to be transmitted from one person to another.[148] For example, whereas the influenza virus is spread through environmental contact and is able to survive outside the host for some time, HIV is not spread through environmental contact and is unable to survive long outside the human body.[149]

HIV transmission varies in efficiency according to various factors such as viral load and route of transmission.[150] Transmission during a blood transfusion occurs in approximately 90 per cent of cases and vertical transmission occurs in approximately 30 per cent of cases.[151] Transmission rates during sexual intercourse vary between approximately 0.5 per cent and 1 per cent per exposure.[152] The rate of transmission

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141 Graham in Nelson *et al* 527; Weiss and Weiss in Smith *et al* 129; identified in 1986, and less virulent. For an interesting discussion on the similarities between HIV II and SIV, see Klein and Ho (n 35 above) 300. It appears that HIV II's genome shows a homology of 70% with SIV, while the genomes of HIV I and HIV II are only 40% similar. Because of the virus's high mutation rate, many biological variants exist, sometimes even within one infected individual (Graham in Nelson *et al* 525). See generally para 2.1 above. The two subtypes vary in their genetic composition.

142 Graham in Nelson *et al* 528 – 531.

143 As above, 528; Klein and Ho (n 35 above) 295.

144 Weiss and Weiss in Smith *et al* 129; Graham in Nelson *et al* 530. See also Van Harmelen and Williamson (2000) 20 *CME* 568 569 – 570.

145 As above.

146 As above.

147 As above.

148 Schoub (n 11 above) 91. Because of the variability of the virus, a relatively large mass of virus is required for successful transmission.

149 See below.

150 See Graham in Nelson *et al* 531 – 536 for more information.

151 As above, 527.

152 As above.

due to an accidental needle-stick injury is as low as approximately 0.3 per cent.[153] The targets for HIV infection and risk factors are discussed briefly below.

For transmission to occur live HIV must survive long enough to pass from an infected to an uninfected person.[154] HIV is very fragile outside the human body as it is quickly inactivated when exposed to air, light, soap and water.[155] Also, when semen or blood dries the infectivity of HIV is lost.[156] Finally, a relatively large mass of virus is required for successful transmission.[157]

HIV is not transmitted through environmental contact[158] and casual contact, such as shaking hands, hugging, living in the same household; sharing a bedroom, bathroom or telephone does not transmit the virus. HIV cannot penetrate intact skin[159] and is not transmitted through respiration.[160] As HIV cannot survive in water, waterborne transmission does not occur. Similarly, as HIV is rapidly inactivated in the stomach, it is not transmitted by ingestion in the gastrointestinal tract.[161] There are no documented cases of HIV transmission through insect bites.[162]

Targets for HIV infection are limited to:[163]

- blood;
- mucosal surfaces such as the vagina, the male urethra and the lining of the anus and the rectum;
- the target of HIV when passing from mother to child during breastfeeding remains unclear, but HIV is understood to pass in the mother's breast milk. Inflammatory conditions such as mastitis cause the presence of plasma-derived components and inflammatory cells in breast milk (such as HIV-1 infected lymphocytes).

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153 As above.

154 Transmission requires direct contact of:
- fluid or secretions containing HIV from an infected person; and
- susceptible cells of another person.

155 Schoub (n 11 above) 91.

156 Graham in Nelson *et al* 536.

157 As above. Several studies have shown that, generally, a high viral load is a risk factor for HIV transmission (see eg Garcia *et al* (1999) 341 *New Engl J Med* 394 and Gray *et al* (2001) 357 *The Lancet* 1149).

158 As above, 536.

159 As above.

160 As HIV is not present in the exhaled breath of the infected person.

161 Schoub 122.

162 As above, 122 - 123. HIV cannot replicate inside an insect as there are no CD4 cells inside an insect. Also, an extremely small amount of blood is transported by the insect and injected.

HIV is transmitted from person to person in the following ways (each is discussed more fully below):[164]

- direct sexual contact;
- sharing of needles and syringes by IDUs which are contaminated by HIV;
- transfusion of contaminated blood and blood products and organ donation;
- trans-placental transfer from mother-to-child;
- breastfeeding by HIV-positive mothers;
- needle-stick injury of health-care workers where needles are contaminated with HIV; and
- any other setting in which an uninfected person is in contact with an infected person's blood or fluids.[165]

a) Direct sexual contact

Sexual intercourse may result in damage or tears to the (mucosal) linings of the vagina or rectum, allowing HIV in semen to pass into the bloodstream of the uninfected person.[166] HIV contained in semen can directly infect the Langerhans cells or macrophages on vaginal or rectal mucosal surfaces.[167] Similarly, HIV in vaginal or cervical secretions can directly infect Langerhans cells or macrophages on the urethral mucosal surfaces or vaginal surfaces.[168]

Vaginal sexual intercourse is the most common mode of HIV transmission worldwide and is the most common mode of transmission in Africa.[169] Trauma to vaginal mucosal surfaces significantly increases the risk of transmission.[170] Male-to-female transmission is two to three times more efficient than female-to-male transmission.[171]

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163 Graham in Nelson *et al* (n 55 above) 531.

164 Graham in Nelson *et al* 531 - 537; see para 3.1 above for sources of HIV in the HIV-infected person.

165 Graham in Nelson *et al* 530.

166 Schoub (n 11 above) 96; Nicklin *et al* (n 2 above) 308.

167 Schoub 94 – 95.

168 As above.

169 Graham in Nelson *et al* 540.

170 As above.

171 Schoub 100. The biological explanation for this is the fact that, during heterosexual sexual intercourse, the vagina receives large volumes of semen which remain in contact with vaginal and cervical mucosa for a relatively long period of time. The penis/urethra has relatively brief contact with vaginal mucosa and retains only a thin film of vaginal or cervical secretions.

The most effective mode of HIV infection is through unprotected receptive anal intercourse.[172] Among men who have sex with men (MSM), a combination of receptive anal intercourse and a high number of sexual partners (who do not wear protection) is the most significant HIV risk factor.[173] The large number of macrophages in rectal mucosa transport HIV to the rich supply of lymphoid tissue in the lining of the rectum.[174] Rectal mucosa is also much thinner and, therefore, more susceptible to damage during sexual intercourse than the vagina.[175]

Oral sex performed on a man carries a very low risk of transmission.[176] There are no documented cases of instances where oral sex performed on a woman and wet kissing have transmitted the virus.[177]

Risk factors of a clinical nature for sexual transmission of the virus include:[178]

- unprotected sex;
- multiple sexual partners engaging in unprotected sex (of course, multiple sexual partners are not a risk factor *per se*, as long as protection is used during each sexual encounter);[179]
- high viral load in the infected partner;[180]
- sex during menstruation;[181]
- practices that cause trauma to the lining of the vagina or rectum, such as 'fisting';[182]
- the presence of other sexually-transmitted diseases at the time of sexual intercourse; [183]
- chronic, generalised infections at the time of sexual intercourse;[184]
- absence of male circumcision;[185] and

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172 Graham in Nelson *et al* 531; Schoub 96.
173 As above.
174 Schoub 96.
175 Graham in Nelson *et al* 531 – 532; Schoub 96.
176 Schoub 100 – 101.
177 As above. Sexual behaviour that carries no risk is dry kissing and mutual masturbation (as long as semen does not come into contact with broken skin). Also, the infection rate for women who have sex with women (WSW) is extremely low.
178 Graham in Nelson *et al* 532; Schoub 100 – 110.
179 Schoub 102.
180 As there is more viral material in the blood, there is a greater chance of the virus being transmitted to another person.
181 Schoub (n 11 above) 107 – 108.
182 As above, 97.
183 Such as genital ulcers.
184 Particularly TB. These are associated with a chronic activation of the lymphocytes, and also immunosuppression, which may enhance susceptibility.

- oral contraceptive and IUDs.[186]

b) Sharing of contaminated needles by injection drug users (IDUs)

In some countries, injection drug use (IDU) is responsible for more instances of HIV transmission than is sexual intercourse.[187] IDUs often share needles, syringes and other drug paraphernalia,[188] all of which are risk factors for the transmission of HIV.[189] Many IDUs also engage in risky sexual behaviours[190] and the drugs themselves are often immunosuppressive and therefore enhance the dug-user's susceptibility to infection.[191]

Prevention programmes among IDUs include needle or syringe exchange programmes, the non-prescription availability of needles and syringes in pharmacies and education programmes that encourage the use of bleach solutions to wash out syringes between use, if they are shared.[192]

c) Transfusion of contaminated blood, blood products and organ donation[193]

This mode of transmission is very infrequent in most developed countries because of thorough screening methods.[194] Also, clotting factor and other blood products are routinely subjected to heat treatment to inactivate HIV.[195]

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185 Schoub 107. Several studies have indicated that male circumcision decreases the risk of HIV transmission - see eg Quinn (2007) 20 *Current Opinion in Infectious Diseases* 38 – 38; Weiss (2007) 20 *Current Opinion in Infectious Diseases* 66 – 72; Roehr (2007) 334 *British Med J* 11.

186 As above. IUDs increase the woman's risk of infection, especially chlamydia. Mechanism of oral contraceptives not clear – may cause immunosuppression.

187 Such as Russia and Thailand.

188 The 'cooker' (equipment used to prepare the drugs) may be contaminated with HIV infected blood. During 'booting' – drawing a small amount of blood back into the syringe before injection – HIV can be transmitted to others who use the same syringe or needle. 'Shooting galleries', 'frontloading', 'backloading' and 'skinpopping' are other high risk practices associated with IDU (for more information, see Graham in Nelson *et al* (n 55 above) 532 – 533).

189 Graham in Nelson *et al* 533. HIV antibody testing of all donated blood, increased sensitivity of antibody tests, and other methods such as thorough screening of prospective donors on risk behaviour, contribute to lowering the chance of HIV-infected blood entering the blood supply.

190 Graham in Nelson *et al* 533.

191 Schoub 113.

192 Of course, programmes that treat drug addiction are very successful in preventing HIV transmission along this route.

193 The acquisition of HIV infection through blood donation has always been regarded sympathetically by the general public. Such infections are seen as 'innocent', whereas sexual transmission is considered less than innocent. Consider also the tendency to call HIV-positive children the 'innocent victims' of HIV. This tendency

The greatest potential risk for acquiring HIV infection through contaminated blood or blood products is at the time when the donor is in the 'window period', during which HIV-infected blood tests false-negative. This risk could be alleviated if use is made of repeat donors and through more sensitive screening tests.[196] The transfusion of contaminated blood and blood products is considered by some scientists to have been a major cause in establishing the epidemic in Africa.[197]

d) Transfer from mother-to-child (MTCT)[198]

HIV may be transmitted vertically to the foetus in utero, intra-partum (during delivery), or post-partum (by way of breastfeeding)[199] from a mother to a foetus or infant.[200] The risk of MTCT ranges from 13 per cent in Europe to 30 per cent in Africa, in accordance with the mode of transmission.[201] Vertical transmission is one of the most important routes of transmission of HIV in sub-Saharan Africa.[202]

Intrauterine or trans-placental infection takes place when the placenta is infected and infection spreads to the foetus.[203] Intra-partum infection takes place[204] when the baby passes through the birth canal and, therefore, is exposed to the mother's vaginal and cervical secretions. The virus is transmitted through intact mucosa or that which has been damaged because of abrasions and lacerations which often occur during birth. Postpartum infection occurs during breastfeeding.[205]

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reveals an element of hypocrisy, especially as such sentiment was rife in the late 1980s in South Africa when HIV infection was considered a 'gay disease'.

194 Graham in Nelson *et al* 534.

195 As above.

196 In the USA, the FDA recommended already in August 1995 that all blood and plasma donations be screened for p24 antigen that can detect HIV infection earlier than the routine ELISA antibody test. This test is also used in South Africa.

197 Opinion is divided on the role of contaminated blood and blood products in the transmission of the disease in Africa (also called 'parenteral transmission'). In this regard, see eg Gisselquist *et al* (2002) 13 *Intl J STD & AIDS* 657 and Walker *et al* (2003) 442 *Nature* 679.

198 Also known as perinatal, vertical transmission or MTCT.

199 Discussed in e) below.

200 Nicklin *et al* (n 2 above) 308; Graham in Nelson *et al* (n 55 above) 533; Schoub (n 11 above) 119.

201 Graham in Nelson *et al* 534; Schoub 119 – 120. This difference may be ascribed to differences in obstetric and breast-feeding practices, inherent factors in the study population and variances in the virulence of different strains of the virus.

202 When selected Caesarean section was combined with the administration of zidovudine (AZT) during the antepartum, intrapartum and neonatal periods, HIV transmission was reduced by about 85%.

203 Schoub 119. Estimated to amount to 23% of cases of MTCT.

204 Estimated to account for 65% of cases of MTCT.

205 Accounting for 12% of cases.

Risk factors for vertical transmission include:[206]

- most significantly, a high viral load in the mother at the time of giving birth or during pregnancy;
- if the mother suffers from sexually-transmitted infections at the time of giving birth or during pregnancy;
- prolonged rupture of the membranes (more than 4 hours prior to delivery);
- invasive obstetric procedures[207] during vaginal labour and delivery that causes tears / lacerations and increases bleeding;
- a premature infant; and
- breastfeeding, particularly if the mother has mastitis or breast abscesses.

Ways in which vertical transmission of HIV may be prevented include:[208]

- elective termination of pregnancy;[209]
- treatment for maternal sexually transmitted infections;
- zidovudine (AZT)[210] treatment

  given to the mother from the fourteenth week of pregnancy through to delivery

  given to the newborn for the first six weeks

  short courses of AZT (from 36 weeks through to delivery) have also been shown to be effective[211]
- short course treatment with Nevirapine[212] where a single dose is given in active labour and a single dose is given to the infant;
- caesarean section delivery before labour and before rupture of the membranes; and
- avoidance of invasive obstetric procedures during vaginal labour and delivery.

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206 Graham in Nelson *et al* 533 – 534.

207 For example, episiotomies.

208 Graham in Nelson *et al* (n 55 above) 533 – 534.

209 Of course this is not really a solution to the underlying problem.

210 In ACTG Protocol 076 (see ch 3), the ARV Zidovudine administered to a selected group of HIV infected women during pregnancy, labour and delivery and to their newborn infants, was shown to reduce the risk of perinatal HIV transmission by two thirds, compared to those mothers who received the placebo. In this regard see Connor *et al* (1994) 331 *New Engl J Med* 1173.

211 As above.

212 a protease inhibitor.

HIV positive mothers who breastfeed can pass on the virus to their babies.[213] Many of the breast-feeding infections may be due to the presence of the mother's blood in the milk because of cracked or injured nipples.[214] HIV transmission through breast-feeding remains an issue in developing countries, such as those in Africa, where poverty, lack of clean water and social prejudice prevent the use of formula feed.

e) Needle-stick injuries of health care workers[215]

The risk of contracting HIV from a deep, penetrating injury with a contaminated needle is about one in 300.[216] Needle-stick injuries represent a far greater risk than that of intact skin or membrane exposure to HIV infected blood.[217] Most health care workers today follow universal precautions, whereby all patients are treated as if they are HIV positive.[218]

3.3.4 The evolution of the epidemic

The HIV epidemic is understood to evolve with the initial infection of a core group, such as MSM, IDUs or sex workers, and spreads from that group to the general population. It is theorised by some that in South Africa the epidemic evolved from an initial (limited) epidemic among MSM and sex workers in the eighties, to the present (large-scale) epidemic of the entire population.[219]

International organisations, such as the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organisation (WHO), co-operate with local governments, networks of AIDS researchers and national AIDS programmes around the world to gather data which enables them to track and estimate the spread of HIV infection. Serosurveillance of so-called sentinel groups,[220] in which HIV antibody

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213 Schoub (n 11 above) 119.

214 As above.

215 The potential threat of HIV to health care workers has assumed 'panic proportions' (Schoub 113) and has caused much unfair discrimination against PLWHIV.

216 Schoub 114. Or about 0.3 %.

217 Graham in Nelson *et al* (n 55 above) 535; Schoub 113.

218 For an extensive discussion of this mode of transmission, see Schoub 113 – 115.

219 See Nelson in Nelson *et al* (eds) (2000) 97 and Schoub 116. This is not necessarily the correct view.

220 Groups who are thought to represent the spectrum of risk activities in a population. Sentinel groups are usually blood donors, pregnant women attending antenatal clinics, members of national armed forces, tuberculosis patients, persons who attend sexually transmitted disease clinics, sex workers, IDUs and MSMs (the last group is regarded as a sentinel group in areas where HIV is transmitted mainly along that route).

tests are performed on representative samples of each of these groups, enables bio-statisticians to track and monitor the epidemic.[221]

There exist two measures of the occurrence of HIV – HIV prevalence and HIV incidence. *HIV prevalence* refers to the proportion of persons in a specified population who are infected with HIV at a specified point in time.[222] *HIV incidence* refers to the proportion of persons in a specified population who are HIV negative who become newly infected with HIV over a specified period of time.[223]

As was pointed out in chapter 1, at the end of 2006 a total of 39.5 million people were estimated to be living with HIV/AIDS worldwide, of whom 37.2 million were adults, (17.7 million of whom were women) and 3.2 million were children under the age of fifteen.[224] Sub-Saharan Africa is the region hardest hit by the epidemic, and within sub-Saharan Africa, Southern Africa is the worst off - one third or 32 per cent of all PLWHIV live in southern Africa and 34 per cent all AIDS deaths in 2006 occurred in Southern Africa.[225]

The following table outlines the prevalence of HIV infection among the adult population of the world (ages 15 – 49):[226]

Sub-Saharan Africa	5.9%
North Africa and Middle East	0.2%
South and Southeast Asia	0.6%
East Asia	0.1%
Oceania	0.4%
Latin America	0.5%
Caribbean	1.2%
Eastern Europe and Central Asia	0.9%
Western Europe and Central Europe	0.3%
North America	0.8%
TOTAL	**1.0%**

The following table outlines the chief modes of HIV transmission worldwide:[227]

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221 Nelson in Nelson *et al* (n 219 above) 97.
222 As above.
223 As above.
224 UNAIDS (2006) *AIDS epidemic update* 1. See para 1 of ch 1 above.
225 As above, 3.
226 As above, 2.
227 As above, 5.

Sub-Saharan Africa	Hetero
North Africa and Middle East	Hetero, IDU
South and Southeast Asia	Hetero, IDU
East Asia and the Pacific	IDU, hetero, MSM
Latin America	MSM, IDU, hetero
Caribbean	Hetero, MSM
Eastern Europe and Central Asia	IDU
Western Europe	MSM, IDU
North America	MSM, IDU, hetero
Australia and New Zealand	MSM

The following table outlines the prevalence of HIV infection among adults in West and Central Africa in 2005:[228]

Senegal	0.9%
Mali	1.7%
Cameroon	5.4%
Central African Republic	10.7%
Cote d'Ivoire	7.1%
Nigeria	3.0%
Democratic Republic of the Congo	3.2%

The following table outlines the prevalence of HIV infection among adults in East Africa:[229]

Kenya	6.1%
Tanzania[230]	7.8%
Somalia	0.9%
Ethiopia	360 000 – 1 100 000
Uganda	6.7%

228 UNAIDS (2006) *Report on the global AIDS epidemic* 506. Only a few countries were included in the table.

229 As above.

230 Figure that of 2002. Not updated in 2005 report.

Finally, the following table outlines the prevalence of HIV infection among adults in Southern Africa:[231]

Botswana	24.1%
Lesotho	23.2%
Swaziland	33.4%
Mozambique	16.1%
Zimbabwe	20.1%
Namibia	19.6%
Malawi	14.1%
South Africa	18.8%

It is clear from the tables above that Southern Africa has the highest rate of HIV prevalence in Africa, and the world. If we combine this high prevalence rate with the fact that Southern African countries, generally, cannot afford expensive anti-retroviral (ARV) drugs, the picture for Southern Africans looks very bleak indeed, and the need for a preventive HIV vaccine becomes both urgent and self-evident.[232]

In the following pages, developments in the treatment of the disease will be examined.

3.4 Developments in the treatment of the infection

At present no drug exists that is able to eliminate HIV infection from the body, nor is there any drug that may indefinitely prevent the eventual onset of AIDS.[233]

At present, HIV/AIDS therapy consists of three major strategies. [234]

- Treatment of opportunistic infections.[235]
- Treatment of HIV-related cancers.
- ARV therapy.

Although there are many drugs which treat bacterial infections, relatively few drugs treat viral infections.[236] ARV drugs are designed to interfere with the viral replication cycle.[237] There are four classes of ARV drugs available:[238]

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231 As above.
232 See paras 3.5 and 4 below.
233 Schoub (n 11 above) 181.
234 Schoub 159.
235 As above.

- Nucleoside analogues or nucleotide reverse transcription inhibitors.
- Non-nucleoside reverse transcriptase inhibitors.
- Protease inhibitors.
- Fusion or entry inhibitors.

Each of these is discussed below.

3.4.1 Nucleoside analogs

AZT (Zidovudine) was the first drug to demonstrate a marked benefit in the treatment of AIDS patients.[239] AZT is incorporated into viral DNA by reverse transcriptase and terminates further viral DNA synthesis and viral replication;[240] upon initiating AZT therapy, the viral load drops ten to 100-fold. However, within a year the viral load returns to its original level as HIV becomes AZT-resistant due to the natural selection of AZT-resistant HIV-variants.[241] AZT is, thus, no longer the sole anti-retroviral drug given to HIV positive persons.[242] Other nucleoside analogs[243] include dideoxycytodine,[244] 3T3[245] and D4T.[246]

3.4.2 Non-nucleoside reverse transcriptase inhibitors (NRTIs)

These are drugs such as nevirapine (Viramune) and delavirdine (Rescriptor). As their name indicates, these drugs are aimed at interfering with HIV's reverse transcription enzyme.[247] After starting on a course of medication, most patients show an initial 1 000 to 10 000-fold decrease in viral load. However, once again

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236 Schoub 154. Antivirals that do exist are mainly those that treat infection by the herpes virus.

237 Schoub 157.

238 Schoub 157; Cloete and Atlas (n 2 above) 22.

239 Weiss and Weiss in Smith *et al* (n 49 above) 141; Rick (n 18 above) 33; Schoub 157; Cloete and Atlas 22; manufactured by GlaxoSmithKline.

240 Weiss and Weiss in Smith *et al* 141; the main toxic effects of AZT are anaemia and low white cell counts.

241 Weiss and Weiss in Smith *et al* 142; Wodarz and Nowak in Domingo *et al* (n 71 above) 214. In mono-therapy, HIV resistant to the drug may emerge within weeks.

242 Of course, with the exception of HIV positive pregnant women among whom AZT lowers the risk of transmission by 70%.

243 PLWV who are resistant to AZT are often not resistant to these.

244 ddC or zalcitabine.

245 Commercially known as Lamivudine.

246 Stavudine. For an extensive discussion of AZT therapy, see Schoub 181.

247 See para 3.1 above. HIV consists of a RNA genome. Inside the infected cell, reverse transcriptase produces a DNA copy of HIV's RNA genome. The virus then uses this DNA copy to replicate inside the invaded cell, producing a DNA provirus that gets

resistant HIV-variants are quickly selected. A single dose of nevirapine has been shown to be effective in reducing mother-to-child transmission of HIV. This fact is of great importance in the developing world.[248]

3.4.3 Protease inhibitors

These drugs inhibit the conversion of immature viral particles into mature viruses.[249] Protease inhibitors include saquinavir (Invirase), indinavir (Crixivan), ritonavir (Norvir) and nelfinavir (Viracept).[250] There is often an initial 1 000 to 10 000-fold decrease in the viral load. Once again resistant HIV-variants are quickly selected.[251]

3.4.4 Fusion or entry inhibitors

Fusion or entry inhibitors, as their name suggests, block the entry of the virus to a host cell.[252]

Because of drug resistance, triple combination therapy[253] has been introduced.[254] HAART[255] is such a triple therapy. HIV often mutates to a variant that is resistant to one drug, but it is less likely that it is able to mutate to a variant that is resistant to two drugs and even less to mutate to a drug that is resistant to three drugs.[256] The most effective combination has been found to be two nucleoside analogs and one protease inhibitor.[257]

Upon being administered HAART, the viral load in the blood of the majority of patients drops below detectable levels and stays at these levels for several years.[258] Even CD4-counts recover and AIDS symptoms and opportunistic infections disappear. When the viral load starts to increase again a new combination of drugs is used.

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inserted into the chromosomal DNA of the host cell. A drug that interferes with this enzyme, therefore, makes it impossible for the virus to replicate.

248 See ch 3 below.

249 They are also known as peptide mimics (Weiss and Weiss in Smith *et al* 314).

250 As above.

251 Wodarz and Nowak in Domingo *et al* 214. Variants resistant to one protease inhibitor are often also resistant to another protease inhibitor.

252 Cloete and Atlas (n 2 above) 22.

253 Also known as AIDS drug cocktails.

254 Wodarz and Nowak in Domingo *et al* (n 71 above) 214 – 215.

255 HAART stands for 'highly active anti-retroviral therapy'.

256 Wodarz and Nowak in Domingo *et al* 214; Rouzine and Coffin in Domingo *et al* 228. Often virus load stays below detectable levels for 2 – 3 years, or longer.

257 As above. Combivir is such a combination therapy.

258 Rouzine and Coffin in Domingo *et al* 226.

However, there are a number of uncertainties and limitations connected to HAART. HAART is not effective in all patients.[259] Also, the extent of the effectiveness is still unclear. HAART was introduced in 1996 and, seven years later, HIV-variants resistant to triple combination are appearing.[260]

There are many drawbacks to HAART. First, life-long therapy is needed.[261] Many patients find the side effects too severe to tolerate such long-term use.[262] It is difficult also to maintain complicated treatment schedules.[263] Strict treatment adherence is critical in preventing the development of drug-resistant variants.[264]

3.5 The need for an effective vaccine

In South Africa, particularly, government seems to lack political will in taking steps to combat the spread of the disease.[265] Because, on the whole, those who are infected tend to belong to a poorer socio-economic sector, they appear 'invisible' to those in power and, so far, the South African government has demonstrated a lack of clear leadership in their response to AIDS.[266]

Current options for the treatment of HIV infection have had limited success. The cost of caring for PLWV remains high, despite the efforts in South Africa of NGOs, such as the TAC, which have increased access to antiretrovirals.[267] As well, in

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259 It seems to be less effective in cases where the patient previously had mono-therapy such as AZT (in which case the patient is only really getting double therapy, not triple therapy).

260 Personal communication, Prof Robert Dubois, Yale University School of Medicine.

261 Weiss and Weiss in Smith *et al* (n 49 above) 317. This therapy is thus obviously not easily affordable in poorer countries, such as those in sub-Saharan Africa.

262 Weiss and Weiss in Smith *et al* 317.

263 In which the patient may have to take as many as 25 pills per day at very precise intervals. Also, there are special requirements connected to the administration of some of the drugs – Indinavir, for example, has to be taken on an empty stomach.

264 Weiss and Weiss in Smith *et al* 316.

265 For instance, the lack of political will in the provision of anti-retroviral therapy. See *MEC for Health, KwaZulu-Natal v Premier, KwaZulu-Natal: In re Minister of Health and Others v Treatment Action Campaign and Others* 2002 (5) SA 717 (CC), 2002 10 BCLR 1033 (CC). See also para 2.3.2 of ch 5 below.

266 See para 2.3.2 of ch 5 below.

267 In *MEC for Health, KwaZulu-Natal v Premier, KwaZulu-Natal: In re Minister of Health and Others v Treatment Action Campaign and Others* (n 265 above), the Constitutional Court found that in not providing Nevirapine in all public health facilities the state had not met its constitutional obligations. The Constitutional Court ordered that to do so, it should remove the restrictions preventing Nevirapine from being made available at public hospitals and clinics that are not research and training sites. It found that there was no reason why the state could not continue to collect data and closely monitor the use of Nevirapine at its chosen pilot sites. The Court stated that this should not prevent the state from providing the drug at other birthing institutions where facilities exist for doing so. The state was also ordered to take

public health care facilities, where antiretrovirals are made available to the public free of charge, PLWV have to meet certain criteria before they become eligible for treatment.[268]

The development of HAART has indefinitely prolonged the lives of countless PLWV, but this therapy is sometimes costly and difficult to administer. Further, new studies indicate that triple-therapy-resistant variants of the virus are developing.[269]

Current ARV therapies are in many instances toxic.[270] Because of this a viable alternative is urgently needed. Similarly, alternative methods for preventing the spread of the disease have met with only limited success. Although safe-sex-public awareness programmes and educational campaigns seem to have worked in some settings,[271] in others they have failed miserably as they neglect to address the underlying socio-economic and cultural issues responsible for the spread of the pandemic.[272]

Among the strategies being investigated to combat infection with HIV, are anti-HIV microbicides, male circumcision and pre-exposure prophylaxes.[273]

A number of microbicides against HIV are currently in Phase II and III clinical trials.[274] Microbicides, in the form of a cream or gel, are chemical products applied to the vagina.[275] An effective microbicide has advantages over male condoms, such as that it can be applied privately, and is in the control of the female sexual partner.[276] As yet, microbicides do not confer lasting protection, and it is assumed

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reasonable measures to extend testing and counselling throughout the public health sector to facilitate the use of Nevirapine.
Donor-funding and other strategies (such as the parallel importation of ARVs) have further lowered the cost of ARVs.

268 Such as a CD4-count of <200 cells per mm^3 irrespective of stage of illness; or WHO Stage 4 AIDS defining illness irrespective of CD4-count, AND patient expresses willingness to adhere to ART regimen (in the case of adults) (Department of Health (2006) 'ART Guidelines' 1 – 2).
In the private sector, one month's supply of the HAART drug Combivir costs R483.00, and Stocrin costs R198.00 (quote by Pharmavalu, Newlands, Pretoria, on file with author). The total cost of HAART in the private sector is therefore about R750.00 per month (which includes a dispensing fee).

269 Schoub (n 11 above) 182.

270 Weiss and Weiss in Smith *et al* (n 49 above) 145.

271 such as Uganda.

272 See ch 5 below, para 2.3.2.

273 And, of course, vaccines. See below.

274 Five are in large-scale trials, another 14 are in safety trials; see Ramjee (2006) 'Microbicides and other prevention technologies' Paper delivered at the XVI International HIV/AIDS Conference, Toronto, Canada, 13 -18 August 2006.

275 Early studies are also being undertaken on efficacy in rectal application (Ramjee 3).

276 See Ramjee (n 274 above) 4.

that a microbicide will need frequent re-applications.[277] In any case, it is not expected that microbicides confer total protection.

Results of previous studies have caused scientists to hypothesise that male circumcision may lower the HIV-infection rate among men.[278] This hypothesis was confirmed by a recent study which showed that male circumcision lowers the infection rate by up to 60 per cent.[279] Although a significant reduction in risk may potentially slow down the progress of the epidemic, circumcision cannot be considered a panacea: it (partly) protects only half of the population (men) and there are religious and cultural objections. More importantly, focussing on circumcision as a preventive strategy will erode the critical message that unprotected sex carries the greatest risk of infection – circumcision, therefore, could be counter-productive in fighting the epidemic: AIDS activists have floated the possibility that by causing people to relax their vigilance, and abandon the use of condoms, male circumcision will allow the disease to spread as rapidly as before.

Various clinical trials are investigating the efficacy of pre-exposure prophylaxes. These drugs (usually antivirals such as Tenofovir) need to be taken regularly, as often as once a day. The scientific and ethical problems associated with using pre-exposure prophylaxes as preventive means include monitoring the adverse effects[280] of the drugs and the implications arising out of the prescription of chronic medication for people in good health.[281]

Given the number of people globally who are infected with HIV, the absence of an effective, low-cost, non-toxic and long-term-efficacious treatment, the lack of hope for the development of a cure, the lack of effective prevention strategies and the prevalence of HIV among economically and socially powerless groups, it is absolutely critical that an effective preventive vaccine is developed. Because vaccines are generally safe, effective and inexpensive ways to prevent disease,[282] the development of an effective vaccine is currently our only hope to halt the spread of the epidemic.

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277 One method currently being developed is a vaginal ring containing microbicides. If successful, this method is expected to provide protection for up to 30 days at a time (Ramjee 9).

278 Quinn (n 185 above) 38 – 38; Weiss (n 185 above) 66 – 72; Roehr (n 185 above) 11. See para 4.2.2 (d) of ch 3 below.

279 Auvert *et al* (2005) 2 *PLos Med* e298.

280 See Ramjee (n 274 above) 17; some antiviral drugs, such as Tenofovir, have serious adverse effects (Ramjee 18).

281 See Ramjee 18.

282 Schoub (n 11 above) 183.

4 THE SEARCH FOR A VACCINE

4.1 Introduction

As indicated above, efforts to slow the spread of HIV have had limited success, and, therefore, it is not surprising that, lately, so much attention has been focussed on the development of an effective preventive vaccine for HIV.

Vaccines are powerful in the control and eradication of infectious disease. Smallpox was finally eradicated on 26 October 1977 because of a vaccine based on the vaccine first used by Edward Jenner in the 18th century.[283] Similarly, poliomyelitis, a devastating viral infection, is today close to eradication because of the use of a highly effective preventive vaccine.[284]

In the following pages, vaccine development will be placed in its historical context, types of vaccines will be discussed, challenges posed by the quest for an effective vaccine against HIV will be considered, and, finally, avenues of hope for the development of an effective vaccine against HIV will be explored.

4.2 A brief history of vaccine science

The beginning of the medical science of immunology is attributed to Emil Behring and Kitasato Shibasaburo who, in 1890, discovered antibodies.[285] However, as early as 1000 years before, a form of vaccination against smallpox was being practiced in Turkey, Greece, China and India.[286]

The first paper on inoculation was read by Dr Clopton Havers to the Royal Society of physicians in 1701.[287] He received a lukewarm response from the Society as little was known about the practice in the West.[288]

Almost twenty years later, during a time when smallpox was one of the most feared diseases in Europe, Lady Mary Wortley Montagu, who learned about the technique of inoculation while in Turkey, elicited the help of Charles Maitland in inoculating her daughter against smallpox in England.[289]

In 1721, Maitland carried out the first 'clinical trial' on inoculation. Six condemned prisoners were inoculated against smallpox on the understanding that

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283 As above, 182; Nicklin *et al* (n 2 above) 317. On 26 October 1977, a Somalian, Ali Maow Maalin, became the last person to be infected with wild smallpox.

284 Schoub 182.

285 Editorial (2000) 342 *New Engl J Med* 42 - 44.

286 As above. See also Mann (1999) 83.

287 As above, 84. Surely an unfair inducement to participation in a clinical trial. Medical and research ethics were at the time still in their infancy.

288 Mann (n 286 above) 83 – 84.

they would be given a reprieve if they agreed to the inoculation. The trial was successful and inoculation was practiced widely in England and Wales for the next fifty years, but not without casualties.[290]

In 1796, Edward Jenner, an English physician, made his contribution to the science of vaccination by discovering that cowpox lent immunity against smallpox, a discovery which would eventually lead to the eradication of smallpox.[291] Jenner observed that milkmaids who had previously been infected with cowpox, a very mild disease, seemed immune to smallpox. He started using fluid from cowpox lesions to vaccinate[292] against smallpox.[293] Around this time, the term 'vaccination' started being used by another English physician, called Dunning, to describe inoculation with cowpox. Soon vaccination became widely accepted, and vaccines for measles, poliomyelitis, rabies and anthrax were later developed as more was learned about the body's immune response.[294]

In 1881, Louis Pasteur, Emile Roux and Charles Chaimberland publicly immunised sheep, cows and a goat against anthrax and, in 1886, Richard Pfeiffer and Almoth Wright independently prepared heat-inactivated vaccines against typhoid.[295]

The next important milestone in the science of vaccination came in 1891 when passive immunisation against pneumococcal pneumonia was introduced by Georg Klemperer. Although his efforts were probably dangerous and ineffective, he was the first scientist to realise the importance of antibodies in immunity.[296]

In 1921, Camille Calmette and Alphonse Guerin administered an attenuated bacterial vaccine against tuberculosis to a newborn baby and, in 1955, salk-inactivated poliomyelitis vaccine proved effective.[297] In 1971, a live (attenuated) vaccine for measles, rubella and mumps was registered in the USA.

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289 As above.

290 As above, 84.

291 n 285 above, 45; Nicklin *et al* (n 2 above) 318; Mackett and Williamson (n 13 above) 5.

292 In this thesis, the terms 'vaccination', 'immunisation' and 'inoculation' are used interchangeably. See para 4.3 below for a definition of 'vaccination'.

293 As above; Cohen (1999) 7 *British Med J* 443; Mackett and Williamson 5.

294 Mann (n 286 above) 88. However, for a discussion of initial public resistance in England against compulsory vaccination programmes, see Mann 90 – 91.

295 Cohen (n 293 above) 443; Mackett and Williamson (n 13 above) 7.

296 n 285 above, 45.

297 The salk-inactivated vaccine was named for its discoverer, Peter Salk; Mackett and Williamson 5; see also Mann 95.

The first vaccine produced by DNA technology is the hepatitis B surface antigen vaccine. Instead of using proteins and polysaccharides this vaccine is based on sequences of DNA that encode microbial antigens that are injected.[298] This vaccine was licensed in 1981.[299] 1991 saw the first trial for DNA vaccines[300] for HIV.[301]

Another recent development in vaccine science is the use of engineered living carriers in the production of vaccines. Portions of the gene coding for the immunogenic protein of the virulent virus are inserted into relatively harmless 'carrier' organisms, such as the cold sore virus or salmonella typhimurium. In this way, a relatively harmless virus is used to introduce the immune system to the virus that is being vaccinated against.[302]

Technological advances have also brought the hope that, in the near future, vaccines will be developed to treat diseases such as diabetes, cancer and multiple sclerosis.[303]

4.3 A definition of vaccination

Vaccination is the artificial introduction of a viral antigen[304] in a modified form into the body in order to induce an immune response.[305] This viral antigen 'primes' the body's immune system not only to recognise the real virus when it is challenged by that specific virus, but also to destroy it. Because the immune system responds to the viral antigen, it is not necessary to introduce the entire virus to the body for immunity to be acquired. [306] Vaccines mimic the organism against which they protect, but they are not so much like that organism that they will cause the specific disease.[307]

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298 Cohen 445.

299 n 285 above, 44.

300 A DNA vaccine functions by directly injecting a gene or genes coding for a specific antigenic protein, resulting in direct production of such antigen(s) within the vaccine recipient in order to trigger an immune response. See para 4.4 below.

301 n 285.

302 Mann (n 286 above) 98.

303 Wilson (2003) 138 *Annals Internal Med* 857.

304 Nicklin *et al* (n 2 above) 317 - 318. An antigen is any substance that stimulates the immune system to produce antibodies. Antigens are foreign substances, such as invading bacteria or viruses, or sections of these substances. Also called an immunogen.

305 Rick (n 18 above) 77; Schoub (n 11 above) 184; Delves and Riott (n 21 above) 42.

306 Schoub 184.

307 Vaccine development therefore focuses on means to reduce the virulence factor of the virus while retaining the immunity stimulation (Rick (n 18 above) 78). Also see Schoub 184.

Vaccines are aimed either at causing sterilising immunity or, if that cannot be achieved, at controlling the infection.[308] Sterilising immunity protects so effectively against the pathogen that it completely prevents the host from being infected. In other words, all signs of the invading organism are cleared from the body.[309] This type of immunity is rarely achieved by vaccination.[310]

Vaccines that control infection are much more common. In this case, infection takes place, usually at the site of the pathogen's entry into the body, but before symptoms develop is quickly aborted by the immune response induced by the vaccine.[311]

When one thinks of vaccination one usually thinks of preventive vaccination. It is important to remember, however, that although vaccines, on the whole, are designed to prevent infection or disease (preventive vaccines), another class of vaccines exists, namely, for the *treatment* of disease (therapeutic vaccines).[312] As this thesis is concerned exclusively with the development of a preventive vaccine for HIV, therapeutic vaccines are not discussed.[313]

Today very effective immunisation programmes exist around the world; some have lead to the total eradication of the disease.[314] These programmes target, traditionally, childhood-onset diseases, such as measles, mumps, whooping cough and rubella; diseases that are mostly associated with teenagers and young adults, such as meningitis; and others, such as typhoid fever, Hepatitis A, B and C, anthrax, yellow fever, poliomyelitis and rabies.[315]

Vaccination to control pathogenic infections may be aimed either at protecting the individual against infection and disease[316] or at protecting the

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308 Schoub (2002) 20 *CME* 561; Van Harmelen and Williamson (n 144 above) 569.

309 As above.

310 As above.

311 As above.

312 Schoub (n 308 above) 561. One such vaccine, Remune, produced by the Trinity Medical Group, has been proven effective in maintaining key clinical markers in HIV+ trial participants one year after HAART was stopped ('Trinity announces Remune study results' *AIDS Weekly* 7 October 2002 21). For a comprehensive review of HIV-1 therapeutic vaccines, see Kinloch-de Loes and Autran (2002) 44 *J Infection* 152 – 159.

313 At present the search for a preventive vaccine enjoys higher priority than the search for a therapeutic vaccine. For information on the development of therapeutic vaccines, and the distinction between therapeutic vaccines and preventive vaccines, see Klein (2003) 21 *Vaccine* 616 – 619 and Schoub (n 308 above) 561.

314 Such the smallpox vaccine, see above.

315 Ada (2001) 345 *New Engl J Med* 1042 - 1044. This list is not exhaustive.

316 Such as vaccination of individuals who travel to certain areas, eg, yellow fever vaccination.

community as a whole by drastically reducing or eradicating the infection from the community.[317] In countries where wide-scale childhood immunisation programmes exist, population or 'herd immunity' is achieved.[318] The term 'herd immunity' refers to the protection of an entire community or population against a disease although only a portion of that population is vaccinated and, therefore, immune.[319] As a proportion of the 'herd' is immune, there are fewer infections and, thus, less chance of exposure for the unvaccinated individual.[320]

The effectiveness of a vaccine programme in controlling and eradicating disease depends on these factors.

- The infection must be limited to humans, leaving no animal reservoir to re-infect humans.[321]
- In the case of a viral vaccine, only a single strain or a few strains of the virus must exist and these should be genetically stable so that its antigenic properties remain more or less the same.[322]
- The virus must not persist in the infected host.[323]
- The vaccine used must be effective.[324]

More attention is given to these requirements and the likelihood of a candidate HIV vaccine being able to meet these requirements in paragraph 4.5 below.

The safety of vaccines has been a concern. Adverse reactions to vaccination include relatively mild reactions, such as swelling of the injection site and mild fever, and more serious reactions, such as seizures and encephalitis which could lead to brain damage.[325] The live (attenuated) oral poliovirus vaccine caused one case of paralysis per million doses of vaccine in the United States; only inactivated poliovirus vaccine is now used, as the cases of paralysis were due to the virus strain used in the vaccine reverting to its virulent state.[326]

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317 Such as organised programmes to eradicate polio and measles. Schoub (n 308 above) 562.
318 As above.
319 As above.
320 Schoub (n 308 above) 562.
321 Ada (n 315 above) 347.
322 Schoub (n 308) 562. See also para 4.5.1 below.
323 As above. In the case of HIV, the virus integrates itself into the host's DNA.
324 Ada (n 315 above) 347.
325 As above, 346.
326 As above. This is one of the documented problems when a live (attenuated) vaccine is used.

Because of these vaccine safety issues, vaccination programmes are not free from opposition among activists, politicians and the public.[327] Vaccines are given to healthy individuals in order to protect them against the risk of future infection. Clearly, the risk of future infection must be great enough to offset exposure to potentially adverse reactions to the vaccine. In the case of HIV, the risk and consequences of infection are great enough to offset this risk in many populations. An exposition on the risk-benefit analysis that is inherent in any decision to vaccinate, however, falls outside the scope of this thesis.

4.4 Types of vaccines

Vaccines may be divided into two major categories.[328]

- Inactivated (or killed) vaccines.
- Live (attenuated)[329] vaccines.[330]

4.4.1 Inactivated (or 'killed') vaccines

As their name indicates, inactivated or 'killed' vaccines are composed of viral material that has been inactivated so that they are unable to infect or replicate in the vaccinated person.[331]

Inactivated viral vaccines use either the entire virus that has been inactivated by means of chemical processes or heat, or parts of that virus, such as a surface antigen.[332] Vaccines utilizing parts of viruses are called subunit vaccines.[333]

Because they cannot replicate and revert to their 'wild'[334] type, inactivated vaccines are the safest type of vaccines. However, increased safety has its cost – these vaccines are often less successful in inducing immune response in the

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327 For a general discussion of, and empirical study on public attitudes to, vaccination programmes, see Ritvo *et al* (2003) 1 *J Immune Based Therapies and Vaccines* 3.

328 Rick (n 18 above) 78; Nicklin *et al* (n 2 above) 317 – 318; Schoub (n 308 above) 561.

329 Weakened or altered.

330 As above. 'Live' is used here to indicate that the virus has not lost the ability to reproduce and infect the host.

331 Nicklin *et al* (n 2 above) 318; Rick (n 18 above) 78; Schoub (n 11 above) 184; Schoub (n 308 above) 561; Klein and Ho (n 35 above) 306; Mackett and Williamson (n 13 above) 99.

332 Rick 78; Nicklin *et al* 319; Ada (n 315 above) 1043; Schoub (n 308 above) 561; Klein and Ho 306. Often, only the relevant immunogenic protein is synthesised by recombinant DNA technology.

333 Schoub (n 11 above) 184; Klein and Ho 306; Nicklin *et al* 319. By definition, a subunit vaccine is a vaccine that contains only part of that virus or other microorganism. HIV subunit vaccines produced by genetic engineering are called 'recombinant subunit vaccines'.

334 Original, infectious virus, as is found in the 'wild'.

vaccinated person and repeat vaccinations may be needed for optimum protection[335] as the immune response is shorter lived.[336]

A recent example of an inactivated vaccine is what is known as a recombinant subunit DNA vaccine. This vaccine uses genetically engineered DNA to produce a synthetic version of a viral surface antigen or it uses genetic material from the virus that cannot harm the vaccinated person.[337] Recombinant DNA vaccines are believed to be much more successful in inducing immunity than other inactivated vaccines.[338]

To enhance the immune response against inactivated vaccines, vaccine developers use adjuvants that can increase the type, strength and durability of immune responses against the pathogen.[339] Some adjuvants also stimulate mucosal immunity.[340] An example of an adjuvant is alum, which increases the strength of antibody responses generated by the vaccine antigen.[341]

In the case of killed subunit or recombinant vaccines it is the foreign protein contained in the vaccine that elicits an immune response and not any replicating activity (as killed viruses cannot replicate).[342]

4.4.2 Live (attenuated) vaccines

Again, as their name indicates live (attenuated) viruses are 'alive' and able to replicate in the vaccinated person.[343] They, however, are weakened by being genetically altered so that the new (vaccine) virus will not cause disease but will continue to stimulate the individual's immune system to recognise and defend against future attacks.[344] The process of changing the wild virus into the vaccine virus is called attenuation.[345]

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335 Rick 78; Schoub (n 11 above) 185; Nicklin *et al* 319.

336 Mackett and Williamson (n 13 above) 41; Wilson (n 303 above) 859; Rick (n 18 above) 78; Klein and Ho (n 35 above) 306. Often several administrations of the vaccine are needed to achieve long-lasting immunity.

337 Nicklin *et al* 319; Schoub 188; Rick 80. The recombinant DNA vaccine against for Hepatitis B is the only such human vaccine licensed to date.

338 Wilson 859; Nicklin *et al* 319.

339 Rick 82; NIH (2003) *Challenges in designing HIV vaccines* <http://www.niaid.nih.gov/factsheets/challenges/challvacc.htm> (30 August 2003).

340 As above.

341 As above.

342 Schoub (n 308 above) 561; Rick 82.

343 Mackett and Williamson 121; Rick 78; Nicklin *et al* (n 2 above) 318; Schoub (n 11 above) 184; Schoub (n 308 above) 561; Klein and Ho 307.

344 As above.

345 As above.

On the whole, live vaccines are much more successful than inactivated vaccines as they produce an immune response very like the one produced by the wild virus and because they provide longer-lasting immunity.[346] However, these advantages carry their own cost. Because live (attenuated) vaccines are able to replicate inside the vaccinated person's cells, they are able to revert to a wild (pathogenic) type and cause disease in the vaccinated person.[347] They also have a limited shelf life.[348]

As was suggested before, most of the successful vaccines used today are live vaccines. These vaccines have either been modified in cell culture (the measles, rubella and polio vaccines) or a close (less virulent) variant of the disease-causing virus has been used (such as in the case of smallpox using cowpox) in the production of the vaccine.[349]

The following table classifies some of the most important vaccines currently in use:[350]

Live vaccines	**Killed (inactivated) vaccines**
Trivalent oral polio (TOPV) Measles Mumps Rubella Yellow fever Varicella BCG	*a) Whole organism vaccines* Diphthera Pertussis (whole) Tetanus Trivalent inactivated polio (TIPV) Influenza (whole) Hepatitis A Rabies *b) Subunit vaccines* Heamophilus Influenza b Pneumococcal conjugate *c) Recombinant* Hepatitis B

346 Nicklin *et al* 318; Mackett and Williamson 121; Schoub (n 11 above) 184; Rick 78. They continue to reproduce inside the cells of the vaccinated person, thereby continually stimulating an immune response.

347 As above; Ada (n 315 above) 1055.

348 Rick 78.

349 Mackett and Williamson 124 – 125; Nicklin *et al* 318; Schoub (n 11 above) 184; Rick 78.

350 Table reproduced from Schoub (n 308 above) 562.

The following table shows some of the most important viral vaccines licensed for use in humans:[351]

Virus	Family	Type of vaccine	Disease (if different from virus)	Year identified	Year vaccine developed
Polio Oral Sabin vaccine Salk vaccine	Picornavirus	Live attenuated Inactivated	Poliomyelitis	1909	1957 1953
Measles	Paramyxovirus	Live attenuated		1954	1963
Mumps	Paramyxovirus	Live attenuated		1934	1967
Rubella	Togavirus	Live, partly attenuated	German measles	1962	1971
Rabies	Rhabdovirus	Inactivated		Discovered 1903; isolated 1960	1970
Influenza	Orthomyxovirus	Inactivated, subunit, and live attenuated		1933	1941
Hepatitis B	Hepadnavirus	Subunit	Serum hepatitis	1965	1986

This table illustrates that, on the whole, a lengthy period of time elapses from the moment that the viral pathogen responsible for a disease is discovered to the point where vaccine research produces a vaccine for that disease. The rabies virus was discovered in 1903, but the vaccine against rabies was only licensed in 1970. The poliovirus was identified in 1909, but the first vaccine became available only in 1953. Similarly, it took 34 years to develop the mumps vaccine.

The table similarly indicates that most viral vaccines currently in use are live (attenuated) vaccines. In the case of HIV such a vaccine is ruled out because of safety concerns.[352]

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351 Klein and Ho (n 35 above) 297.

352 See para 4.5.4 below.

More than twenty years have passed since the isolation and identification of HIV. There is, as yet, no vaccine available against HIV infection. The next section explores a few of the obstacles in the search for a preventive HIV vaccine.

4.5 Scientific challenges posed by the search for an effective preventive HIV vaccine

That clinical research is a long and difficult undertaking is shown by the fact that, although more than twenty years have passed since the first documentation of HIV in 1983, only a few vaccines have progressed to Phase III clinical trials. One such vaccine, produced by VaxGen, has proven a failure.[353]

From the discussion in paragraph 4.4 above, it should be clear at the outset that each type of vaccine (inactive or live) has its own drawbacks. Inactive vaccines are less able effectively to induce immunity, whereas live vaccines pose serious risk to the vaccinated person in that they mutate and cause disease.

HIV is an extremely complex virus and, therefore, vaccine development is difficult. An effective preventive HIV vaccine requires both a neutralising antibody response which will eliminate free virus and a killer (cytotoxic) T-lymphocyte (CTL) response which will eliminate virus-infected cells.[354]

An effective preventive vaccine to prevent infection by HIV should have the following qualities. It should be:

- safe;
- easy to administer;
- stable under adverse storage conditions;
- inexpensive; and
- capable of inducing long-lasting immunity, against a broad range of strains of HIV.[355]

A few of the most important scientific, logistic and economic obstacles in the way of developing a preventive HIV vaccine that meets these requirements are discussed below.

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353 Wilson (n 303 above) 857.

354 Van Harmelen and Williamson (n 144 above) 569; Klein and Ho (n 35 above) 304. The traditional method of developing a vaccine, in which the focus is on the stimulation of a strong antibody response, has proven ineffective in the case of HIV. Also see the discussion of the human immune system, para 2.3 above.

355 Graham and Wright (2003) 33 *New Engl J Med* 1331; Klein and Ho (n 35 above) 310.

4.5.1 Variation and mutation of HIV and other characteristics

Not only do a number of HIV subtypes exist, but great genetic variety is seen in strains isolated from the same individual.[356] The ability of HIV to mutate and recombine, and so escape the immune system, is likely to pose a serious obstacle to the successful development of a vaccine.[357] A successful vaccine against HIV, therefore, will have to protect against the emergence of resistant strains – in other words, it will have to protect even against a virus that is yet to evolve.[358] To many this seems a daunting task and one of the most significant obstacles in striving to develop a vaccine.

Initially, scientists thought that a subunit vaccine consisting of a HIV viral envelope protein, such as gp120, could provide immunity.[359] It was thought that the antigen contained in the vaccine would trigger the production of specific neutralising antibodies.[360] This assumption has been shown to be mistaken, as HIV simply evades the neutralising antibodies so generated. HIV coats itself in host-derived sugars when it buds out of an infected cell[361] and, as these sugars are seen as 'self' by the immune system, HIV is able to 'hide' from the immune system.[362]

The RNA of HIV is reverse transcribed into DNA that is integrated into the host genome. This makes it unlikely that any vaccine will be able to completely clear HIV infection.[363]

HIV infects helper T-cells, the very cells that orchestrate the immune system's response. It is difficult to design a vaccine that, to be effective, needs to activate the very cells that are infected by the virus.[364]

Certain viral proteins have adverse biological functions[365] that need to be inactivated before inclusion in vaccines. This has proven difficult to do.[366]

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356 Schoub (n 11 above) 189.

357 Graham and Wright (n 355 above) 1333. It seems that HIV is able to survive a great deal of sequence variation while still maintaining its ability to replicate and its structural integrity.

358 For a detailed discussion on this topic, see Lukashov *et al* in Wong-Staal and Gallo (eds) (2002) *AIDS vaccine research* 93 – 120.

359 Smith (2003) 2 *Med Immunology* 2.

360 Van Harmelen and Williamson (n 144 above) 569.

361 This process is called glycosylation.

362 Van Harmelen and Williamson 571.

363 As above, 573.

364 NIH (2003) *Challenges in developing AIDS vaccines* 1 <http://www.niaid.nih.gov/daids/vaccine/challenges.htm> (30 August 2003).

365 Such as stimulating tumour growth.

366 n 358.

Because of the virus's genetic diversity, a successful vaccine will have to stimulate not one but a broad range of neutralising antibodies against HIV. To date this has been impossible.[367]

4.5.2 A lack of models of protection to give clues to the mechanisms of immunity

Even though at the time little was known about human immunology, Edward Jenner was able to produce an effective vaccine against smallpox as early as the 18th century. What Jenner lacked in knowledge of the immune system, however, was made up for by the fact that he had a model of protection to study. Jenner was presented with a population of milkmaids who were protected from smallpox because of their prior exposure to cowpox. He had, literally, but to observe this group and draw conclusions about the cause of their resistance.[368]

In the case of HIV there exists no group of individuals who continue to be protected against HIV though they have repeatedly been exposed to the virus. A study of long-standing HIV negative sex workers in Nairobi has not provided clarity on the mechanism of their resistance.[369]

Although the role of neutralising antibodies and cytotoxic T-cells in the immune response against HIV has been documented, it is not known exactly which components of the immune response are necessary for protection from natural infection.[370]

4.5.3 Lack of experimental animal models to study the disease

Experimental animal models enable scientists to study infection and disease safely. Even though they do not always mimic human disease completely, animal models give important information on immune response and vaccine safety.[371] In the case of HIV very few animal models exist. The most successful animal model to date has

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367 Nabel (2001) 410 *Nature* 1002 1005.
368 As above, 1002.
369 Mackett and Williamson (n 13 above) 14; see Rowland-Jones *et al* (1998) 102 *J Clinical Investigation* 1785.
370 Mackett and Williamson (n 13 above) 14; Graham and Wright (n 355 above) 1331.
371 Wong-Staal and Gallo (n 358 above) iv. See also Pauza and Wallace in Wong-Staal and Gallo 287.

been that of the Rhesus macaque, in which infection with SIV[372] resulted in a syndrome very similar to AIDS.[373]

However, this animal model underscores the complexities of the interaction between retroviruses and their hosts, as neither the infection in animals nor the progression of the disease completely mimics HIV infection in humans. Structural and genetic differences between HIV and SIV make it difficult to transpose what has been learnt from animal studies to the human disease. [374]

4.5.4 Live (attenuated) HIV vaccines would be unsafe

The most successful vaccines that have been developed to date are live (attenuated) vaccines.[375] As was indicated above,[376] these vaccines consist of live viral material that is able to infect and replicate inside the host. In the case of a fatal infection, such as HIV, this poses a significant safety risk and, therefore, a live (attenuated) vaccine for HIV has been ruled out.[377] This approach, however, is being pursued in studies in animals and live (attenuated) mutant virus vaccines with deletions in the *nef* gene have been shown to have promise.[378]

4.5.5 The importance of logistics and economics

Although not scientific by nature, these obstacles to the development of a vaccine are significant. Vaccine trials are lengthy affairs and vaccine development is a costly exercise.

It takes almost 20 years from the moment a concept vaccine is produced up to the end of a Phase III vaccine trial. Many vaccines never make it to Phase III trials as they do not produce the necessary immune response *in vitro*.[379] Because of the long time frame involved, by the time a candidate vaccine finally reaches Phase

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372 Simian Immunodeficiency Virus.

373 In this regard, see Barouch *et al* (2002) 415 *Nature* 335 – 339. It is also important to remember that the animals that are needed in HIV vaccine experimentation are usually rare, protected species, unlike other laboratory animals such as rats and rabbits.

374 Graham and Wright 1333.

375 Klein and Ho (n 35 above) 306.

376 See para 4.4.2 above.

377 Smith (n 359 above) 1; Klein and Ho 306.

378 Graham and Wright 1334. In particular, see endnote 48 of their article. See also Klein and Ho 306.

379 'In vitro' refers to an artificial environment created outside a living organism (eg in a test tube) used in experimental research to study a biologic process or disease. 'In vivo' refers to the living body, or research done 'inside' a living organism.

III trials, scientific thinking may have changed no longer to reflect much hope that the vaccine antigen used in the vaccine will induce immunity successfully.

Thousands of volunteers at high risk for HIV infection are needed to take part in Phase III vaccine trials. This involves significant organisational and financial investment on the part of the pharmaceutical company. Often there is no expectation of a return on this investment.[380]

However, despite these obstacles, there do seem to be a few promising vaccine candidates. The next section explores a few of these possibilities.

4.6 Avenues of hope: various options for candidate preventive HIV vaccines

The disappointing results of the recently completed Phase III VaxGen candidate preventive HIV vaccine trial[381] have dampened many scientists' hopes that a successful preventive HIV vaccine will be found soon. However, scientists gain knowledge from clinical research; even failed trials.

Presently, despite our incomplete understanding of immunity to HIV and certain safety concerns, a number of candidate vaccines are entering Phase I and II trials, and a few are even entering Phase III trials. The results of completed Phase I and II trials give some room for optimism. The next section looks very briefly at a few of the candidate vaccines that are currently under investigation.

The following table summarises HIV vaccine strategies presently being investigated:[382]

Strategy	Description
Subunit vaccines	Recombinant viral proteins (eg *env*, p24, *tat*)
Live (attenuated) vaccines	Containing deletions of *nef* and/or *vpr* genes
Whole killed	Chemically inactivated HIV viruses
Peptide-based vaccines	Chemically synthesised HIV protein fragments and/or defined immunogenic epitopes
Pseudovirions	Non-replicating and non-infectious virus-like particles consisting of, for example,

380 Consider, for example, VaxGen's Phase III AIDSVAX trial. The trial was recently completed without any indication that the candidate vaccine that was tested provided protection against infection.

381 See McCarthy (2003) 361 *The Lancet* 755.

382 This table is taken from Bojak *et al* (2002) 7 *DDT* 36 39.

	gag, pol and *env*
Replicons	Non-HIV viruses engineered to carry genes encoding HIV proteins
Live bacterial vectors	Harmless bacteria engineered to carry genes encoding HIV proteins
Live viral vectors	Non-HIV viruses engineered to carry genes encoding HIV proteins, eg canary pox
DNA vaccines	Naked plasmid-DNA containing one or more HIV genes
Combined vaccines	Combination of different vaccines in a mixed modality immunisation schedule (eg DNA vaccines plus live viral vectors)

The following paragraphs mention specific candidate vaccines that are promising and that have entered clinical trials. (Also see chapter 5 for a more complete representation of the HIV vaccine trials being conducted in South Africa and around the world).[383]

Below, some important current candidate AIDS vaccines in Phase 1 and 2 clinical trials are classified according to vaccination approach, antigenic content and formulation:[384]

Vaccine antigens	**HIV strain of origin**	**Adjuvant, conjugate, or delivery system**
V3 (gp120) (a surface antigen)	Multiple	Alum, microspheres, IFA
Gp120 (surface antigen)	MN, SF-2	Alum, others
Gp 160	LAI, MN	Alum, alum + DOC
env *env, gag, pol*	LAI, MN LAI, MN	Vaccinia, canarypox[385]
Gp160, p24	MN	Virus- particle
P24	LAI	Self-assembling particle
gag (p24)	MN	Lipid conjugate

A vaccine developed by scientists at Oxford University and at the University of Nairobi is currently in Phase II trials in London and in Kenya. This vaccine, aimed at

383 Para 2.3.1 of ch 5.

384 This table is adapted from Graham and Wright (n 355 above) 1335.

385 Canarypox is a virus that infects birds and is used as a live vector in vaccine design as it is able to carry a large number of foreign genes. The canarypox virus cannot grow in human cells; an important safety aspect.

boosting cell-mediated immunity, consists of a number of the genes of HIV, such as *gag*, *pol*, *nef* and *env*. The vaccine is described as a 'prime boost' DNA vaccine.[386]

Another vaccine candidate soon to be entering clinical trials is Merck's 'HIV-1 gag replication defective adenovirus'. A cold virus that has been modified is used as a vehicle to deliver a fragment of the synthetically reproduced HIV-gene, called *gag*.[387] The Phase III trials of this candidate are to start in 18 cities around the world, including in South Africa.[388]

In March 2002, GlaxoSmithKline Biologicals announced the start of its first human trials of an adjuvant HIV vaccine, NefTat and gp 120.[389] This candidate vaccine succeeded in protecting rhesus monkeys against SIV, a virus similar to HIV.[390]

Another pharmaceutical company, AlphaVax, recently announced the start of the first human trials of its HIV preventive vaccine in the United States and South Africa.[391] The AlphaVax vaccine (called AVX101) uses a non-propagating form of an alphavirus vector[392] to express HIV genes.[393] It is hoped that these will elicit broad-based immune responses, including cellular immunity.[394]

The next section examines aspects of clinical research relevant to the thesis. Research methodologies to produce a vaccine are investigated and the structure of clinical trials used to develop a HIV vaccine is explained.

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386 Weidle *et al* (2002) 359 *The Lancet* 2264; 'AIDSVAX trial not the end of the story' *The Scientist* (Daily News) 28 February 2003.

387 The HIV Vaccine Trials Network *Press release 19 September 2003* <http://www.hctn.org/pressroom/press_releases.sht?id=36> (4 October 2003).

388 As above. Another candidate vaccine utilising the *gag* gene, is AVX101. This candidate vaccine has entered phase I trials in South Africa and the USA. AVX101 is an alphavirus replicon vaccine. See ch 5 below.

389 See 'GlaxoSmithKline Biologicals announces start of human trial of novel HIV vaccine' *AIDS Weekly* (2002) 11.

390 As above.

391 'Trials of new HIV vaccine begin in US, South Africa' *Biotech Week* 27 August 2003 42.

392 A 'vector' is a bacterium or virus that does not cause disease in humans and which is used in genetically engineered vaccines to transport genes coding for antigens into the body to induce an immune response.

393 n 388.

394 As above.

5 CLINICAL RESEARCH AND HIV VACCINE DEVELOPMENT

5.1 Introduction

In this section clinical research, generally, and vaccine efficacy trials, specifically, are explored in order to come to some understanding of the methodological framework underlying HIV-related clinical research. Problems and risks related to HIV vaccine efficacy trials are examined with a view to providing the scientific underpinning for the third, fourth and fifth chapters that focus on ethical issues and human rights issues in HIV-related clinical research and vaccine efficacy trials.

5.2 Clinical research

Levine defines the term 'research' to denote 'a class of activities designed to develop or contribute to generalizable knowledge'.[395] Such generalised knowledge consists of 'the theories, principles, or relationships (or the accumulation of data on which they may be based) that can be corroborated by accepted scientific observation and influence'.[396]

The term 'clinical research', in turn, refers to research 'involving human subjects, that is designed either to enhance the professional capabilities of individual physicians or to contribute to the fund of knowledge in those sciences that are traditionally considered basic ...'[397] Clinical research, thus, is research carried out on humans, and, by definition, therefore excludes research carried out on human blood or tissue samples[398] and research on animals.

The definition above also emphasises that the individual research participant might not benefit directly from the research that is being done – research may be undertaken to contribute to the 'fund of knowledge'. This is the case in clinical research aimed at testing a new drug, in which the participant is allocated to the control, or placebo, group. [399]

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395 Levine (1986) 3.

396 As above; Chen *et al* (2003) 138 *Annals Internal Med* 669. The term 'research' is often contrasted with the term 'practice'. 'Practice' relates to activities that are focussed on the individual patient or client with the aim of diagnosing, treating and curing that patient. The best interests of the individual patient are most important. In the case of research, the aim is to develop knowledge to help future patients.

397 Levine (n 395 above) ix; also see Rick (n 18 above) 4.

398 Rick 4. Even though these may often form part of research carried out on humans, for instance, where blood is drawn from participants to establish whether an immune response is present against a candidate vaccine.

399 A dummy treatment.

Furthermore, it is important to note that clinical research is sometimes carried out on healthy individuals who are exposed to risk solely to expand scientific knowledge.

The aim of clinical research is to benefit the individual or society as a whole. Without research on human subjects major medical breakthroughs would never have been achieved. Clinical research in the past has led to the development of drugs, such as antibiotics and antivirals, and procedures, such as heart and lung transplants. Clinical research is a necessity and the effects of neglecting such research would be disastrous. The World Medical Association's Declaration of Helsinki recognises the value of research for medical progress and the inevitability of that research having to include human participants: 'Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects'.[400]

The benefits of HIV-related research, generally, and of finding an effective preventive vaccine for HIV, specifically, are enormous, both to the individual and to society. Not only will the successfully vaccinated individual be protected against future infection by a deadly disease but, because of the 'herd' immunity, non-vaccinated members of society will be protected as the 'pool' of infection will have been decreased.[401] Clinical research to find a preventive vaccine is thus a necessity.

Two major types of clinical research may be distinguished.[402]

- Observational research.
- Experimental research.[403]

The two methods will be discussed briefly below.

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400 Declaration of Helsinki, adopted by the 18th World Medical Association assembly, Helsinki, Finland, in 1964, and revised subsequently, reprinted in Levine (n 395 above) 427.

401 See para 4.3 above.

402 Grimes and Schulz (2002) 359 *The Lancet* 57 - 58.

403 A third method, qualitative research, is also sometimes distinguished. Qualitative research attempts to interpret, or give meaning to, different phenomena. It studies participants in their natural surroundings and attempts to draw conclusions from these observations. With qualitative research the focus is on the research participants' interpretation of events, and not on that of the researcher. There is no attempt at objectivity - this method attempts to arrive at various, subjective interpretations of the world. A few qualitative research methods are focus groups, case study evaluation and qualitative interviews. As this method is rarely used in clinical research in a medical or scientific setting, it is not included in this discussion.

5.2.1 Observational research

Observational research involves the observation of a certain state or event without interfering.[404] This research method is clearly distinguishable from that of experimental research in which the effect of a specific intervention is studied. Observational research is sometimes referred to as epidemiological research, as this method is frequently used in epidemiological studies.[405] For example, observational research is frequently employed to determine the prevalence of diseases in a certain geographical area, the infection rate at a certain point in time, and so on.

Observational research is either descriptive or analytic.[406] Descriptive studies describe states or events without indicating their cause or effect. In descriptive studies there are no control or experimental groups.[407] Analytic studies, on the other hand, look for links between cause and effect in an attempt to arrive at an understanding of the interplay between different factors.[408] Analytic studies use a comparison or control group.[409] They are always quantitative in nature.[410]

Three types of analytic, observational clinical research methods exist, namely, cross-sectional studies; cohort studies; and case-control studies.[411] The direction in time of an analytic study determines its subtype.

A study that determines both exposures and outcomes at the same point in time is a cross-sectional study.[412] An example of a cross-sectional study is the measurement of the serum cholesterol levels of men admitted to hospital with myocardial infraction, compared to those at the hospital next door.[413]

Cohort studies compare two groups, whereby one group is exposed to risk and the other is not, and follow these groups.[414] For example, the study begins with an exposure (such as oral contraceptive use) and follows women for a period of time to measure outcomes (such as breast cancer).[415] In this way the ratio and rates of

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404 Foster (2001) 23; Grimes and Schulz (n 402 above) 58.
405 As above.
406 As above.
407 Grimes and Schulz (n 402 above) 58. A case report is an example of a descriptive study. When more than one patient, or 'case', is described, the study is known as a case-series report.
408 As above.
409 As above.
410 As above.
411 As above; Foster (n 404 above) 23.
412 Grimes and Schulz 58.
413 As above.
414 Foster 23.
415 Grimes and Schulz 58.

disease may be calculated.[416] Cohort studies may be either concurrent or non-concurrent.[417]

Case-control studies are the opposite of cohort studies. Case-control studies start with the effect or outcome (breast cancer) and look back in time to find a cause (oral contraceptive use).[418]

5.2.2 Experimental research

Experimental research attempts to exclude the weaknesses of observational research that affect its scientific validity, such as researcher and participant bias.[419] This is done through a clinical trial.

Clinical trials are 'organized studies to provide large bodies of clinical data for statistically valid evaluation of treatment'.[420] Such experimental research methods include randomised controlled clinical trials and non-randomised controlled trials.[421]

The randomised controlled clinical trial (RCCT) is the most widely used (experimental) research method.[422] A RCCT is used to 'compare the efficacy and safety of two or more interventions or regimes'.[423] This definition highlights the fundamental characteristic of the method – that it makes a comparison. For example, a new drug or treatment is compared to an existing drug or treatment, a placebo, or nothing at all.[424] Research participants receiving the existing (standard) drug or a placebo are referred to as the control group, while the participants receiving the new treatment are referred to as the experimental group.[425] Sometimes a RCCT compares different doses of the same drug.[426]

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416 Foster (n 404 above) 23.

417 Grimes and Schulz (n 402 above) 58.

418 Grimes and Schulz 58; Levine (n 395 above) 210; Foster 23.

419 Devereaux *et al* (2003) 413 *Clinical Orthopaedics and Related Research* 25 - 26.

420 Anderson (ed) (1998) 1E13. The International Conference on Harmonization (ICHJ) offers a more lengthy definition of a clinical trial:
Any investigation in human subjects intended to discover or verify the clinical, pharmacological and / or other pharmacodynamic effects of an investigational product, and / or to identify any adverse reactions to an investigational product, and / or to study absorption, distribution, metabolism, and excretion of an investigational product with the object of ascertaining its safety and / or efficiency (Rick (n 18 above) 140).

421 Experimental designs that need mention but which do not really warrant inclusion as they are used in combination with RCCTs and non-randomised controlled clinical trials, are historical control data as a control in trials and dose-response design trials.

422 From now on referred to as RCCT.

423 Levine 185.

424 Foster 22.

425 As above.

426 As above.

An important characteristic of RCCTs is that they attempt to control for any chance of an outside (non-experimental) factor influencing the results of the trial. This is done by ensuring that the sample size is sufficiently large. The fact that the trial is often 'blinded', tries to exclude observer or participant bias.[427] In a 'double blind' RCCT, neither the researcher nor the participant knows who is given the 'real' intervention and who is receiving the standard care or the placebo.[428]

Randomisation also contributes to the elimination of outside influences.[429] Randomisation is the practice of allocating participants to different experimental groups by random selection.[430] In large trials the selection is done by computer.

Before research participants are randomised into different groups, efforts are made to ensure that they are as homogenous a group as possible. The eligibility criteria of trials attempt to ensure this. For example, only healthy persons of a certain cholesterol level or a certain age are included in a specific trial.[431]

RCCTs were initially designed to test new drugs[432] but are now used for a wide range of purposes, such as the study of existing drugs and the development of new surgical interventions.[433] This RCCT trial design is considered the approximate of the controlled experiment in basic science and is the 'gold standard' of clinical research.[434] The RCCT is of interest to this study as vaccine efficacy trials are conducted in this way.

When true randomisation is not used, the study design is that of a non-randomised controlled clinical trial. Instead of randomisation, another assignment scheme may be used, such as alternate assignment.[435] This study design is

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427 For example, a principle investigator whishing the trial drug to be proven effective may actively (and even subconsciously) select participants who stand a better chance of benefiting from the experimental regimen and ensure that those participants are part of the 'experimental' group; trial participants who know that a new drug is being tested on them may feel an 'improvement' in their condition which may be absent as they are part of a placebo group.

428 At the end of the trial, the trial is 'unblinded' to reveal who is receiving which intervention. This is also done where serious adverse events are reported. Also, for a discussion of some of the ethical implications of trials where placebos are used, see ch 3 below.

429 Such as a researcher allocating participants that she thinks may benefit most from the experimental treatment to the experimental group.

430 Levine 185.

431 As above.

432 As above.

433 As above. RCCTs are also used to test the efficacy and safety of new vaccines, see para 5.4 below.

434 Grimes and Schulz (n 402 above) 58.

435 As above.

considered less scientifically rigorous than that of a randomised controlled trial.[436] After the participants to a non-randomised control clinical trial have been assigned to the treatment and control groups the study resembles that of a cohort study.[437] The disadvantage of this trial design is that selection bias may occur.[438]

In the following section aspects of clinical research methodology significant to the development of new HIV drug regimens will be outlined, before attending to the design of clinical trials in the development of a preventive HIV vaccine.

5.3 Drug development through clinical research

This section explores the methodology of clinical research aimed at developing a new drug for the treatment of HIV and distinguishes vaccine efficacy trials from trials to develop other experimental drug regimens.

The development of a new drug or experimental treatment proceeds through the following phases. They are:[439]

- Basic research.
- Pre-clinical evaluation.
- Clinical trials (involving human trial participants).

5.3.1 Basic research

What this involves is research into the different attributes of the pathogen that produces the disease.[440] Thus, HIV's virulence, pathogenicity and infectivity have been established, as well as the exact mechanisms of the human immune response to HIV.[441] Knowledge gained from basic research leads to the identification of a drug strategy that, for example, it is suspected will be successful in lightening the burden of HIV-disease. The drug is then produced for pre-clinical testing.

5.3.2 Pre-clinical evaluation

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436 As above.
437 As above.
438 As above.
439 Levine (n 395 above) 6 – 7.
440 As above.
441 As above.

Pre-clinical testing is done to evaluate the drug's ability to treat the disease. Usually, such testing is done in vitro or on animals. In the case of HIV-related drug research the lack of a suitable animal model has hampered research.[442]

Animals are given the experimental drug or treatment, after which they are closely monitored. Not only are the animals' clinical responses examined during this stage but the levels at which the drug becomes toxic are also measured.[443]

Only once a drug has been shown successfully to elicit the required response in animals, as to be safe, is it tested on humans to ascertain its efficacy and safety.

5.3.3 Clinical trials

Clinical research to test drug safety and efficacy in humans is done by means of controlled clinical trials:[444]

- *Phase I: Clinical pharmacology*

This phase is intended to be the first introduction of the drug into humans and is aimed at determining levels of toxicity, the appropriate dosage and its safety.[445] Drug dynamic and absorption studies are performed during this phase. Normally, healthy volunteers are recruited during this phase.[446] Furthermore, usually no control group is included and only a limited number of participants are enrolled – from as few as 10 to about 100.[447] Subjects are monitored closely to check their tolerance to the drugs and any side-effects.[448] Depending on the complexity of the trial, the cost of a Phase I trial is estimated at around US$ 10 million.[449] The trial may last from several months to a year.[450]

- *Phase II: Clinical investigation*

This phase consists of controlled clinical trials to ascertain the effectiveness and relative safety of the developmental drug.[451] Only once a drug has passed through Phase I trials, and was proven safe and non-toxic, may it proceed to Phase II trials.

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442 See above.
443 Levine (n 395 above) 6.
444 As above. Not all drugs progress through all four phases. Most often the clinical trials of drugs are terminated during early phases when drugs are proven toxic or inefficacious.
445 Levine 6; Rick (n 18 above) 144.
446 Rick 144. However, in some instances, critically ill patients or with terminal diseases are presented with the option to be included in the trial after due consideration of the risk-benefit ratio.
447 Rick 144.
448 As above.
449 As above.
450 As above.

Phase II trials differ from Phase I trials as the effectiveness of the drug is also assessed. A series of doses of varying strengths may be given to participants.[452] Participants are randomised to a control group or an active group.[453] Once again a relatively small number of participants are enrolled – from about 50 participants to 500 participants.[454] Phase II trials result in the information needed to determine the effective dose and the dosing regimen with regard to frequency and duration.[455] The success rate of Phase I and II studies is around 30 per cent.[456] A Phase II trial may take one to two years and costs as much as US$20 million.[457]

- *Phase III: Clinical trials*

These are large-scale trials and may be controlled or uncontrolled.[458] The trials are most often RCCTs. This phase aims at establishing efficacy and the possibility of the existence of adverse effects, and uses the safe, effective dosage and administration schedule determined by the preceding phases.[459] Phase III trails are considered large-scale trails as they usually include thousands of participants.[460] These trials are usually conducted in different geographic locations (known as multi-centre trials).[461] The trial has to be methodologically sound in order for meaningful results to be presented at the end of the trial.[462] Statistical proof to show the efficacy of a drug or vaccine has to be established.[463]

- *Phase IV: Post-marketing clinical trials*

These trials are done after the new drug has been marketed to the public, and include clinical trails aimed at elucidating increased adverse reactions or events; testing of the drug in populations not previously included in the trials;[464] and trials to test drug efficacy for an indication other than what was initially tested for.[465]

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451 Levine 6; Rick 145.
452 Rick 145.
453 As above.
454 As above.
455 As above.
456 Rick 145.
457 As above.
458 Levine (n 395 above) 6 - 7.
459 As above.
460 Rick 145.
461 Rick 146.
462 As above.
463 Rick 147.
464 such as in children. Levine 6 – 7; Rick 147.
465 Levine 6 - 7.

Although they follow the same basic pattern as usual clinical trails to test drug efficacy, vaccine efficacy trials differ from drug efficacy trials in a few very important respects.

- Most important, in the case of trials to establish the efficacy of a new drug, the trial participants usually suffer from the particular disease the drug is being tested for - obesity drugs are tested on obese participants, cancer drugs are tested on cancer sufferers and new drugs to treat diabetes are tested on participants suffering from diabetes. This is not the case in vaccine trials. Vaccine trials are usually performed with healthy volunteers who may be at risk for contracting the disease[466] but who are otherwise healthy.
- Participants in a vaccine trial, thus, are taking part primarily to benefit their community or society and not themselves.[467] Of course, as a community that is at risk of HIV infection, they will ultimately benefit from the development of a successful vaccine.
- Because participants are healthy and are taking part in vaccine trials for the benefit of others, one would expect that they should be placed at a lower degree of risk than is expected of participants already suffering from a specific disease who are taking part in a trial to develop a new drug to better treat their own condition.
- Because vaccine trials utilise volunteers who are only at risk for contracting a disease and who are not sufferers of that specific disease, vaccine efficacy trials usually last longer and require more volunteers in order to be regarded as scientifically valid. [468]

5.4 Preventive HIV vaccine efficacy trials[469]

In turn, preventive HIV vaccine efficacy trials carry significantly greater risk to their participants than is the case with other vaccine efficacy trials. This section explores HIV vaccine efficacy trials, and attempts to establish exactly why participation in a

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466 Especially during Phase III trials. However, this risk may never materialise, as not all participants are ever exposed to the virus.

467 Even though they will benefit if a successful vaccine is developed.

468 Where everybody is a sufferer of a disease it is relatively easy to show that a certain drug works better than another. In the case of vaccine efficacy trials, because not all participants will be challenged by the pathogen, many more volunteers are required.

469 Only the stages of vaccine efficacy trials are discussed here – the process of gaining regulatory approval for conducting a human trial is discussed in ch 5, in which specific reference is made to this process in South Africa.

HIV efficacy trial poses greater risk than participation in any other vaccine efficacy trial. Finally, these risks are enumerated.

5.4.1 Stages and duration of HIV vaccine efficacy trials

Additional to the outline given in 5.3.3 above, the following applies to HIV vaccine efficacy trials in particular. Pre-clinical research to develop a new vaccine proceeds along the same pattern as indicated above.

- *Phase I: Clinical pharmacology*

As indicated above, this phase determines the levels of toxicity and appropriate dosage of the candidate HIV vaccine.[470] Human participants are exposed to the candidate vaccine for the first time during a Phase I trial. This phase lasts about eighteen months and requires a smaller number[471] of trial participants than subsequent phases.[472] Also, as efficacy is not at issue here, trial participants do not need to be at high risk of HIV infection. Phase I trials usually consist of ten to twenty patients or volunteers in each study arm.[473]

- *Phase II: Clinical investigation*

This phase attempts to determine the safety and effectiveness of the candidate HIV vaccine. Trials are done on larger numbers[474] of closely monitored participants, some of whom should be at high risk for infection. Phase II trials last 24 months.[475] The details of the immune response to the vaccine are studied during this phase.[476] This phase attempts to answer the question: Does the candidate vaccine produce the desired immune response?[477] These studies are mostly multi-centred.[478]

- *Phase III: Clinical trials*

These are large-scale, double blind, placebo-controlled, randomised clinical trials, aimed at finding out whether the candidate HIV vaccine is effective in preventing infection by HIV.[479] The possibility of the existence of adverse effects is also examined.[480] Large numbers of volunteers are used during this stage, usually more

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470 Abdool Karim (2002) 20 *CME* 588 589.
471 Fewer than a hundred, mostly twenty to 50 participants.
472 Abdool Karim (n 470 above) 588.
473 As above, 589.
474 100s of participants.
475 Abdool Karim 589.
476 As above.
477 As above.
478 As above.
479 Abdool Karim 589.
480 As above.

than a thousand.[481] The question to be answered is this: Is the candidate vaccine effective? Because the efficacy of the candidate vaccine needs to be established these volunteers should be at high risk for infection.[482] This aspect of Phase III clinical trials has important ethical implications which will be discussed later.[483]

5.4.2 Preventive HIV vaccine efficacy trials versus other vaccine efficacy trials

The most important differences between HIV vaccine efficacy trials and drug efficacy trials of vaccines for other diseases stem from the nature of the disease itself. The following comments are restricted to scientific and social aspects of HIV vaccine efficacy trials. Important ethical problems associated with HIV vaccine efficacy trials are dealt with subsequently.[484]

- *Stigmatisation of HIV/AIDS and its sufferers*

HIV/AIDS is not like any other disease. Despite many attempts to educate and inform the public, HIV/AIDS sufferers remain stigmatised. Because those at highest risk for HIV infection often belong to marginalised groups in society, such as IDUs, sex workers and MSM, HIV/AIDS is considered a shameful disease. Also, because HIV/AIDS is largely a sexually transmitted disease, and because sex is not discussed openly in many societies, HIV/AIDS is regarded as unmentionable.

HIV infection is regarded as avoidable. Unlike other viral diseases such as polio and measles, which are not really preventable in the true sense of the word, HIV infection is associated with promiscuity and sexual adventure. Politicians often refer to children as the 'innocent' victims of AIDS; adult victims, by implication, are not 'innocent'. It is likely that these assumptions about HIV/AIDS - perceptions that have created endless obstacles to effective prevention and treatment programmes - will influence the public's perception of HIV vaccine trials and their participants as well.

- *Severity of the disease*

HIV/AIDS is a potentially fatal disease. Any HIV vaccine efficacy trial, therefore, will need to conform to the highest safety standards in order to protect healthy participants against vaccine-related adverse effects. Fears of contracting HIV

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481 The VaxGen Phase III trial involved 5009 volunteers.
482 Abdool Karim 589.
483 See ch 5 below.
484 As above.

because of trial participation may inhibit participants form volunteering for preventive HIV vaccine efficacy trials.[485]

- *Natural history of infection*

Because it is a lenti-retrovirus, HIV infection does not advance along the same pattern of infection as other viruses. It is a slow, progressive disease. Because of its integration into the host cell's DNA and because of the high rate of error in the reverse-transcription process, HIV manages to escape the body's standard immune responses. A HIV vaccine design and efficacy trial will have to take cognisance of this fact.

- *The urgency of the need for an effective vaccine*

There is no room for error in the search for an effective preventive HIV vaccine. Each vaccine concept and trial takes years to deliver results. During this time many more people will be dying. Had HIV had not been a fatal disease, the need for an effective vaccine would not have been that urgent.

Because of their particular nature, HIV vaccine efficacy trials offer some benefits and pose specific risks for participants. These are mentioned below, paving the way for a detailed examination of the benefits and risks of participation (in chapter 5 below).

5.4.3 Advantages versus risks to participants: A preliminary overview[486]

In a setting where resources usually are stretched, the most important benefit of HIV vaccine trial participation is the fact that vaccine trial participants gain access to increased health care and attention. They are given treatment for STDs and counselling to reduce high-risk behaviour, possibly preventing infection in the future.

Risks borne by participants of HIV preventive vaccine efficacy trials are physical, psychological and social in nature and differ according to vaccine design and trial design.[487] Some risks are more serious than others.

Physical risks in HIV preventive vaccine trials include the possibility of adverse autoimmune reactions to the vaccine and the possibility that the participant will suffer from a worse infection should she ever become infected with HIV.[488] Other

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485 See paras 2.3.1 and 3.4.1 of ch 5 below.

486 Also see para 2.3.1 of ch 5 below for a more extensive discussion on the topic.

487 Some vaccines are safer than others, see para 4.4 above; and some trial designs may have more adverse effects, such as those using placebos, see ch 3 below.

488 Graham and Wright (n 355 above) 1335. See para 2.3.1 op ch 5 below.

risks are adverse reactions to the vaccine itself;[489] pain, skin irritations, fever, and malaise.[490] HIV vaccination may require repeated inoculations, each producing these adverse effects.

Live vaccines carry the risk that the vaccine virus may mutate sufficiently to revert back to its virulent form. Although pre-clinical research is being done on live vaccines, there is no indication that these vaccines will be tested on humans. Should this be, however, trial participants would be exposed to serious risk of harm.[491]

Finally, participation in a HIV preventive vaccine efficacy trial may result in immune tolerance which, in turn, will prevent the trial participant from being successfully immunised against HIV in the future.

Psychological risks to participants in HIV preventive vaccine efficacy trials include stress, anxiety and depression due to having to discuss intimate sexual matters with trial administrators, the stress inherent in being subjected to repeated HIV testing,[492] and also strain in the participants' sexual relations with others, especially when the participants' sexual partners (mistakenly) believe that the participants may infect others with the virus.[493]

After being vaccinated, participants may test HIV-positive on standard ELISA assays even though they are not infected with HIV. This could have serious consequences for participants' prospects of successfully taking out insurance, finding employment, and so on.[494] They may be perceived by a misinformed public to *be* HIV positive. Participants in Phase III trials are usually high-risk individuals and this perception may cause them to be stigmatised and discriminated against. The communities from which these participants are drawn may be similarly stigmatised.

6 CONCLUSION

This chapter aims to provide the scientific foundation for the ethical and rights-based analyses in subsequent chapters.

In order to do this HIV has been classified and described. The natural progression of the disease has been outlined and the peculiarities of the HIV and AIDS syndrome and progress made in its treatment have been investigated. It has

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489 Such as an allergic reaction to one of its components. See para 2.3.1 of ch 5 below.

490 UNAIDS (2000) *Ethical considerations in HIV preventive vaccine research* 28. See para 2.3.1 op ch 5 below.

491 See para 4.4 above.

492 UNAIDS (n 490 above) 29. See para 2.3.1 op ch 5 below.

493 As above.

494 As above. See ch 5 below on attempts to prevent this risk from materialising.

been pointed out that, although relatively effective, HAART is not a long-term solution to halting the epidemic.

It was argued that an effective HIV preventive vaccine is the only way of controlling and eradicating HIV. In order to arrive at a successful vaccine clinical research will have to be undertaken. Such clinical research, by definition, will involve human participants, exposing them to risks and adverse effects.

The sections on challenges posed by HIV vaccine development and on the problems and risks related to HIV vaccine efficacy trials show that there is a long road ahead in the search for an effective HIV preventive vaccine; a road along which science will have to be assisted by ethics and human rights principles.

The focus of some sections in this chapter has been on the scientific framework of HIV preventive vaccine efficacy trials. These sections have been included in preparation for the analysis in chapter 5, which focuses on preventive HIV vaccine efficacy trials in South Africa.

In the following two chapters there is a more general emphasis on HIV-related clinical research in Africa. As background to the more general discussion of clinical research in these chapters this chapter contains an overview of clinical research methodology.

The discussion turns to an examination of ethical issues with regard to HIV-related clinical research in Africa.

CHAPTER 3

ETHICAL ISSUES IN CLINICAL RESEARCH IN AFRICA: PRINCIPLES AND PRACTICE

Outline

1 Introduction

2 Principles of clinical research ethics
2.1 Introduction
2.2 Conceptual framework
2.3 Philosophical background
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3 Ethical guidelines and documents
3.1 Introduction
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4 From principles to practice: The regulation of clinical research elsewhere and in Africa
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5 Conclusion

1 INTRODUCTION

This chapter explores the origin and nature of the ethical principles deployed in the protection of research participants in clinical research. An analysis of the protection afforded by fundamental ethical principles, namely, autonomy, beneficence (including nonmaleficence), and justice, as embodied in various international and domestic documents, is presented.

The protection afforded by international documents, such as the Nuremberg Code, the International Ethical Guidelines for Biomedical Research involving Human Subjects, the Belmont Report and the Declaration of Helsinki, is scrutinised. The scope of domestic documents, such as the Medical Research Council's Guidelines on ethics for medical research and the Department of Health's Guidelines for good practice in the conduct of clinical trials in human participants in South Africa, and the objectives of the different local research ethics committees are investigated.

The chapter presents an analysis of the ethical dilemma at the centre of the controversy over the placebo-controlled trial of AZT in preventing MTCT of HIV in Uganda, and indicate problematic issues arising out of three other drug trials.

Finally, it examines ethical concerns relevant to research participants in Africa.

The purview in the chapter is broad; it focuses on clinical research relating to HIV in Africa in general, and preventive HIV vaccine efficacy trials are mentioned merely in passing.

2 THE PRINCIPLES OF CLINICAL RESEARCH ETHICS

2.1 Introduction

In deciding the 'ethical' nature of clinical research, one determines whether it conforms to the commonly considered norms of ethical research. Levine defines an ethical norm as 'a statement that actions of a certain type ought (or ought not) to be done'[1]. Certain acts are believed to be ethically 'wrong' (and should not be done), whereas others are ethically 'right' (and may be done).[2] Ethical norms have been codified as guidelines in the various international and domestic ethics documents. The following is an example:[3]

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1 Levine (1986) 19.
2 As above.
3 Art 1 World Medical Association Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research involving Human Subjects, adopted by the

> Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.

Ethical norms, such as the one quoted above, derive from three[4] ethical principles; namely, respect for persons (or respect for autonomy), beneficence (which includes nonmaleficence), and justice.[5] These ethical principles correspond to the three ethical concerns or questions in research namely, which research qualifies as both scientifically valid and necessary research, which is in the best interests of the participants, and the autonomy of the research participant.[6] In the following pages the origin of these ethical concerns and the ethical principles they involve are explored.

2.2 Conceptual framework

Beauchamp and Childress define the term 'ethics' as 'a generic term for various ways of understanding and examining the moral life'.[7] 'Ethics' has been referred to as the academic study of moral concepts and theories.[8] In departments of philosophy, 'ethics' is termed 'moral philosophy' or 'moral theory'.[9] Some writers, such as Beauchamp and Steinbock, use the terms 'ethics' and 'morality' interchangeably.[10]

However, the term 'morality' requires elucidation. Beauchamp and Childress define morality as being those norms about right and wrong human conduct that are so widely shared that they form a stable social consensus.[11] Morality thus includes standards of conduct, such as moral principles, rules, rights and virtues.[12]

A set of norms shared by all 'morally serious' persons is referred to as the 'common morality' by Beauchamp and Childress.[13] Further, morality includes moral

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18th World Medical Assembly, Helsinki, Finland, in 1964, and revised subsequently; from now on referred to as the 'Declaration of Helsinki'.

4 Writers, such as Beauchamp and Childress, refer to *four* fundamental ethical principles. They consider beneficence and nonmaleficence as two separate principles; this thesis considers the two concepts as one ethical principle; the one implying the other.

5 Levine 11; Beauchamp and Childress (2001) 12.

6 Foster (2001) 9 – 10.

7 Beauchamp and Childress (n 5 above) 1.

8 Beauchamp and Steinbock (1999) 4.

9 As above.

10 Beauchamp and Steinbock (n 8 above) 4.

11 Beauchamp and Childress (n 5 above) 2 – 3.

12 As above, 3.

13 Beauchamp and Childress 3. Such as notions that it is wrong to steal, lie, etc.

ideals (that a group readily accepts), communal norms (that bind members of a certain community), and virtues, and so on.[14]

A distinction is made between universal morality and community-specific morality,[15] in which universal morality refers to the norms in common morality, whereas community-specific morality indicates moral norms that are specific to a particular cultural, religious or institutional setting.[16]

Professional morality is the set of norms or a standard of conduct that is generally acknowledged by members of a profession who acknowledge the moral duties and responsibilities of that profession.[17] As Beauchamp and Childress point out, professional morality in the medical and related professions stems from the 'institutions, practices and traditions of medicine'.[18] Codes of medical, nursing and research ethics attempt to formalise these moral duties and responsibilities.[19]

Government agencies sometimes formulate codes that contain normative ethical guidelines,[20] and these guidelines may be legislated.[21] Such guidelines reflect public policy, for example, guidelines regulating biomedical research carried out on foetal tissue.[22] Public policies are a reflection of moral and ethical considerations,[23] and exist within 'social disagreements, uncertainties, and different interpretations of history'.[24]

Because public policies are derived in a situation of uncertainty, any set of principles and guidelines they embody is devoid of sufficient specific information so as to provide guidance in all the varying practical, political and cultural situations.[25] In the words of Beauchamp and Childress: [26]

> Principles and rules provide the moral background for policy evaluation, but a policy must also be shaped by empirical data and by information available in fields such as medicine, nursing, economics, law and psychology.

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14 As above.
15 As above. 'Morally serious' is Beauchamp and Childress' term.
16 As above. The influence of community-specific moral norms on ethical decision-making is discussed in detail in chs 4 and 5.
17 Beauchamp and Childress 5.
18 As above.
19 As above.
20 As above, 7.
21 As above. If they are legislated they acquire the force of law.
22 As above, 8.
23 As above.
24 As above.
25 As above, 9.
26 As above.

Approaches to ethics are either normative or nonnormative.[27] 'Normative ethics' is an attempt to identify the general moral norms to be used for deciding conduct that is ethically acceptable.[28] In other words, normative ethics attempts to provide a theoretical or foundational basis for how people ought to behave.[29] Various ethical theories provide ways to identify and justify these moral norms.[30]

'Nonnormative ethics', on the other hand, divides into two broad categories – descriptive ethics and metaethics. Descriptive ethics is the factual investigation of moral conduct and beliefs with the purpose of finding out how people reason and act.[31] Metaethics is a theoretical analysis of the language, concepts, and methods of reasoning in ethical discourse; [32] it investigates the meaning of ethical terms such as 'duty', 'good' and 'obligation'.[33]

Applied (also practical) ethics aims to 'implement general norms and theories for particular problems and contexts'.[34] The term 'applied' is an indication of the use of theory and analysis to examine moral problems in professions, institutions and public policy.[35] In applied ethics, theory and principles are starting points and a general guide to the development of norms of appropriate conduct.[36]

Bioethics, a discipline that is relatively recent, is a sub-field of applied ethics.[37] It has its beginnings in the late 1960s and early 1970s,[38] and, partly, was born from student demands at Anglo-Saxon universities in the 1960s for an education that was 'relevant', and, partly, as a result of advances in medical science and the novel ethical questions they raised.[39]

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27 As above, 1.

28 Beauchamp and Childress (n 5 above) 2. The concern of this thesis is limited to the approach that is normative ethics.

29 Beauchamp and Steinbock (n 8 above) 4.

30 Beauchamp and Childress 2.

31 As above.

32 As above.

33 Beauchamp and Steinbock 4.

34 As above.

35 Beauchamp and Childress 2.

36 As above.

37 The terms 'bioethics' and 'biomedical ethics' are used interchangeably in this thesis. The term 'bioethics', is preferred as it encompasses more than 'biomedical ethics'– 'bioethics' stresses that we do not limit our concern to the practice of medicine by doctors, but other disciplines are included.

38 See David Rothman's account of the history of modern bioethics in Rothman (1991) *Strangers at the bedside: A history of how law and bioethics transformed medical decision making.*

39 Beauchamp and Steinbock (n 8 above) 3. Advances in medical science include assisted reproduction, genetic testing and manipulation, and technologies to prolong life.

The concern of bioethics is with an ethics that should guide physicians and scientists. Its aim is the protection of patients and of research participants. A broad range of literature on topics in bioethics has developed to include the doctor-patient relationship; informed consent; clinical research; euthanasia; genetic testing; and reproductive choices.[40]

2.3 Philosophical background

The various ethical (or moral) theories or philosophical traditions rely on different values in deciding whether an action is right or wrong, yet each contributes something to our understanding of ethical reasoning. Beauchamp and Childress maintain that knowledge of these ethical theories is an indispensable requirement for a reflective study of bioethics.[41]

The following classical philosophical traditions are regarded as fundamental in ethical decision-making: utilitarianism, Kantianism and liberal individualism.[42] Communitarianism and the ethics of care are discussed as well, as they add significantly to an understanding of the limitations of restricting philosophical reasoning to utilitarianism; Kantianism and liberal individualism. Each tradition is summarised below (with the exception of liberal individualism, which is dealt with in detail in the next chapter).

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40 As above.

41 Beauchamp and Childress (n 5 above) 337.

42 Aristotelian virtue ethics, Utilitarianism and Kantian/Rawlsian ethics are described as traditional or classical ethical theories. Recently, these traditional ethical theories have been challenged by the proponents of a range of special interests; feminism, race, sexuality, multiculturalism and environmentalism. Traditional ethics articulates general and universal principles of right and good, from the social forces or abstracted beliefs that govern established relations between persons, races, genders and classes. The 'newer' ethical theorists pose different questions, have different goals, use different tools of analysis and, therefore, believe they are challenging the prescribed paradigm in traditional ethical discourse. They point out that in the real world, groups are divided by gender, race, poverty, sexual orientation, and that these divisions constitute the 'problem' of ethics, presenting in a non-ideal, non-ordered post-modern society. This is an attempt to unmask the ideological stereotypes and normative contradictions they claim are embodied in established systems of race, gender, sexuality and so on (Doppelt (2002) 6 *The J Ethics* 383 – 386).
This thesis, however, does not undertake a philosophical analysis of ethical theory, nor does it provide an exhaustive account of modern ethical theory. It investigates the traditional ethical theories that are the foundation of bioethical discourse. The challenges posed by the ethics of feminism and multiculturalism will be mentioned in passing, and particularly in ch 5 below.
For more on the challenges posed by modern theory, see Doppelt 'Can traditional ethical theory meet the challenges of feminism, multiculturalism, and environmentalism?' (2002) 6 *The J Ethics* 383 – 405 and Callahan 'Principlism and communitarianism' (2003) 29 *British Med J* 287 – 291.

As with all forms of generalisation, in simplifying, a summary is an inadequate representation and may even be inaccurate, however, the aim here is not to present a comprehensive or even an introductory account of the traditions, but, rather, it is to present preliminary accounts of ethical decision-making.

2.3.1 Utilitarianism

Utilitarianism is a concept developed in the writings of Jeremy Bentham (1748 – 1832) and James Mill, and refined by John Stuart Mill (1806 – 1873);[43] although its origins are much earlier.[44]

John Stuart Mill adhered to the basic principles of the utilitarian philosophy of James Mill and Bentham, the chief principle of which is that goodness is whatever produces the greatest happiness for the greatest number.[45]

Utilitarianism is considered a consequence-based theory in that it examines the consequences of actions to determine whether the actions were good or bad.[46] Utilitarianism thus holds that actions are right or wrong according to the balance of their good and bad results.[47] An action is justified for utilitarians if it produces an increase in the general welfare of a large number of people. A central aspect of utilitarianism is the principle of utility as its sole measure and, therefore, the basic principle of ethics.[48]

Utilitarians may disagree as to which values or consequences should be maximised.[49] The principle of utility may ascribe happiness, freedom and health as the ultimate good. Whereas Bentham and Mill employ the term 'pleasure' in their definition of the greatest good, more contemporary utilitarians, such as G E Moore and James Griffin, list success, friendship, beauty, knowledge, health, personal autonomy, understanding and deep personal relationships as goods that should be fostered. [50]

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43 Beauchamp and Childress (n 5 above) 341.
44 Beauchamp and Steinbock (n 8 above) 13.
45 Grayling (2003) 174.
46 Grayling 177; Beauchamp and Steinbock 13; Gillon (1994) 21.
47 Beauchamp and Childress 340.
48 As above, 341.
49 As above; Gillon (n 46 above) 21; Grayling (n 45 above) 177.
50 As above.

John Stuart Mill's refinement of utilitarianism lies in the greater emphasis on individual liberty and autonomy. Individual autonomy is to be respected, even though the person acts against her own interest:[51]

> The only purpose for which power can be rightfully exercised over any member of a civilised community, against his will, is to prevent harm to others. His own good, either physical or moral, is not sufficient warrant. He cannot rightfully be compelled to do or forbear because it will be better for him to do so, because it will make him happier, because, in the opinion of others, to do so would be wise, or even right.

To the objection levelled against utilitarian philosophy to the effect that people desire many things other than happiness, John Mill responds that they are desired for their part in bringing happiness:[52]

> Whatever is desired otherwise than a means to some end beyond itself, and ultimately to happiness, is desired as itself a part of happiness and not desired for itself until it has become so.

Utilitarians disagree as well about whether the principle of utility should apply to particular acts in particular circumstances, or to general rules that determine which acts are right or wrong.[53] Rule utilitarians examine the consequences of adopting particular rules by determining whether a particular act conforms to a particular justified rule.[54] If the rule on which the act is based is justified, then that act serves the greater good even though the outcome in a particular case may not be for the best.[55] For example, if the general rule of telling the truth is regarded as a just rule, then, though following the rule has as its result in a particular case an unjust outcome, it should still be followed.[56]

Act utilitarians, on the other hand, focus on acts and not on general rules; using the principle of utility directly.[57] Their interest is in the particular circumstances of the particular action.[58] For example, a general rule, such as telling the truth, may not, in all circumstances, produce the best outcome.[59] Therefore, the underlying circumstances should be examined to find out whether the best outcome was achieved by the rule.[60]

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51 Mill (1864) (Robson (ed) (1984)) *On liberty* 1.
52 Mill (1864) (Crisp (ed) (1998)) *Utilitarianism* 2. Also see Grayling 179.
53 Beauchamp and Childress 343.
54 As above.
55 As above, 344.
56 As above.
57 As above.
58 As above.
59 As above, 344.
60 As above.

Beauchamp and Childress base a critique of utilitarianism on the problem of individuals who have 'immoral' or 'unacceptable' preferences. Thus, it is necessary to formulate an acceptable range of individual preferences.[61] In terms of utilitarianism, in the abstract, immoral acts could be justified if they achieve a good outcome.[62]

Further, it is felt that utilitarianism is too demanding of the individual, in that, in certain circumstances, the individual may be expected to commit acts of self-sacrifice to serve the greater good.[63]

A serious criticism is that inherent to utilitarian theory is the principle that the wishes of the majority override the interests of the minority.[64]

Nevertheless, utilitarianism makes a significant contribution to bioethical thought:[65] the principle of assessing satisfaction or utility and a concern with the consequences of a course of action so that good outcomes may be maximised are at the basis of the beneficence principle in bioethics.[66]

2.3.2 Kantianism

Through the consideration of aspects of an action other than its consequences (as is the case with utilitarianism) here is a moral theory which is deontological. The Prussian philosopher Immanuel Kant (1724 – 1804) is regarded as the father of this school of thought, which is referred to as Kantianism.[67]

Kant argues that morality is grounded in the faculty of reason, rather than seeking its origin in tradition, religion, intuition or emotion.[68] Human beings, according to Kant, are rational and able to make rational decisions.[69] The morality of an individual's action consists not in its outcomes, but on the moral acceptability of the rule or maxim according to which a person acts.[70] To be morally good, a person's action must arise from the realisation of the morally correct thing to do.[71] Kant thus holds that the 'right' (moral) action is justified by a person's intrinsic

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61 As above, 345 - 346.
62 As above. For example, to achieve a good outcome such as ending a war it would be considered justifiable to torture prisoners of war.
63 As above, 346.
64 As above, 347.
65 As above, 248.
66 As above, 348.
67 Beauchamp and Childress 348 – 349; Gillon (n 46 above) 16.
68 Beauchamp and Childress 349; Gillon 16.
69 Beauchamp and Childress 349.
70 As above.
71 As above.

values: we do the right thing because we have a moral obligation to do so, not because of an extrinsic motivation.

Kant's thought is opposed to the idea of utilitarianism and its consequentialism. Kant established a notion of the 'categorical imperative' in accordance with which the morality of actions is to be judged: 'Act only according to that maxim whereby you can at the same time will that it should become a universal law'.[72] There is a voluntary choice to act in a way we would want all others in similar situations to act,[73] so that actions done out of duty alone have moral worth.[74] Feelings, such as sympathy, are not therefore a source of moral behaviour.[75]

Central to Kantian ethics is the idea that people are ends in themselves; worthy of respect and dignity[76] '[p]ersons are ... not merely subjective ends ... but are objective ends, ie, exist as ends in themselves'.[77] In expanding upon this principle, he declares:[78]

> the ground of all practical legislation lies objectively in the rule and in the form of universality, which (according to the first principle) makes the rule capable of being a law (say for example a law of nature). Subjectively, however, the ground of all practical legislation lies in the end: but according to second principle) the subject of all ends is every rational being as an end in himself. From this there now follows the third practical principle of the will as the supreme condition of the will's conformity with universal practical reason, *viz*, the will of every rational being as a will that legislates universal law.

As rational agents, people have choices and make decisions.[79] Above all, they are prized for their dignity.[80]

> [M]an as a person—that is, as the subject of a morally practical reason, is exalted above all price. For as such a one (*homo noumenon*) he is not to be valued merely as a means to the ends of other people, or even to his own ends, but is to be prized as an end in himself. This is to say, he possesses a dignity (*an absolute inner worth*) whereby he exacts the respect of all other rational beings in the world, can measure himself against each member of his species, and can esteem himself on a footing of equality with them ...

The principle of the 'absolute inner worth' of human beings is the foundation for the requirement of informed consent in bioethics.[81] Kant defines autonomy this way:[82]

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72 Kant (1785)(transl Ellignton, 1994) 30.
73 Beauchamp and Steinbock 18 – 19; Gillon (n 46 above) 16 - 17.
74 Beauchamp and Steinbock 19.
75 As above.
76 As above, 20; Gillon 16.
77 Kant (n 72 above) 36.
78 Kant 38.
79 As above.
80 Kant (n 72 above) 7. My emphasis.
81 Beauchamp and Childress 351.

> Autonomy of the will is the property that the will has of being a law to itself. [Morality] is the relation of actions to the autonomy of the will [...] That action which is compatible with the autonomy of the will is permitted; that which is not compatible is forbidden.

Several contemporary philosophers have developed a Kantian account of ethics, such as Alan Donagan, Robert Nozick, Bernard Williams and, most notably, John Rawls.[83]

Nevertheless, Beauchamp and Childress criticise Kantian theory for being too abstract to be useful in deriving the specific ethical principles that are needed by professional ethics.[84] Kant's 'rationality' and 'humanity', in this view, are empty formulations, too flimsy to be the basis upon which a set of moral norms is determined, or a set of specific obligations is derived.[85]

Yet, Kant has contributed to ethical thought the principle that ethical and moral rules cannot apply unequally to different groups to suit the occasion. A moral rule gives rise to a certain action, and all groups need to be treated in the same way in terms of that action. For example, if informed consent is required for clinical research, one cannot dispense with the requirement despite dealing with a group from whom it is impossible to obtain consent.[86]

The following two contemporary theories – communitarianism and the ethics of care - may be regarded as a reaction to, and a criticism of, the traditional ethical theories which are relied upon by Beauchamp and Childress and which are considered the basis for bioethical thought.

2.3.3 Communitarianism

Communitarianism is a term applied to a group of contemporary philosophers who are in reaction against the emphasis on the individual as autonomous moral agent in utilitarian, Kantian and liberal philosophy.[87] Communitarians include philosophers and political theorists such as Michael Sandel,[88] Charles Taylor and Alasdair

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82 Kant 44.

83 Beauchamp and Childress (n 5 above) 351 – 352. For an excellent account of some of the main tenets of Kant's philosophy, also see Häyry (2005) 31 *J Med Ethics* 645.

84 Beauchamp and Childress 355.

85 As above; Gillon (n 46 above) 17.

86 As above. For instance where one carries out research on prison populations without their consent. See also ch 5 in this regard.

87 Beauchamp and Childress 365. See ch 4 below.

88 Sandel is responsible for the work *Liberalism and the limits of justice*, published in 1982.

MacIntyre[89] whose writings refer to the thought of philosophers such as Aristotle, Hume and Hegel.[90]

Utilitarianism and Kantian theories of ethics have at the centre of their inquiry the individual.[91] As indicated in the discussion above, the utilitarian strives for the realisation of the greatest happiness for the greatest number, but does so with reference to an individual conception of happiness.[92] Kantian theory disavows that the individual should be sacrificed to community interests.[93] The primacy that has been ascribed to the individual and to personal autonomy is challenged in communitarian-based ethics.

Communitarianism asserts that the individual arrives at moral action even in traditional ethical accounts, such as utilitarianism and Kantianism, only because of her adherence to communal values, social goals, conventions, traditions and loyalties.[94] According to the communitarian, the dimension of community, neglected in utilitarian, Kantian and liberal moral thinking, should be re-established. Callahan's view is representative of this way of thinking:[95]

> Communitarianism, as I construe the term, is meant to characterise a way of thinking about ethical problems, not to provide any formulas or rigid criteria for dealing with them. It assumes that human beings are social animals, not under any circumstances isolated individuals, and whose lives are lived out within deeply penetrating social, political, and cultural institutions and practices.

Callahan further comments that communitarianism assumes that no sharp distinction can be drawn between the public and the private sphere.[96] It is important that there be a private and protected sphere, but what counts as private will be a societal decision, not something inherent in the human condition.[97]

Communitarians reject the idea that there are universal, timeless ethical truths arrived at by the application of reason, and that these truths form the basis for ethical decision-making.[98] Instead, communitarians argue that our moral thinking has its roots in the history, values and traditions of particular communities;

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89 MacIntyre's work, *After virtue: A study in moral theory*, written in 1981, criticises Beauchamp and Childress' work on the ground that it searches for a foundation for ethical theory externally – in the philosophy of Kant and others - in a domain that transcends the variabilities of space and time (see Tong in Wolf (ed) (1996) 69).

90 As above, 69.

91 Beauchamp and Childress (n 5 above) 362.

92 Beauchamp and Steinbock (n 8 above) 21.

93 As above, 21.

94 Beauchamp and Childress 362.

95 Callahan (n 42 above) 288.

96 As above.

97 As above.

communities that are composed of people who share the same traditions, beliefs and values.[99] The shared values and traditions of the community offer the starting point from which ethical problems should be solved, and are critical of a theoretical or principled approach:[100]

> As these critics [communitarians] see it, principlism[101] is what its name implies: a prescription for bioethical reasoning that favors 'top-down' reasoning (from theories to principles to rules to particular moral judgments), even if it is also capable of 'bottom-up' reasoning (from particular moral judgements to rules to principles to ethical theories).

Communitarians, like utilitarians, want to advance the common good, but, whereas the utilitarian promotes the welfare of a collection of individuals, the communitarian seeks to promote the welfare of the shared values and ideals of a community.[102] The communitarian bioethicist asks, 'What is most conducive to a good society?' and not 'Is it harmful or does it violate autonomy?'[103]

Even though members of a community may have a different concept of what the ideal of a good society is, they have certain ideals in common.[104] For example, most of society's members share the value of a belief in the benefit of educating young people. The communitarian argues that the values that advance these benefits should be pursued actively by a community. In communitarian ethics, the needs of the community may take precedence over those of the individual.[105]

MacIntyre holds the view that the practices and traditions of local communities are primary above abstract ethical theory and normative thought.[106] For example, for MacIntyre, the virtues of the medical practitioner flow not from abstract ethical theories and codes, but from 'communal and institutional care, practical wisdom, and education'.[107] In this view the history and traditions of medicine require physicians to act in a certain way.[108]

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98 Beauchamp and Steinbock (n 8 above) 21.
99 As above.
100 Tong in Wolf (n 89 above) 69.
101 'Principlism' is the term used to refer to Beauchamp and Childress' four principles-approach.
102 As above.
103 Callahan (1990) 105 - 113, quoted in Beauchamp and Childress 367.
104 Beauchamp and Childress 367.
105 As above.
106 Beauchamp and Childress 366.
107 As above.
108 As above.

Many philosophers regard the communitarian rejection of classical ethical theories as unjustified, arising out of an erroneous interpretation of these theories.[109] Beauchamp and Childress point out that the communitarian establishes two false dichotomies in a zero sum game: the first is the primacy of either the individual or the community; and, the second, is the protection of either the autonomous individual in decision-making or of a communal determination of social goals against the individual.[110] The dichotomy is a false one in that the choice does not lie in the elimination of the alternative, as Beauchamp and Childress explain: [111]

> A more accurate picture is that we inherit social roles and goals. We then critique, adjust, and attempt to improve our beliefs over time through free discussion and collective agreements. Individuals and groups alike progressively interpret, revise, and sometimes even replace traditions with new conceptions that adjust and foster community values.

2.3.4 Ethics of care

Proponents of the ethics of care (care ethics), as well as sharing communitarian questioning of the values of liberal individualism,[112] emphasise traits valued in personal relations, such as sympathy, compassion, fidelity and love:[113]

> Ethics-of-care writers argue that real people live in families and that real caring relationships are not impartial, impersonal, or equal. Instead, they embody fundamental inequalities of power, capacity, judgment, information, and responsibility. Moreover, such relationships are based on a particular connection between those involved — which implies that any one person cannot and should not care for all human beings equally. These writers argue that philosophy has ignored family life in particular, and caring in general, because it has been written mainly by men who do not fully understand, or take seriously enough, the centrality of such relationships to human experience.

The ethics of care is contrasted to an ethics of rights and obligations,[114] in such a way that it undermines a notion of a universal ethical principle, as well as that the analysis of the greater good is the consequence of impartial decision-making principles. [115]

A theorist who writes form the point of view of an ethics of care is Annette Baier. Baier finds in contemporary female philosophers a voice that is 'reflective and

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109 As above, 368.
110 As above.
111 As above.
112 As above, 369.
113 Roberts and Reich (2002) 359 *The Lancet* 1057.
114 Beauchamp and Childress 369.
115 As above, 370.

philosophical'.[116] Baier rejects the notion expressed in traditional ethical theories that emphasises universal principles and uses a Kantian contractarian model to emphasise justice, rights and law.[117] She asserts that traditional ethical theories do not take into account an ethic of love and mutual trust.[118] Baier asks,[119]

> [w]hat would be a suitable central question, principle, or concept, to structure a moral theory which might accommodate those moral insights women tend to have more readily than men, and to answer those moral questions which, it seems, worry women more than men?

Central to Baier's thought is the idea that women cannot fit their moral experience into a conception of morality based exclusively upon obligation and contract.[120] Women's life experiences are often characterized by their caring relations with those who are less powerful and highly dependent, such as relationships with children and the sick and the dying.[121] When individuals are highly dependent, their relations with others on whom they depend for care are often non-voluntary and thus they require something from their caregivers other than a contractual agreement.[122]

Classical liberal theories which rest on impartiality of judgment, thus, are challenged by these theorists, for their neglect of the partiality that care ethicists claim for our relationships with others, such as in the relations with the doctor, nurse or friend.[123]

Care ethicists argue that the liberal focus on fairness leads to the neglect of morality and that universal principles can be irrelevant and constrictive.[124] This amounts to an argument that each situation which confronts the medical practitioner or researcher calls for a response beyond generalised moral norms and principles.[125]

The ethics of care is in favour of the idea of a mutual interdependence and, therefore, emotional responsiveness. Mutually interdependent relations (such as those between a medical practitioner and patient; researcher and research participant) demand a response which does not reflect a detached respect for that person's rights, but responsibility and empathy.[126] In opposition to theories based on

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116 As above.
117 As above, 371.
118 As above.
119 Baier (1985) 19 *Nous* 55.
120 Peter and Morgan (2001) 8 *Nursing Enquiry* 5.
121 As above.
122 As above.
123 Beauchamp and Childress 371 - 372.
124 As above.
125 373.
126 As above.

reason and through the emphasis on emotion, the ethics of care points out that a moral life also has an emotional dimension alongside the cognitive, with the stress on an 'engaged and contextual moral thinking'.[127] This, they claim, other forms of ethical thinking lack because obligation rather than sympathy is central to their thought.[128]

The discussion above is but a brief account of the philosophical foundation underlying biomedical ethics. Below we turn to the principles of biomedical ethics.

2.4 Principles

Beauchamp and Childress hold that the 'common morality' expresses a set of moral norms, including principles that are basic to bioethics.[129] The principles of bioethics (responsible for the name 'principlism') were introduced by Beauchamp and Childress with the aim of reconciling the divergence between utilitarian and deontological models of thought. These principles underpin ethical theory in some form[130] and function as a guideline for bioethics.[131] They are intended to link moral decision-making to 'mid-level' principles rather than to universal rules (such as those espoused by Kant and Mill).

Although the principles are too general in quality to address the particulars of diverse circumstances, at least they can provide a starting point for moral judgement. These principles are outlined below.[132]

2.4.1 Respect for persons

By implication, respect for persons is respect for autonomy; or that people who are capable of doing so make their own decisions.[133] Clearly, individuals need the

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127 374 - 375.

128 On care ethics, also see Marian A Verkerk 'The care perspective and autonomy' (2001) 4 *Med, Health Care and Philosophy* 289.

129 Beauchamp and Childress, 12.

130 Callahan (n 103) comments that the attraction of what he calls 'principlism' (the three principles) lies in the following:
'But these theories [utilitarianism, Kantianism, etc] turned out to be too broad and cumbersome to be useful for clinical decision making or policy formation. Principlism, as a middle level approach, seemed much more helpful and more attuned to different kinds of ethical problems. It seemed to have a special appeal to physicians not too interested in ethical theory, but in need of a way of thinking through their ethical dilemmas'.

131 Beauchamp and Childress 374.

132 For a criticism of 'principlism', see ch 5 below.

133 Smith (1999) 6.

information that enables them to make informed decisions.[134] Beauchamp and Childress indicate that respect for autonomy is an acknowledgement not only of another person's right to hold views and to make choices, but also that their actions are based on personal values and beliefs.[135]

In a research environment, what this recognition means is that a participant will enter studies only after they have been provided with adequate information and have freely given their informed consent.[136] Respect for persons implies that those unable to make autonomous decisions, such as the very young, the mentally ill and others, should be protected.[137]

This principle originates in the philosophy of Kant (among others), who asserts that that respect for persons flows from a recognition that all persons have unconditional worth.[138] John Stuart Mill supports the argument that there is a moral obligation to respect the autonomy of human beings on the utilitarian grounds that such respect increases human welfare except when they do harm to others.[139] He asserts the centrality of the principle to his thinking:[140]

> The object of this Essay is to assert one very simple principle, as entitled to govern absolutely the dealings of society with the individual in the way of compulsion and control ... That principle is, that the sole end for which mankind are warranted, individually or collectively, in interfering with the liberty of action of any of their number, is self-protection. That the only purpose for which power can rightfully be exercised over and member of a civilised community, against his will, is to prevent harm to others. Hic own good, either physical or moral, is not sufficient warrant.

2.4.2 Beneficence

Beneficence (or nonmaleficence) defines an obligation to improve the state of well-being of others and to do them no harm.[141] This principle arises from the maxim '*primum non nocere*', or 'first, do no harm'.[142] Philosophers have long debated whether the obligation not to do harm is as important as the obligation to benefit or to do what is good.[143]

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134 Smith 6; Beauchamp and Childress 63.
135 As above, 63.
136 Smith (n 133 above) 6.
137 As above.
138 Beauchamp and Childress 63. See also Gillon (n 46 above) 63 – 64 where which he presents Kant's argument in favour of respecting autonomy.
139 Gillon 64 – 65.
140 Mill 'On liberty' (n 51 above).
141 Smith 7; Gillon (n 46 above) 73 – 76, 80; Beauchamp and Childress (n 5 above) 113.
142 Beauchamp and Childress 114.
143 Eg Foot, quoted by Gillon 81: 'other things being equal, the obligation not to harm people is more stringent that the obligation to benefit people'.

In a research context the principle is an assurance that the risks to the research participant do not outweigh the possible benefits gained by the research.[144] Important areas in which the principle is to be considered relate to the decision to withdraw or withhold life-sustaining treatment and to physician-assisted suicide.[145] The prohibition on the use of placebos, if an effective treatment exists, stems from this principle.[146]

2.4.3 Justice

The term 'justice' refers to the obligation to treat everyone justly, in accordance with what is that person's due, and with what is reasonable and fair.[147]

Several philosophers have proposed ways in which social goods in society, such as access to health care, should be distributed. Utilitarianism, for example, aims to maximise public utility.[148] In these proposals the term 'distributive justice' is used, and a distinction is made between formal and material principles of justice.[149]

Justice involves decision-making about the allocation of scarce medical resources.[150] In a research setting the principle of justice takes into account fair access to participation in trials, as well as the access of the research population to the benefits of research.[151]

2.5 Conclusion

Ethical discourse is about the use of terms such as 'virtue', 'obligation', 'justification', 'morality', 'permissible action', and so on. A set of ethical principles is the foundation for an individual or group to believe that they have an obligation either to do or not to do something. Such an obligation stems from a perception that it is binding upon them. Many of the terms that are used in the context in which they are used may be unfamiliar to those whose discourse is rights-based.[152]

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144 Smith (n 133 above) 7; Gillon 83 - 84.

145 As above. For a detailed discussion on these implications, see Beauchamp and Childress 113 – 157. Beauchamp and Childress also criticise the conflating of beneficence and nonmaleficence. See 114.

146 See para 4.2.2 below.

147 Smith 7; Gillon 86 – 89; Beauchamp and Childress 226.

148 Beauchamp and Childress 230.

149 See Beachamp and Childress 226 – 229 and Gillon 86 - 91.

150 For a comprehensive discussion, see Gillon 93 – 98.

151 Smith 7. See para 4.3.3 below.

152 See ch 4 for a more detailed discussion on the differences and commonalities between ethics and legal rights.

These principles of bioethics (which express essential aspects of ethical theories, including utilitarianism, Kantian ethics, liberalism) are intended to aid in the process of reasoning about bioethical problems. The process in this case is a deductive (or top-down) approach; that is, the four general principles of bioethics are applied to specific, practical problems.[153] Bioethicists apply the abstract principles to practical problems in order to arrive at an ethically 'correct' decision in a practical situation. This reliance on principles by bioethicists has led to the term 'principlism' being applied by various writers to their theory and methodology.

Beauchamp and Childress claim that the validity of the four bioethical principles is grounded in what they call 'common morality' - an undefined and quite elusive term.[154] They support a 'universal core of morality' to be distinguished from *community-specific* morality, which includes moral norms deriving from 'particular cultural, religious, and institutional sources'.[155] An important implication of the accepted universality of common morality is that Beauchamp and Childress's bioethical principles are (in theory) applicable to clinical research conducted anywhere in the world.[156]

In addition, a degree of *indeterminacy* is incorporated into Beauchamp and Childress's bioethical model: their bioethical principles are very general and abstract in nature. They express no *exact content* that may lead to *specific* moral judgments and courses of action:[157]

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153 Also responsible for the term 'applied' ethics: 'Justification occurs if and only if general principles and rules, together with the relevant facts of a situation, support an inference to the *correct or justified judgment*' (Beauchamp and Childress (n 5 above) 178). My emphasis.
The deductive model of bioethics is rivalled by the *casuistic* model. This model advocates a case-by-case evaluation of bioethical problems. It is a *bottom-up* approach that accepts that the primacy of practical decision-making is based on precedent *and* common moral judgments. Casuists maintain that the very matrix of general principles and rules (ie the conceptual framework of the deductive model) is created out of moral judgments that can only be made through an initial stage of moral reasoning over the specific, and not the general; that is, through induction, and not deduction. General moral rules can be fully understood only in terms of the paradigmatic cases which define their meaning. For an explication of the precepts and limits of casuistic model, see Beauchamp and Childress (n 5 above) 391 - 397. Also see Arras 'Getting down to cases: The revival of casuistry' in Jecker *et al* (eds) (1997) *Bioethics: An Introduction to the History, Methods, and Practice* 175 - 183.

154 See para 2.2 above; 'common morality' is defined as 'the set of norms that all morally serious persons share ... and [which] bind[s] all persons in all places' (Beauchamp and Childress 11).

155 Beauchamp and Childress 11.

156 As above.

157 Plomer (2005) 12.

> Principles may have a fairly determinate and undisputed meaning in core areas, but the precise interpretation and scope of application of the principles at the boundaries or in disputed contexts may be indeterminate and uncertain, particularly when the principle is divorced from its theoretical origins.

Bioethical principles (and the respective rules) have to be contextualised, or *specified*, and their relative weight and strengths must be *balanced* when their combined contents prove antagonistic.[158]

In the following paragraphs, the crystallisation of ethical principles into guidelines and documents will be analysed.

3 ETHICAL GUIDELINES AND DOCUMENTS

3.1 Introduction

The three fundamental ethical principles outlined above, namely, respect for persons, beneficence and justice, as the foundation of a research or bioethics, are embodied in the various international and domestic ethical guidelines and documents. In the following pages, international documents, such as the Nuremberg Code, the Council for International Organizations of Medical Sciences' International Ethical Guidelines for Biomedical Research involving Human Subjects, the Belmont Report and the Declaration of Helsinki are scrutinised; as well as domestic documents, such as the Medical Research Council's Guidelines on Ethics for Medical Research of 2004 and the objectives of research ethics review committees in South Africa. The discussion remains at a general level, laying the foundation for more details in Chapter 5 below.

3.2 International codes of ethics

3.2.1 Nuremberg Code

The Nuremberg Code, written in 1946 as the final part of the judgment in the Nuremberg trials,[159] is the first comprehensive set of guidelines on how to conduct

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158 Beauchamp and Childress 17 - 19.

159 The Nuremberg trials include the trials of the doctors responsible for some of the inhumane experiments conducted at the orders of the Nationalist Socialist German Government during World War II. The judges at the Nuremberg Tribunal provided a list of requirements for doctors conducting experimental research, now known as the Nuremberg Code. This list prescribes the conduct of physicians holding them to a minimum standard of ethical behaviour as required by universal moral, ethical and legal concepts, the violation of which would bring down upon them the condemnation of society (in this regard, see Levine (n 1 above) 425).

ethical research on humans.[160] The Nuremberg Code is a consequence of the outrage that was felt at the conduct of doctors under National Socialism in Germany, who, in the guise of science, performed cruel and inhuman medical experiments on German and non-German nationals, including Jewish and other 'asocial'[161] people during the Second World War.[162] The Nuremberg criminal trials were aimed at holding specific individuals accountable for their barbarous acts against humanity; and recording the acts committed into history.[163]

The Nuremberg Code contains ten principles.[164] The first principle is an acknowledgement that the voluntary consent of human participants is absolutely essential.[165] The Code recognises that human experimentation, if conducted ethically, is valuable in generating knowledge that cannot be obtained by any other means, but forbids research that is random and unnecessary in nature.[166] Furthermore, unnecessary risk and harm should be avoided,[167] and the risk taken should not outweigh the possible benefits of the research.[168] Investigators should be qualified to conduct the research,[169] and be prepared to terminate the research project at any time if it should become clear that harm or injury is being suffered or may be suffered by the research participant.[170] The research participant may withdraw at any time from the experiment.[171]

3.2.2 Declaration of Helsinki

The World Medical Association's (WMA)[172] Declaration of Helsinki is an international code of ethics overseeing biomedical research involving human participants that is

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160 Levine 425; Foster (n 6 above) 141. The Code deals with non-therapeutic research only (ie research that does not investigate an illness or condition from which the participants suffer).

161 For example, prisoners, Jewish people and people undergoing treatment for psychiatric illnesses.

162 As above.

163 See Taylor in Mann *et al* (eds) (1999) 284 – 285.

164 For commentary on the legal / ethical force of the Nuremberg Code, see para 4.2 of ch 5 below.

165 Nuremberg Code, reprinted in Levine (n 1 above) 425 - 426.

166 Art 2 Nuremberg Code.

167 Art 3 Nuremberg Code.

168 Art 6 Nuremberg Code.

169 Art 8 Nuremberg Code.

170 Art 10 Nuremberg Code.

171 Art 9 Nuremberg Code.

172 The WMA was created in September of 1947. It was inspired by the events at the Nuremberg trials, and consists of a large group of private physicians who gathered to establish an international association, the World Medical Association. The WMA's primary focus is on global issues confronting physicians. It was created to ensure the

framed to govern the status and behaviour pf physicians. The Declaration of Helsinki was adopted by the WMA's 18th Assembly, held in Helsinki, Finland, in 1964, and has been revised several times, most recently in October 2000.[173]

The Declaration of Helsinki represents the efforts of the WMA to develop an international consensus on the ethics of medical research involving humans, and is a guide for physicians involved in research on humans. It consists of three sections, namely, I Basic Principles; II Medical Research Combined with Professional Care; and III Non-therapeutic Biomedical Research involving human subjects (non-clinical biomedical research). Significantly, unlike the Nuremberg Code, the Declaration of Helsinki distinguishes clinical (therapeutic) from non-clinical (non-therapeutic) research.[174]

The first section, 'Basic principles', establishes that research on humans should conform to generally accepted scientific principles, and that it must be based on adequately performed animal experimentation and a thorough knowledge of the literature.[175] The research protocol should be reviewed by an independent committee;[176] the responsibility for the human participant rests with the investigator;[177] the risk and the importance of the possible benefits must be in proportion;[178] the interests of the research participant should always prevail over those of society;[179] the research participant's free informed consent should be obtained;[180] and the research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles are complied with.[181]

The second section focuses on clinical research, and states that the new method that is being tested should be more advantageous than the current

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'independence of physicians, and to work for the highest possible standards of ethical behavior and care by physicians ...' (see WMA Policy <http://www.wma.net/e/about.html> (15 December 2006). Since its inception the WMA has actively participated in the international community to protect the interests of physicians and to promote its own ideals in shaping public health policy through information gathering and dissemination in the international health arena.

173 Levine 427. 'Clarifications' have also been added to the 2000 revision, accepted in October 2002.

174 See ch 5 below.

175 Art I.1 Declaration of Helsinki.

176 Art I.2 Declaration of Helsinki.

177 Art I.3 Declaration of Helsinki.

178 Art I.4 Declaration of Helsinki.

179 Art I.5 Declaration of Helsinki.

180 Art I.9 Declaration of Helsinki.

181 Art I.12 Declaration of Helsinki.

method;[182] the control group should be assured of the best proven diagnostic and therapeutic method;[183] and the refusal of the patient to participate should never interfere with the doctor-patient relationship.[184]

The third section focuses on nonclinical research, and stresses that the researcher should remain the "protector of the health and life" of research participants;[185] participants should be volunteers;[186] the research should be discontinued if harmful;[187] and the interests of society should never take precedence over the well-being of the participant.[188]

3.2.3 Belmont Report

The American National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research[189] in 1979 published the Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (Belmont Report).[190]

The National Commission felt that the Nuremberg Code and subsequent ethical codes were inadequate to cover complex situations and that they often conflicted with each other.[191] The purpose of the Belmont Report was to identify broader ethical principles to provide 'a basis on which specific rules could be formulated, criticised, and interpreted'.[192]

The Belmont Report summarises the ethical principles that are fundamental to the specific ethical rules formulated in documents such as the Nuremberg Code: respect for persons, beneficence and justice.[193] The Belmont Report is divided into three sections, namely, Section A: Boundaries between Practice and Research; B:

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182 Art II.2 Declaration of Helsinki.
183 Art II.3 Declaration of Helsinki.
184 Art II.4 Declaration of Helsinki.
185 Art III.1 Declaration of Helsinki.
186 Art III.2 Declaration of Helsinki.
187 Art III.3 Declaration of Helsinki.
188 Art III.4 Declaration of Helsinki.
189 The American National Commission was established in 1974 by the National Research Act (Levine (n 1 above) 15). The Act established the National Commission as advisory to the US Department of Health, Education and Welfare and stipulated that it was to be replaced by a long-term National Advisory Council (see Grady (1995) 41). Between 1975 and 1979 the National Commission published numerous reports, one of which was the Belmont Report (Grady 41).
190 FR Doc 79-12065 (filed 17 March 1979); <http://ohrps.osophs.dhhs.gov/humansubjects/guidance/belmont.htm> (4 March 2004).
191 Grady (n 189 above) 42.
192 As above.

Basic Ethical Principles; and C: Applications. In Section B, the Report lists and discusses the three principles that underlie ethical decision-making in research on human participants: respect for persons, beneficence, and justice, and provides a conceptual framework to these principles.[194]

3.2.4 International Ethical Guidelines for Biomedical Research involving Human Participants

The Council for International Organizations of Medical Sciences (CIOMS)[195] in conjunction with the World Medical Association (WMA) published its International Ethical Guidelines for Biomedical research involving Human Subjects (CIOMS guidelines) in 1982, and has updated these guidelines in 1993 and 2002.[196]

The 21 CIOMS guidelines are extensive in scope, and issues discussed range from the ethical justification and scientific validity of research,[197] ethical review,[198] informed consent,[199] benefits and risks of study participation,[200] vulnerable individuals and groups,[201] children and women as research participants,[202] equity regarding burdens and benefits,[203] choice of control in trials,[204] confidentiality,[205] compensation for injury,[206] strengthening of international and local capacity for ethical review,[207] and the obligations of sponsors to provide health-care service.[208]

The CIOMS guidelines are more comprehensive than the Declaration of Helsinki, and, for the first time, express an awareness of problems related to

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193 Levine 12; Smith 5; Grady 42.

194 Levine 12.

195 The Council for International Organizations of Medical Sciences (CIOMS) is an international, nongovernmental organization established by the WHO and UNESCO in 1949.
The main objectives of CIOMS are to promote international biomedical activities, serve the scientific interests of the international biomedical community, and maintain relations with the WHO and the United Nations. While CIOMS does not have the power to make binding regulations, it does have the ability report to the WHO and to influence decisions made by the WHO (see 'What is CIOMS?' <http://www.cioms.ch/frame_what_is_cioms.htm> (16 December 2006).

196 Levine (n 1 above) 12.

197 Guideline 1 CIOMS guidelines.

198 Guideline 2 & 3 CIOMS guidelines.

199 Guideline 4 – 7 CIOMS guidelines.

200 Guideline 8 & 9 CIOMS guidelines.

201 Guideline 13 CIOMS guidelines.

202 Guideline 14 – 16 CIOMS guidelines.

203 Guideline 12 CIOMS guidelines.

204 Guideline 11 CIOMS guidelines.

205 Guideline 18 CIOMS guidelines.

206 Guideline 19 CIOMS guidelines.

207 Guideline 20 CIOMS guidelines.

research in developing countries. Also, the Guidelines show a concern for the obligations of sponsors in developed countries to provide health care services to their research populations in poor, developing countries.

3.3 Domestic codes of ethics

3.3.1 Introduction

A number of codes of ethics governing biomedical research on human participants exist in South Africa.[209] These are the Medical Research Council's (MRC)[210] Guidelines on ethics for medical research, the Department of Health's Guidelines for good practice in the conduct of clinical trials in human participants in South Africa and, specifically relevant to HIV and AIDS-related research, Ethical considerations for HIV/AIDS clinical and epidemiological research, also issued by the Department of Health. These documents are outlined below, following which the nature and functions of the different research ethics committees in the country are examined.

3.3.2 MRC Guidelines on ethics for medical research

The MRC Guidelines on ethics for medical research (MRC Guidelines),[211] one of the most important codifications of research ethics in South Africa,[212] is issued in terms of section 17(1) and 17(2) of the Medical Research Council Act.[213] Section 17(1) of the Act determines that the MRC Board must regulate and control research on or experimentation upon humans. Section 17(2) empowers the Board to determine ethical directives to be followed in research and experimentation, and to take the necessary steps to enforce the ethical directives.

The MRC Guidelines govern all research carried out by or on behalf of the MRC, and research funded by the MRC, and approved by its ethics committee.[214] Ferdinand Van Oosten is of the opinion that the MRC Guidelines are to be followed

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208 Guideline 21 CIOMS guidelines.

209 Discussed in ch 4 below.

210 The South African Medical Research Council (MRC) was established in terms of two Acts of Parliament (19 of 1969 and 58 of 1991). Its most important functions were defined as promoting 'the improvement of the health and the quality of life of the population of the Republic and to perform other such functions as may be assigned to the MRC by or under this Act'. Such improvement was to be attained 'through research, development and technology transfer'. See also <http://www.mrc.ac.za/history/general.htm> (15 December 2006).

211 4th (revised) edition published in 2004, previous editions are those of 1977, 1987, and 1993.

212 Van Oosten (2000) 63 *J Contemporary Roman Dutch L* 5 7.

213 Act 58 of 1991.

also by other research institutions, if that particular body does not have its own ethical guidelines in place.[215]

The fourth edition of the MRC Guidelines was published recently. There are five books in the revised series:[216] Book 1, entitled Guidelines on Ethics for Medical Research: General Principles; Book 2, entitled Guidelines on Ethics for Medical Research: Reproductive Biology and Genetic Research; Book 3, entitled Guidelines on Ethics for Medical Research: Use of Animals in Research; Book 4, entitled Guidelines on Ethics for Medical Research: Use of Biohazards and Radiation; and, finally, Book 5, entitled, Guidelines on Ethics for Medical Research: HIV Vaccine Trials.

Book 1 of the MRC Guidelines sets out the reasons for the revised publication. In the Preface it is stressed that in the 4th edition the MRC Ethics Committee has decided that the guidelines must have a South African emphasis, and that the individual's dignity and the importance of informed consent is to be strongly highlighted, as informed consent is entrenched in the Bill of Rights.[217] The argument that developing communities must not be exploited and the view that participating communities must benefit from research done on or with them are foregrounded.[218]

Book 1 of the MRC Guidelines consists of twelve guidelines and deals with issues such as the medical justification for research;[219] the legal and moral justification for research (which includes an extensive section on consent);[220] the way in which research ought to be conducted.[221] As such, it includes a large section on research participants;[222] ethical issues in qualitative research;[223] the assessment of ethics in research;[224] the monitoring of research;[225] international collaboration in research;[226] and, finally, ethical guidelines for epidemiology.[227]

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214 Van Oosten (n 212 above) 7.

215 Van Oosten 9. He bases his opinion on the fact that the MRC is a national research institution and the fact that the MRC Guidelines have statutory authority.

216 The reason for splitting the previous single volume into five sections is explained in the Foreword the Book 1 – five different editions will make the task of future revising and updating the Guidelines considerably easier. Also, researchers with specific interests will be able to access a single volume that relates to their interests.

217 MRC Guidelines 5.

218 As above.

219 Guideline 4.

220 Guideline 5.

221 Guideline 6.

222 Guideline 7.

223 Guideline 8.

224 Guideline 9.

225 Guideline 10.

226 Guideline 11.

227 Guideline 12.

3.3.3 Guidelines for good practice in the conduct of clinical trials on human participants in South Africa

The Department of Health (DH) issued the Guidelines for good practice in the conduct of clinical trials in human participants in South Africa (Good practice guidelines) in September 2000. The Preamble to the Good practice guidelines states that they are aimed at providing 'South Africa with clearly articulated standards of good clinical practice in research that are also relevant to local realities and contexts'.[228] Although the Good practice guidelines purport to be applicable to both academic and contract research in South Africa, it is important to remember that they have no statutory power, unlike the MRC's that are issued in accordance with a statute.[229]

The Good practice guidelines are contained in nine chapters. An introduction, which discusses the reasons for and scope of the guidelines, is followed by an explanation of the role of bodies such as the ethics committee during ethical review. This, in turn, leads to an examination of the protection of study participants,[230] the responsibility of the principle investigator and participating investigators,[231] the responsibilities of the sponsor[232] and quality assurance,[233] data management and statistics,[234] multi-centre studies[235] and ethics committees.[236] Guideline 9 is of particular importance to the current study, as it focuses on ethical considerations for HIV/AIDS clinical and epidemiological research. This guideline is discussed in detail below.

3.3.4 Ethical considerations for HIV/AIDS clinical and epidemiological research

Ethical considerations for HIV/AIDS clinical and epidemiological research (HIV/AIDS research guidelines) was issued by the DH in 2002, with the view to complementing the MRC guidelines with respect to research related to HIV and AIDS.[237] It is

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228 Preamble, Good practice guidelines.
229 See 3.2.2 above.
230 Guideline 2.
231 Guideline 3.
232 Guideline 4.
233 Guideline 5.
234 Guideline 6.
235 Guideline 7.
236 Guideline 8.
237 Preamble, HIV/AIDS research guidelines.

published as guideline 9 of the Department's Good practice guidelines.[238] According to the introduction, the HIV/AIDS research guidelines emanate out of a series of consultations held by the Task Group on Ethical Guidelines for HIV research.[239] The HIV/AIDS research guidelines do not deal specifically with HIV vaccine trials, as the challenges posed by this type of research are to be dealt with in a later document.[240]

After providing a brief background which emphasises that South Africa is a middle income country reflecting severe economic disparities and that the majority of its population is of a low socio-economic status, the authors of the HIV/AIDS research guidelines explain why conditions in South Africa are so favourable for conducting HIV and AIDS-related clinical research. Apart from the rapid proliferation of an HIV/AIDS epidemic, South Africa offers clinical and scientific expertise, academic institutions of good standing, good laboratory and clinical facilities and an industrial country's infrastructure. It also has high standards in communications and other relevant technologies.[241] The authors further reiterate the importance of conducting HIV and AIDS-related clinical research, because the information that is gained could have critical implications for South Africa and the rest of the world.

The HIV/AIDS research guidelines highlight ethical issues in HIV and AIDS-related clinical research in South Africa. Among the issues elaborated are that research should be appropriate to South Africa,[242] high research and ethical standards should be applied when research is conducted in vulnerable and non-vulnerable communities,[243] during HIV-related drug trials there should be a consciousness that trials are often the only way in which HIV positive persons are able to access expensive antiretroviral medication and this could compromise their ability to give informed consent, and that efforts should be made to increase the autonomy of research participants in this setting.[244]

The need for placebo-controlled trials is discussed, and the authors of the HIV/AIDS research guidelines comment that it may be justifiable to use placebo-controlled trials in communities where there is no access to the medications that are standard care in resource-rich settings.[245]

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238 See above.
239 Introduction, Guideline 9.
240 Introduction, Guideline 9.
241 Para 9.1 Introduction, Guideline 9.
242 Para 9.2.1.
243 Para 9.2.2.
244 Para 9.3.1. This issue is discussed in ch 5 below.
245 Para 9.3.2. For a detailed discussion on this ethical dilemma, see para 4 below.

Because HIV and AIDS-related clinical research and drug trials could cause short and long term ill effects, the patient information section of the informed consent document should specify what action is to be taken in the event that the study drug or drugs are withdrawn as a consequence of the side effects. The HIV and AIDS research guidelines recommend that in those circumstances appropriate therapy that is required to manage the adverse drug effects should be made available to participants. This therapy should be made available within the study framework and at no cost to the patient, unless exceptions have been agreed upon by all parties. [246]

If a patient withdraws from a study, or upon completion of a study, patients should be advised about the ongoing management of their condition. Ongoing therapy should be according to the local standard of care. Costs of this care should be borne by the local health service, the patient's medical insurance or the patients themselves.[247]

The HIV/AIDS guidelines further stipulate that, because many patients who participate in HIV and AIDS treatment trials have no alternative access to drug therapy, in cases where a patient has a therapeutic response to a study drug, that patient should be offered ongoing treatment. In designing studies, consideration should be given to the costs of long-term provision of study drugs and of clinical monitoring, including the costs of medical staff. The duration of drug therapy in a study should be clearly stated in the patient information section of the informed consent document.[248]

Next, the HIV/AIDS guidelines discuss HIV testing. Situations in which it is necessary to carry out HIV testing are outlined,[249] and the HIV/AIDS research guidelines acknowledge that HIV testing has important implications and consequences for the individual. The guidelines stress that informing individuals that they are HIV positive has an impact on their quality of life and that it should be considered a major intervention.[250] The HIV/AIDS research guidelines outline the ethics of confidential HIV testing[251] and deal with issues such as unlinked anonymous testing[252] and linked anonymous testing.[253]

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246 Para 9.3.3.
247 Para 9.3.4.
248 Para 9.3.5.
249 Para 9.4.
250 Para 9.4.
251 Para 9.4.1
252 Para 9.4.2.

Furthermore, population-based studies to prevent HIV transmission,[254] the difficulty of obtaining informed consent in populations where literacy levels are low,[255] incentives offered to research participants to take part in a trial,[256] and issues relating to the researcher herself, such as incentives that may influence the objectivity of the researcher,[257] and the release and implementation of research results[258] are other topics that are dealt with. Finally, the HIV/AIDS guidelines deal briefly with HIV vaccine research,[259] the involvement of people living with the virus[260] and the need to give special consideration to subgroups in society, such as women, children and prisoners, when conducting HIV and AIDS research.[261]

3.3.5 Research ethics committees

The 1970s witnessed the birth of the research ethics committee (REC), or, as it is called overseas, the institutional review board.[262] RECs are set up to oversee the ethical conduct of clinical research and they are the primary mechanisms intended to protect the interests of research participants. Lisa Eckenwiler writes as follows about the role of RECs:[263]

> Institutional review boards (IRBs) represent a particular approach to answering to people – the public generally, research participants more directly – in terms of responsibilities that have come to be recognised within the research community. Their efforts, indeed, can be understood as a special case of an important move made in moral life: reasoning about the interests of others in coming to conclusions about what is ethically acceptable.

Guideline 9 of the MRC Guidelines requires that all research involving healthy volunteers and patients must be subject to independent ethical review and that this should be conducted by a REC.[264]

Guideline 6.1.9 of the MRC Guidelines sets out the objectives of RECs. They are to:

- maintain ethical standards of practice in research;

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253 Para 9.4.3.
254 Para 9.5.
255 Para 9.6.
256 As above.
257 Para 9.7.1.
258 Para 9.7.2.
259 Para 9.8. See ch 5 below for a detailed discussion of this paragraph of the HIV/AIDS research guidelines.
260 Para 9.9.
261 Para 9.10.
262 Often abbreviated as IRB.
263 Eckenwiler (2001) 11 *Kennedy Institute Ethics J* 37.
264 Guideline 9.1 MRC Guidelines.

- protect research participants and investigators from harm or exploitation;
- preserve the research participant's rights over society's rights; and
- provide reassurance to society that this is being done.

Two principles guide the appointment of members of RECs:[265]

- Committees should command the technical competence and judgment to reconcile the physical and psychological consequences of participation with both the welfare of the research participants and the objectives of an investigation.[266]
- Committees should accommodate lay opinion in a manner that provides effective representation of the non-clinical community as well as clinical interests. Lay opinion includes representation by a lawyer, social worker, religious leader, teacher or similar person of standing able to contend with pressures from individuals within the broad health profession.[267]

Two kinds of RECs function in South Africa.[268] They are the Ethics Committee of the MRC and the ethics committees at various universities and other bodies.[269]

a) The ethics committee of the MRC

Sections 17(1) and 17(2) of the South African Medical Research Council Act[270] empower the Board of the MRC to issue ethical directives which must be followed during research and experimentation on or with humans, animals, human or animal material, and which is performed by its employees and by persons performing research or experimentation for or on behalf of the MRC, or with research funding of the MRC.[271]

b) Other ethics committees

Apart from the MRC's Research Ethics Committee, ethics committees are in place at various academic and other institutions where research is conducted. For instance, the medical faculties of the universities in South Africa each has its own ethics committee. Van Oosten submits that if research is carried out under the auspices of other RECs, such as research conducted at the different universities, and no ethical

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265 Guideline 9.9.1.
266 Guideline 9.9.1.1(i).
267 Guidelne 9.9.1.1(ii).
268 Van Oosten (n 212 above) 6.
269 As above.
270 58 of 1991.
271 Van Oosten 7.

guidelines are in place at that institution, such research should also be governed by the MRC guidelines.[272]

The Department of Health's Good practice guidelines make provision for the establishment of a National Health Research Ethics Council.[273] Once it is established, this body will have overall responsibility to promote, ensure and monitor compliance by approved ethics committees in South Africa with relevant legislation, regulations and guidelines. This body is to be established under the new National Health Act,[274] and will report directly to the Minister of Health.

3.4 Conclusion

The preceding pages surveyed the documents that are a crystallisation of the principles expressed by ethical theory as discussed in paragraph 2. Briefly, the various national and international ethics guidelines and documents have been outlined and the functioning of South African research ethics committees is examined.

The following section moves away from theoretical principles and documents to an examination of how these principles function in practice. The effectiveness of the protection of participants in clinical research over the past decades offered in various ethical guidelines is assessed. Proceeding from the general discussion, the focus shifts to ethics and HIV/AIDS-related clinical research in Africa.

4 FROM PRINCIPLES TO PRACTICE: THE REGUALTION OF CLINICAL RESEARCH ELSEWHERE AND IN AFRICA

4.1 Introduction

In the preceding pages an outline was presented of various ethical theories and their crystallisation into the ethical principles that are included in domestic and international ethics guidelines and documents. What follows is an examination of the manner in which ethical documents have been employed to protect the interests of research participants in HIV and AIDS-related clinical research in the world in general and in Africa, specifically.

Firstly, an overview of the failures of ethical guidelines to safeguard research participants in the rest of the world is given, as well as an outline of the protectionist

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272 Van Oosten 9.

273 Guideline 1.5.3 Good practice guidelines. In this regard, also see the discussion of the National Health Act 61 of 2003 in ch 5 below.

measures which were devised in response to the subsequent outcry. Next, the influence of the HIV/AIDS epidemic on the ethics of clinical research is explored. A much-publicised ethical dilemma - the controversy over the use of a placebo in the AZT trials to prevent MTCT of HIV in Uganda - is analysed and reference is made to difficulties that arose in three other trials. Finally, ethical concerns specifically relevant to clinical research in Africa are discussed and the question is posed whether research participants in developing countries are differently situated from those in developed countries.

4.2 Imperfect practices: Past failures of ethical guidelines

4.2.1 A short history

a) Early failures

Although the history of clinical research may be traced back for many centuries, little attention was paid early on to what was later to become known as bioethics or research ethics. Even the early part of the 20th century saw modest attention in the literature to bioethics. This may be due to several reasons: partly because doctors and scientists did not clearly distinguish between 'research' and 'treatment' and partly because doctors enjoyed a considerable amount of public trust. They were rarely criticised by research 'participants' or their patients.[275]

The middle of the 20th Century saw the adoption of the Nuremberg Code, establishing the primacy of the welfare and interests of the research participant, and the embodiment of its principles into a variety of codes of conduct, including the Helsinki Declaration. The emphasis was on informed consent after disclosure by the investigator of the risks of research. Henceforth, reputable organisations and journals required that researchers include statements affirming that the principles of the Declaration of Helsinki were followed during research, and, specifically, that informed consent had been obtained from participants.

However, abuses of ethical guidelines and research participants continued, showing that a mere reliance on informed consent does not protect research participants against exploitation. In the 1950s, an experiment at Willowbrook State School, in which researchers injected the Hepatitis B virus into mentally-retarded children in order to study the natural progression of the disease, aroused public

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274 Act 61 of 2003.

275 See ch 5 below on the concept of 'paternalism' in research, as well as n 306 below.

concern.[276] Participants were fed extracts from the stools of infected children, and participants who were 'enrolled' in the trial at an earlier point in time, and who were already ill, received injections of 'purified' virus.[277] The parents of children were only able to have their children admitted to hospital upon their agreeing to the children being part of the research.[278]

In the 1960s, details of an experiment at the Jewish Chronic disease Hospital in Brooklyn, New York, came to light.[279] In this instance, researchers injected cancer cells into research participants without informing those participants of the risk or obtaining their informed consent.[280] The researchers defended their actions by saying that they could not tell patients that they were going to receive cancer cells as that would have frightened them unnecessarily.[281] These researchers wanted to gain information on the nature of the human transplant rejection process.[282]

In 1966, an exposé by Henry Beecher, published in the *New England Journal of Medicine,* identifies 55 cases[283] over the preceding ten years in which there were instances of 'unethical and questionably ethical procedures', which put research participants at risk.[284] A staggering 22 cases had their findings incorporated in articles that were published in the *New England Journal of Medicine*.

Beecher argues that two factors determine whether research is ethical - the informed consent of the participant and an 'intelligent, informed, conscientious, compassionate, responsible investigator'.[285] Beecher points out that the 'gain anticipated from the experiment must be commensurate with the risk involved'.[286] Most of the instances Beecher describes involve poor, disadvantaged research participants. Subsequent publications have detailed even more severe abuses, such as those Pappworth[287] and Katz[288] describe.

The 1970s saw the disclosure of one the most serious abuses of research subjects to date: the Tuskegee syphilis study. The study began in 1932, lasted for

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276 Levine (n 1 above) 70.
277 Levine 70; Grady (n 189 above) 40 – 41.
278 Levine 70; Grady 40.
279 Levine (n 1 above).
280 Levine (n 1 above) 71; Grady (n 189 above) 40. It was later asserted by researchers that informed consent was negotiated orally, but not documented.
281 Levine 71; Grady 40.
282 Levine 71.
283 The results of which were published in international journals.
284 Beecher (1966) *New Engl J Med* 1354 – 1360.
285 Beecher 1360.
286 As above.
287 Pappworth (1967) *Human guinea pigs*.

40 years, and is probably the most publicised of the abuses during this period and has caused an outcry around the world.[289] The study recruited 400 black men of a low socio-economic background from Alabama with the promise of free medical care for a study into the natural progression of the disease.[290] 200 of these men were suffering from syphilis, the remaining 200 were healthy and served as controls.[291] The standard treatment for syphilis at the time was an injection of arsenic and bismuth.[292]

None of the men gave informed consent to the treatment; in fact, they were told that some of the experiments, such as spinal taps, were not part of the research at all, but 'special free treatment'.[293] Although penicillin was discovered in the 1940s to be an effective therapy for syphilis, and the fact that syphilis sufferers' life-spans were reduced by 20 per cent when the disease was left untreated by antibiotics, the men taking part in the study were not told, and were left untreated.[294]

Also in the 1970s, the aim of the San Antonio Contraceptive study was to discover which side-effects of oral contraceptive use were due to the drug itself, and which were due to the 'symptoms of everyday life'.[295] Mexican-American women (poor and who had no other access to contraceptives and who had multiple pregnancies), who attended a clinic seeking contraceptive advice, were enrolled in the study.[296] None of the women were advised that they were part of a research study, and that, in some instances, they received placebos instead of contraceptives.[297] Eleven of the 76 research participants became pregnant during the study because of receiving a placebo instead of an active contraceptive.[298]

In the 1990s the Kennedy Kriegler Institute at Johns Hopkins University conducted a research study on lead paint exposure.[299] In order to test their interventions, the presence of small children was required, and researchers from the University encouraged landlords of lead-contaminated housing to rent to families (with otherwise healthy young children) who were told the homes had been abated

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288 Katz (1972) *Experimentation with human beings*.
289 Levine (n 1 above) 69.
290 Levine 69; Grady 40.
291 As above.
292 As above.
293 As above.
294 Levine 70.
295 Levine 71.
296 As above.
297 As above, 72.
298 Levine 72.
299 See Spriggs (2004) 30 *J Med Ethics* 176.

of lead paint.[300] Those families were subsequently recruited to participate in a (fictitious) research study in which blood testing of the children would be done; however, the families were not informed that testing for the presence of lead was to be part of the study.[301] Children living in study houses were also encouraged to continue living in the houses. The levels of lead that accumulated in the children's blood determined the success of the various methods of lead abatement.[302]

Exposure to lead has a detrimental affect on the health and cognitive development of young children.[303] When the true nature of the research study came to light, mothers of two of the children filed court cases, complaining that they were not fully informed of the risks and hazards involved in the study, and were not warned promptly of the high levels of lead in their homes and in their children's blood - information that would have influenced their willingness to continue in the study.[304] The judge in the case likened the lead paint study to the infamous Tuskegee experiments.[305]

From the above examples it is clear that despite the existence of the Nuremberg Code and the Declaration of Helsinki, as well as other international and national codes, they were not sufficient to safeguard the research participants' rights. Researchers either ignored the ethical rules laid down in these documents outright, or thought that their non-ethical actions were justified in the interests of science.

b) Protectionist[306] attitudes in the 1960s and 1970s

The incidents described above and the public outcry which followed the disclosure, led to the United States Senate passing the National Research Act in 1974. This Act requires independent review of all research by an institutional review board before it

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300 As above.
301 As above.
302 Spriggs (n 299 above) 177.
303 As above.
304 As above.
305 See above.
306 According to Carole Levine, during the 1960s and 1970s, the paradigm for ethical analysis in the United States focussed on the risks and burdens of research; she notes that the history of the regulation of clinical research in that country 'was born and reared in protectionism' (Levine 'Changing views of justice after Belmont: AIDS and the Inclusion of "vulnerable" subjects' in Vanderpool (ed) (1996) 106). Research participants had to be protected against abuse by authorities who regarded themselves as better able to judge what is best for participants.

can be funded.[307] The Act also establishes the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research. The National Commission published the Belmont Report[308] in 1979 as an attempt to synthesise the ethical guidelines that are basic to human subject research.

The Belmont Report and the work of bodies such as the National Commission illustrate a pre-occupation with the need to protect the research participant against the evils of irresponsible research. This protectionist attitude lasted until the mid-nineteen eighties when the beginnings of the HIV epidemic brought a change to how research participants are perceived by investigators and how they perceive themselves. This change in attitude is discussed below.

c) The impact of the HIV epidemic

Regarding the extent of the impact of the HIV/AIDS epidemic on medical ethics, Kenneth Boyd writes that the impact of AIDS on medical ethics can possibly be compared to the impact of war on medicine itself:[309]

> In wartime, everydayness is seen in a different light, new solutions are found to old problems, and few wars have ended without some contribution having been made to medical progress. The arrival of AIDS had similar effects on medical ethics. Few clinicians were untouched by it; nor, as in all modern wars, was the civilian population.

The ravages of HIV/AIDS during the mid-nineteen eighties brought dramatic changes to the way in which research participants are viewed by researchers and the way in which research itself is seen.[310] For the first time participation in a clinical research is seen as a benefit, and not a burden.[311] People were desperate for a cure and saw research participation as a way of accessing treatments.

HIV/AIDS activists were instrumental in this shift in perception. Participation in clinical research brought people living with the virus access to investigational new drugs and medical care.[312] The perception of the benefit of research and participation in clinical trials was so strong that participants and their physicians even in some cases falsified participants' medical records in order to comply with the

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307 The Act is a domestic piece of legislation; therefore, it governs research carried out in the United States, or funded by an agency in the United States and carried out elsewhere.

308 See para 3.1.3 above.

309 Boyd quoted in Pinchin *et al* (2000) 26 *J Med Ethics* 6.

310 Beauchamp and Childress (n 5 above) 203.

311 As above.

312 As above.

inclusion criteria of clinical trials for new drugs and treatments.[313]

Developments during the 1980s and 1990s in patient advocacy and activism have their origins in the problems of stigma and alienation felt by PLWHA.[314] Pinchin *et al* comment as follows:[315]

> An emerging solidarity, reinforced by the cumulative personal losses, soon led to action to protect each other through prevention programmes, based on peer-education and influence. These were impressively relevant, focused and unfettered by the constraints limiting official campaigns. Issues of access to care and to information followed, leading to treatment activism, driven by a strong desire for more satisfactory outcomes.

At this time people living with HIV/AIDS in the developed world became an informed, scientifically-educated group. Rather than being inactive recipients of the researchers' protectionist attitudes, they demanded to be part of the process of decision-making. This attitude was often born out of a sense of desperation.[316]

> Physicians in this field have been struck by the way in which people affected have wanted to be involved in decision making. While this has often been ascribed to their social groups, it probably was more a reflection of their younger age and a generation change in expectations of health care. While medicine and medical ethics were already moving towards a more explicit recognition of personal autonomy, AIDS has accelerated and catalysed the process. Faced initially with a disease of overwhelming severity that would so shorten their lives, and the limitations of treatment, it is understandable that patients wanted to explore the options and to make the vital choices.

Thus, AIDS activists demanded early access to research findings, even during the early stages of clinical trials.[317] In turn, this demand resulted in a pool of research participants who were well-informed about the research that was being carried out and about treatment options.[318]

The standard process of ratification the US Federal Drug Administration (FDA) follows was seen by AIDS activists as slow, restrictive and paternalistic.[319] People living with HIV/AIDS criticised the FDA for dragging its feet while people were dying – '[c]oncerns about the conduct of clinical trials and delays in drug availability and licensure became a public expression of the ethics of emergency'.[320] Clinical trial methodologies, such as placebos and randomisation, were seen by AIDS activists as

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313 Beauchamp and Childress 204.
314 Pinchin *et al* (n 309 above) 3.
315 As above.
316 Pinchin *et al* 3.
317 Beauchamp and Childress (n 5 above) 203.
318 As above.
319 As above.
320 Pinchin *et al* 4.

'disempowering, arbitrary and irrational'.[321]

In response to the demands of AIDS activists, the FDA developed expanded access to experimental drugs, allowing the treatment use of experimental drugs that had not yet been approved for seriously ill patients.[322] Furthermore, the FDA allowed for fast-track (expedited approval) of investigational medication for people with life-threatening conditions.[323] For the first time it was considered acceptable for people with life-threatening illnesses to take greater risks in taking medication that had not yet received approval. AZT is one of the drugs that was fast-tracked in this way.[324]

The AIDS pandemic thus brought about a new definition of the research participant's right to be seen as autonomous and capable of making decisions about participation in research, ushering in a new era in research ethics in the 1980s. The perceived paternalism of the previous decades was thoroughly rejected and the shift in attitude was reflected in policy and in revisions to the major international documents.[325] During this period, the debate centres on the inclusion of women and ethnic minorities in clinical trials, which demonstrates clearly the shift towards regarding research participation as a benefit rather than a burden.

However, clinical trials in Africa on the perinatal transmission of HIV, and other medical questions, soon put back in the spotlight the failings of research ethics to adequately protect the interests of the research participant. The following section is an outline.

4.2.2 Four cases in point: Failures of ethical guidelines to protect research participants in Africa

a) Placebo-controlled trials of Zidovudine to prevent MTCT of HIV in Uganda

i) Overview

Mother-to-child transmission of HIV (MTCT) is the manner most common for young children, world-wide, to become infected with HIV.[326] The search for drugs that would limit this form of transmission has been a priority in the battle against HIV/AIDS.

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321 As above.
322 Beauchamp and Childress 203.
323 As above.
324 As above.
325 As above.

In 1994, a large randomised, double-blind, placebo-controlled trial[327] (conducted mainly in the USA) showed the efficacy of the ARV zidovudine or AZT (during the trial known as the PACTG[328] 076 regimen) in reducing MTCT of HIV by almost two thirds, from 25 per cent to 8 per cent.[329] After the results of the trial were published, this regimen became the standard care to prevent MTCT of HIV in the developed world.

In the developing world, however, the situation was less reassuring. Because of the high cost of AZT ($800 per patient at the time of the trials, now far less)[330] and the fact that it has to be administered for several weeks before birth to the mother, intravenously during labour, and as a syrup to the child after birth, meant its administration is an impracticality in countries where mothers often do not attend clinics until immediately before labour or only if complications arise. Further, many rural clinics in these countries do not have the technology to administer intravenous medication.[331] Many mothers never attend a clinic at all. Moreover, the original clinical trial was performed in a setting where mothers were urged not to breastfeed, whereas, in Africa, most mothers breastfeed.

A shorter and cheaper regimen that could be used in a resource-poor setting thus had to be found if the administration of AZT was to be an achievable goal for developing countries. In order to successfully develop a shorter, cheaper regimen, sixteen randomised, double-blind placebo-controlled trials of shorter AZT regimens were undertaken in developing countries, such as Uganda, Tanzania, Ethiopia, Zimbabwe, Thailand and the Dominican Republic. Fifteen of these studies used a placebo in the control arm of the study.

ii) The ethical dilemma

The September 1997 issue of *The New England Journal of Medicine* published the results of a randomised, double blind, placebo-controlled trial determining the efficacy and safety of a shortened, simplified course of AZT[332] in reducing the risk of

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326 See ch 2 above.
327 See para 5.2.2 in ch 2 on the scientific methodology of these trials.
328 Paediatric AIDS Clinical Trial Group.
329 Connor *et al* (1994) 331 *New Engl J Med* 1173. Other interventions such as caesarean section were shown to reduce the risk even further.
330 Bayer (1998) 88 *American J Public Health* 568.
331 See Connor et al (n 329 above) and Bayer (n 330 above) 568 – 569.
332 This trial had taken place long before nevaripine and newer drugs became the preferred treatment in such instances.

MTCT of HIV in Uganda.[333] This article, and the editorial written in response to it by the journal's editor, Marcia Angell, sparked off one the most astringent ethical debates of the nineties.

HIV-infected pregnant women who had not received anti-retroviral therapy and who had a CD4 count of above 2300 per millilitre of blood were enrolled in the Ugandan trial.[334] Trial participants were given AZT before and during birth, and AZT was administered to the child for six weeks after birth. This trial was placebo-controlled, in other words, the control group received no treatment while the experimental group received AZT.

The controversy lay in this fact – even though AZT had been shown to be effective in preventing MTCT (in the previous trials of the 076 regimen), and, therefore, had become the best proven treatment, it had not been given to the control group. They were given a placebo – violating the ethical principle of beneficence.[335]

In her editorial, Marcia Angell asserts that 'only where there is no known effective treatment is it ethical to compare a potential new treatment with a placebo'.[336] If an effective treatment exists (as is the case here), then it is not ethically permitted to use a placebo. Members of the control group should have been given the 'best known treatment'.[337]

In the context of this view, if the trial had been conducted in the United States, or another developed country, the practice would have been considered unethical.[338] Marcia Angell posed a question concerning the ethical nature of conducting a trial in a developing country in a manner that is considered unethical in a developed country.[339] Angell argues from the viewpoint that research participants in a developing country should receive the same standard of care as that provided in the developed world (in other words, the women should not have been given a placebo). Relying on the Declaration of Helsinki, Angell is asserting the requirement

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333 Also see Lurie and Wolfe (1997) 337 *New Engl J Med* 854.

334 As above.

335 Art II.3 Declaration of Helsinki requires the investigator to provide the 'best proven treatment'.

336 Angell (1997) 337 *New Engl J Med* 847.

337 Art II.3 Declaration of Helsinki.

338 Bayer (n 330 above) 568. Such a trial would be considered unethical because it is not trying to find an intervention that is at least as effective as, or better than the prevailing standard of care (the 076 regimen of AZT).

339 Angell (n 336 above) 848.

that control groups receive the 'best' current treatment, not the local one:[340]

> The shift in wording between 'best' and 'local' may be slight, but the implications are profound. Acceptance of this ethical relativism could result in widespread exploitation of vulnerable Third World populations for research programmes that could not be carried out in the sponsoring country.

Based on the conclusion that that she derives from her perception of the practice of 'ethical relativism', Angell maintains that the justifications used by the researchers for the need for the trial is reminiscent of that used in the Tuskegee study; that the research participants will, in any case, not have access to AZT (as it is too expensive):[341]

> Women in the Third World would not receive antiretroviral treatment anyway, so the investigators are simply observing what would happen to the subjects' infants if there were no study. And a placebo-controlled study is the fastest, most efficient way to obtain unambiguous information that will be of greatest value in the Third World.

Her argument is that the limited resources of the developing world cannot justify an attempt to find an affordable intervention if the standard of care is at a level different to that provided in the developed world.[342]

Marcia Angell is not alone in criticising the Ugandan research. In the same issue of the *New England Journal of Medicine*, Peter Lurie and Sidney Wolfe attacked the Ugandan research as unethical on the grounds that it will lead to the preventable infection of hundreds of infants.[343] They regard the research as directly violating the research participants' right not to be exposed to unnecessary risk.[344] In their view, the research violated several existing international research ethics guidelines.

Lurie and Wolf criticise the study because participants in these trials do not have access to antiretroviral treatment, while women in the United States, where similar studies were conducted, do have access to antiretrovirals. They use a similar study in Thailand, in which three shorter AZT regimens were being compared to a regimen similar to the 076 regimen (instead of a placebo),[345] as an example of how the same research could have been conducted in an ethically acceptable manner.[346]

The Thailand study is an equivalency study; a methodology that is used when

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340 Angell 848.
341 As above.
342 As above.
343 Lurie and Wolfe (n 333 above) 853.
344 Lurie and Wolfe 854.
345 The subjects in the experimental arm thus received the shortened experimental regimen, while those in the control arm were not given a placebo, but the active, longer course of AZT.
346 As above.

a particular regimen has already been proven effective and the aim is to determine whether the second regimen is as effective, but is less toxic or expensive.[347] In response to pressure from the USA NIH[348] to change the study to one that is placebo-controlled, the principle investigator in Thailand argued that an equivalency study (using an active control) is feasible in Thailand.

Lurie and Wolfe assert that the wrong research question was being asked in the Ugandan study. Instead of asking, 'Is the shorter regimen better than nothing?' (which would perhaps justify a placebo control), the question asked should have been, 'Can we reduce the duration or prophylactic treatment (AZT) without increasing the risk of perinatal transmission of HIV, that is, without compromising the demonstrated efficacy of the standard ACTG 076 regimen?'[349] They stress that an equivalency study would have yielded more useful results than the placebo study. Therefore, their argument is that the scientific rationale for the research was flawed.[350]

In response to Lurie and Wolfe's argument for the use of an equivalency study, proponents of the use of a placebo maintain that differences in the duration and administration of antiretrovirals agents in the shorter regimens justify the use of a placebo.[351] Lurie and Wolfe assert in response that the data gained from the original 076 trial provides sufficient information, and the equipoise necessary to regard the study as ethical is retained:[352]

> These findings seriously disturb the equipoise (uncertainty over the likely study result) necessary to justify a placebo-controlled trial on ethical grounds.

On similar grounds they dismiss the claim that in Uganda (and the other countries), because the medication was administered orally, in contrast to intravenously in the original trial, this justifies the use of a placebo.[353] They insist that previous pharmacological studies have indicated that the uptake of the drug is the same whether administered orally or intravenously.[354]

Lurie and Wolfe examine the 'standard of care' argument. The version of the argument they contest implies that placebo-controlled studies are acceptable in the

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347 As above.
348 National Institutes of Health.
349 This was indeed the research question that was posed in the Thailand study. See Lurie and Wolfe 853.
350 As above.
351 As above.
352 As above, 854.
353 As above.

developing world as the standard of care here is either to rely on unproven treatment or to have no care at all.[355] In their view, this is a misunderstanding of the concept 'standard of care', as the standard of care that is used as a yardstick should be that of the treatment available in the sponsoring country:[356]

> Acceptance of a standard of care that does not conform to the standard of care in the sponsoring country results in a double standard in research. Such a double standard, which permits research designs that are unacceptable in the sponsoring country, creates an incentive to use as research subjects those with the least access to health care.

Lurie and Wolfe's arguments against using placebos may be summed up as follows.

- A placebo-controlled study is no longer ethically justified as AZt has been proven to be effective in preventing mother-to-child transmission of HIV.
- Research participants in developing countries who take part in research of this nature should have access to the prevailing standard of care in the sponsoring country.
- An AZT control arm should be used, regardless of prevailing local circumstances.

The *New England Journal of Medicine* published a response to Laurie and Wolfe.[357] In their response Vermus and Satcher stress that, because of the poverty of developing countries, placebo-controlled studies were used to obtain a speedy result.[358] They argue that placebo-controlled trials alone are able to provide definitive and clear answers about whether the interventions have worked.[359] They maintain that no clear answer would be gained by testing two or more interventions of unknown benefit against each other as it would not become clear whether either intervention would be more effective than no intervention.[360]

Ronald Bayer, in his article dealing with the controversy relating to the trials, comments that Vermus and Satcher neglect the real ethical difficulty inherent in the trials in their response. In this view, the real ethical difficulty relates to how one[361]

> should balance the claims of research subjects and their offspring against the claims

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354 As above, 855.
355 As above.
356 As above.
357 In their October 1997 edition, written by Harold Vermus and David Satcher: Varmus and Satcher (1997) 337 *New Engl J Med* 1003.
358 As above.
359 As above, 1005.
360 As above.
361 Bayer (n 330 above) 568.

> of those who might be placed at risk if the use of non-placebo designs were to require trials of more extended duration. Time is not an ethically neutral consideration, given that, in the time period before definite answers become available, untreated mothers and their offspring continue to suffer the risk of vertical transmission.

iii) Commentary

The debate in the *New England Journal of Medicine* cannot merely be characterised as an argument between ethical universalists, who believe a single ethical standard should be applied throughout the world, and ethical relativists, who hold the opinion that a different set of ethical principles should apply in local circumstances. Nor is it an argument about the practical application of ethical principles in different circumstances, economic conditions and social situations.[362] Rather, the two groups represent contesting methodologies.

One group suggests that methodological considerations make it necessary to use a placebo control group in clinical research, whereas the other believes that ethical standards and the rights of research participants are sacrificed for methodological considerations.[363] As Emmanuel proposes; is there a compromise or middle ground between the two groups' views?

In philosophical terms, at issue are two approaches to ethical reasoning. Angell, Lurie and Wolfe present the deontological or Kantian approach, by their assertion that actions should not be judged by their consequences. Vermus and Satcher, from a consequentialist or utilitarian point of view of determining whether an action is right or wrong, argue that the best possible outcome is achieved by the use of a placebo.[364]

Supporters of the placebo-controlled clinical trial, in instances where a known treatment exists, point out that a variable response to drugs in certain populations - unpredictable and small effects and high rates of spontaneous improvement in effect in patients – means these trials are necessary and, thus, ethically acceptable.[365] Without a placebo group to ensure validity, there is no assurance as to whether the known therapy is, in fact, better than the placebo, or if there is no difference between the investigational and standard treatment.[366] Most ethicists agree that

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362 See Bayer's argument to this affect, above.

363 Emanuel (2001) 345 *New Engl J Med* 915.

364 See paras 3.2.1 and 3.2.2 above.

365 Emanuel (n 363 above) 915. The argument below is based on Emmanuel's article.

366 Of course, new treatments that are no better than existing treatments may still be valuable, such as is the case when the new treatment has fewer side-effects or is more effective in older people or children.

there are instances where placebo-controlled trials are unethical by definition, such as if a life-saving treatment is withheld.[367]

However, as there is no agreement with regard to when a placebo-controlled trial will be ethical even though a known treatment exists, controversy, such as the one discussed above, is bound to arise. In some instances research participants suffer psychological and physical harm if they are refused a known treatment.[368] In those circumstances, placebo-controlled studies may be said to place the demand of scientific rigour above the need to care for the well-being of the patient.

Advocates of active controls propose that, as prescribed in the Declaration of Helsinki, these should be used whenever possible. Nevertheless, their implementation is not straightforward.

- Active control studies do not always produce a result or may produce misleading results, thus making the trial worthless.[369] In that case the study may be termed unethical, because one of the first requirements for an ethical study is that it should be scientifically rigorous in producing an answer to a specific research question.
- In some cases, the harm done by not treating the participant with the existing treatment is so small that there exists no ethical duty to do so.[370]
- Trials using effective controls (such as equivalency trials) may need to enrol many more participants than is the case with placebo-controlled trials and last longer. Thus, many more people will be exposed to possible harm, such as an undiscovered side-effect of the investigational drug (that may be more toxic or just useless), than is the case with a placebo-controlled trial.[371]

Ethical guidelines require that clinical research that is ethically acceptable be scientifically valid and minimise the risks that research participants are exposed to. Emanuel argues that advocates of placebo-controlled trials are opting for scientific validity, and their opponents for minimising risks.[372] He suggests that there is a middle ground between these positions; asserting that placebo-controlled trials are ethically justifiable only when the methodological reasons for them are compelling,

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367 Emanuel 915; also see Beauchamp and Childress (n 5 above) 142 – 143; 145 – 146; 159 – 160.
368 eg when they suffer from a disease that is treatable.
369 Emanuel (n 363 above) 915.
370 As above. Also see Beauchamp and Childress 133.
371 Emanuel 916.
372 As above.

that patients receiving the placebo will not be exposed to serious harm, and that attempts should be made to minimise the risks associated with receiving the placebo.[373]

Has the ethical dilemma presented by the placebo-controlled trials of AZT to prevent MTCT of HIV in Africa been solved? The methodological reasons for the trials may be compelling – if we wait for the results of a much longer equivalency trial, many more children may die while waiting for a shorter, more effective course of AZT. However, the second requirement that the participants receiving the placebo must not be exposed to serious harm, has not been met by the short course maternal-infant transmission trails. Babies that could have been born HIV negative have been infected; if they were in the active arm of an equivalency trial, they would have received AZT and have been spared. Nevertheless, this benefit is offset by the fact that an equivalency trial lasts longer, so that more babies will be born with the virus in a country where the 076 regimen of AZT is too expensive.

A further problem with the placebo-controlled trials of AZT to prevent MTCT of HIV in Africa is that that they do not meet the distributive justice principle.[374] According to this principle, the sponsoring agency (conducting the trials) should ensure that, after successful testing, a product developed from the results is made 'reasonably available' to inhabitants of the community in which the research was carried out. Exceptions to this requirement are justified, but must be agreed to by all parties before the research begins.[375]

Crouch and Arras, in the *Hastings Center Report*, assert that a violation of this principle amounts to an unjustifiable exploitation of the developing nation for no morally legitimate reason.[376] If it is the case that even the shorter course of AZT is unavailable to the research participants and their community (it is still too expensive), then the information gained from the trial is rendered useless for the community in which the trial was conducted, and, therefore, they were exploited.[377]

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373 As above, 917.

374 See Cooley (2001) 22 *Theoretical Med* 151 for a full discussion of distributive justice and clinical trials in the developing world.

375 Guidelines 8 & 9 CIOMS guidelines. Also see para 3.1.4 above.

376 Crouch and Arras (1998) 28 *Hastings Center Report* 26.

377 As above 27. Also see chs 5 and 6 below. Timing in HIV-related research also is an issue. Because the science develops so fast, and because new antiretrovirals are developed continually, research which is not *per se* exploitative at the beginning of a trial may become so when, during the course of that trial, another, much more efficacious drug is developed.

There are concerns regarding this argument: mostly they are the consequence of the formulation of the distributive justice principle, which is so ambiguous as to make it practically impossible to use.[378]

Cooley asserts that because of the imprecise language in which it is written, the CIOMS principle (of justice) is unlikely 'to help anyone legitimately evaluate medical experiments or to assist people in determining their moral obligations'.[379] Behaviour that is interpreted as impermissible by one researcher may be regarded as permissible by another.[380] According to Cooley, the phrase 'any product developed will be made reasonably available to inhabitants of the underdeveloped country in which the research was carried out' has three aspects to it which are unclear.[381] First, who determines the meaning of 'reasonably available'? Who determines whether something is reasonably available, and on what does that person base her decision? Cooley asks.[382] A reasonable sponsor may regard something as reasonably available if it is made available to the members of the community who took part in the research,[383] in the context that the sponsoring company has to make a profit for its shareholders, and cannot give the drug away.[384] Many products, besides, can only be used appropriately when ancillary services are available - mothers in labour would not only need AZT administered to them, but they would also need the technology to have the medication administered intravenously.[385]

Second, who should be the beneficiaries of the knowledge gained by the research undertaking? To how many inhabitants should the sponsoring company make the drug available: the research participants; the community in which the research took place; the town or village; the province or country?[386]

Third, the meaning of the term 'community'. Is it the people of the immediate area where the drug was tested or is it the citizens of the country where the drug was tested?[387]

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378 Cooley (n 374 above) 152.
379 As above.
380 As above.
381 As above.
382 As above.
383 As above, 153.
384 As above, 153 – 154.
385 As above, 154. In the 'Nestlé baby formula' case, the sponsoring company provided the formula but not the expensive refrigeration or clean water, and many infants were in fact harmed in consequence.
386 As above, 155.
387 As above.

Importantly, Cooley argues that research participants in the developing world decided autonomously to participate in the clinical trial of AZT.[388] The women who participated were given better medical attention, and the opportunity to have their children born HIV negative.[389] The research participants thus acted in their own interests when deciding to participate in the trial.[390] To argue that they were exploited reflect a paternalistic attitude towards the women who made the choice to participate in the research.[391]

Moreover, a utilitarian argument indicates that the trials were a waste of time and resources from their very inception.[392] The populations of many developing countries still are unable to afford even the cheaper version of the drug, so that there was no reason to conduct the study in the first place, which is unethical from its inception.[393] If a cheaper drug is as expensive at $50 as the other version is at $800 a person, in the sense that it is still beyond the per capita expenditure on health care, then only the research participants benefit.[394] For this reason, Cooley regards the placebo-controlled trials of AZT to prevent MTCT of HIV in Africa as unethical.[395]

Cooley's arguments are appealing, because straightforward, and his criticisms of Angell and Lurie and Wolfe are valid, but his dismissal of the principle of distributive justice as being too vague is insufficiently serious. He ignores the great disparity in health care between the developed world and the developing world. In his article 'Distributive justice and clinical trials in the third world', Solomon Benatar makes out a convincing case for retaining the principle of distributive justice, despite its ambiguity and imprecision.[396] Of the annual global expenditure on health care, 87 per cent is spent on 16 per cent of the population who bear 7 per cent of the global disease burden;[397] of the $56 billion that is spent worldwide on medical research and development, 90 per cent is spent on diseases that account for 10 per cent of the

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388 As above 160.
389 As above.
390 As above.
391 As above, 161. This argument, regarding the autonomy of the participants in the trial, will be re-examined later.
392 As above.
393 As above. Only should the drug become affordable, will this argument become invalid.
394 As above.
395 As above, 162.
396 See Benatar (2001) 22 *Theoretical Med* 169 – 176.
397 Benatar 170.

global burden of disease;[398] per capita expenditure ranges from $5 in developing countries to $4000 in the developed countries such as the USA.[399] These statistics demonstrate the reason for the CIOMS guidelines to stress that distributive justice is an essential part of collaborative medical research in the world today.[400] An overly-simplified notion of utility which ignores the concern of distributive justice appears unfair against the background of such inequities.[401]

Benatar is of the opinion that the decisions are best left in the hands of those who are directly affected:[402]

> What makes them think that their insights provide adequate or sufficient means of assessing what is best for those living under dehumanising conditions in which the requirements for achieving improved health are so different from their privileged world?

A narrow utilitarian approach, he concludes, undermines the human dignity of those involved in research in the developing world.[403] Benatar dismisses as unfounded the criticisms levelled by Cooley and others and associates them with imperialistic attitudes.

Because the shorter regimes that were developed by the research outlined above are not being implemented, either because of a lack of resources or a lack of the political will to implement them, that research is not regarded as ethical in the contexts of the remarks of Solomon Benatar and Peter Singer:[404]

> Research ethics must be deeply rooted in the context of global health ... it must ultimately be concerned with reducing the inequalities in global health and achieving justice in health research and care.

An important aspect of the Ugandan trials escaped notice: during the controversy surrounding the trial, it was never questioned whether, considering that their only means of accessing health care was participation in the trial, the women in the trial gave informed consent to participation. This aspect of the trial is discussed in more detail later in the thesis.[405]

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398 World Health Organisation *Report of the ad hoc committee on health research relating to future intervention options World*, quoted in Benatar 170.
399 Benatar 172.
400 Benatar 171.
401 Benatar 172.
402 Benatar 172.
403 Benatar 175.
404 Benatar and Singer (2000) 321 *British Med J* 824.

b) Pfizer's Trovan experiments in Nigeria

i) Overview

In February 1996, an epidemic outbreak of cerebrospinal meningitis occurred in Kano, Nigeria. The WHO's web-site indicated that by March, 17 668 cases had been reported and that more than 2 500 people had died from the disease.[406] The epidemic left over 18 000 victims suffering from the disease.[407]

An international pharmaceutical company, Pfizer, quickly acted to alleviate the epidemic. It delivered desperately-needed medical supplies, as well as medical staff, to Nigeria.[408] It also started trials of an experimental drug for the treatment of viral meningitis, called Trovan.[409] At the time Trovan was not approved for human experimentation by the FDA in the United States.[410] Trovan is one of the few drugs to have been withdrawn from the US market due to known serious side effects in the last five years.[411] Further, it is not approved for experimentation using children.[412]

Pfizer set up research headquarters in Kano, next to the facility of Doctors Without Borders (DWB), using DWB bed space and a section of DWB's treatment centre.[413] The doctors brought in by Pfizer were unaccustomed to offering medical care in a city of more than two million people ravaged by pollution, disease and death.[414] During the two weeks they spent in Kano, Pfizer's researchers treated over 200 children for spinal meningitis: 100 children used an oral or intravenous form of Trovan;[415] the remaining children were treated with the antibiotic Ceftriaxone, a drug already approved for use with children in the United States.[416]

At first, the Pfizer researchers selected the most suitable children for treatment, but, as the epidemic raged, they began treating any child presenting.[417] The ages of the children ranged from a few months to eleven years and varied in

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405 See ch 6 below. Also see Macklin's exposition of the trial in Macklin (2004) 13 – 24.

406 WHO (19 February 1996) *Disease Outbreak News* <http://www.who.int/disease-outbreak-news/n1996/feb/n19feb1996c.html> (15 December 2006); Carr (2003) 35 *Case Western Reserve J of Intl L* 15.

407 The damage done by the virus causes long-term after-effects, such as the loss of sight and hearing and paralysis.

408 Carr (n 406 above) 15.

409 Trovan had never before been tested on children.

410 In fact, Trovan has been one of the few drugs in the last five years that have been withdrawn from the US market due to known serious side-effects (see Carr 16).

411 As above.

412 Carr (n 406 above) 16.

413 Carr 18.

414 As above.

415 As above.

416 As above.

417 As above.

levels of infection from the early stages of the disease, to partial paralysis, to near death.[418]

Due to the large number of patients treated in such a short time and the high illiteracy rate in Kano, many of the patients did not sign consent forms.[419] Many of the patients consented verbally, relying on an interpretation provided by a nurse; but frequently the nurses did not translate all the details on the consent form to the families.[420] It is alleged that the treatment with Trovan resulted in the deaths of eleven of the 100 children; several more allegedly were left blind or deaf.[421]

ii) The ethical dilemma

When the media started to investigate claims regarding unethical and illegal research practices by Pfizer, they uncovered a variety of violations of international research ethics. Research documents had been forged;[422] there was no oversight and approval of research procedures during the trials;[423] and the researchers failed to administer effective treatment to desperate participants.[424]

In 2001 the families of the children that had participated in Pfizer's Trovan research in Kano brought a case against Pfizer in a US court, claiming that Pfizer had violated international and national laws in carrying out experimental research on humans. The case against Pfizer in the US represents the first in history in which individuals are suing in a foreign court a private corporation for wrongful experimentation in violation of US and international law.[425]

iii) Commentary

It is clear from the discussion above that various international ethical guidelines were breached. Importantly, there was no informed consent to participate in Pfizer's

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418 As above.
419 As above.
420 As above.
421 Carr (n 406 above) 19.
422 Forged documents included individual consent forms, governmental permission forms and oversight approval forms (Carr 16, fn 8). Also see Bosely 'New Drug 'Illegally Tested on Children': Pfizer Accused of Irregularities During Clinical Trial in Nigeria', *The Guardian*, 17 January 2001, 19. Parents of the children participating complained that they did not know that the drug that was being given to their children was experimental.
423 As above.
424 As above.
425 As above.

clinical trials, as it appears that the consent process was flawed.[426] Informed consent is a prerequisite for the ethical conduct of clinical research; it is included as the first principle in the Nuremberg Code, in the CIOMS Guidelines and in the Declaration of Helsinki.[427]

On the other hand, it may be argued that in the face of a devastating epidemic Pfizer did the best it could – it expedited medical staff and supplies; its effort was a humanitarian one rather than an example of gross abuse of research participants and a violation of ethical guidelines. This argument lacks validity because Pfizer used their 'humanitarian' effort to test Trovan on children in violation of Nigerian and international ethical guidelines. That Nigerian researchers and politicians collaborated to conceal the fact that ethical approval had not been given by a Nigerian ethics committee,[428] only serves to exacerbate the violation.

The Nigerian Trovan experiment shows that in spite of the existence of international ethical guidelines to protect participants in clinical research, and even after increased media awareness and scrutiny of clinical trials, abuse of research participants continue.

c) The Tenofovir trials in Cameroon and Nigeria

i) Overview

Tenofovir is an experimental antiretroviral pre-exposure prophylaxis aimed at preventing infection with HIV.[429] The first randomised trial to assess the safety and efficacy of Tenofovir was planned for developing countries, such as Thailand, Cambodia, Cameroon and Nigeria.[430] The study was funded by the US NIH and the Bill and Melinda Gates Foundation. It was to recruit 960 sex workers.[431]

The Cambodian trial was shut down before recruitment began due to protests by AIDS activists and sex-worker advocacy groups,[432] thus demonstrating increased vigilance among these groups in the aftermath of the Ugandan MTCT trials. Activists protested that there were no safety data supporting the long term use of Tenofovir in healthy participants; they thus objected to starting phase II trials when phase I

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426 See Carr's description on 15 – 43.
427 See ch 5 below, paras 3.3 and 4.
428 See Carr (n 406 above) 16.
429 Mills *et al* (2005) 331 *British Med J* 1403.
430 As above.
431 As above.
432 As above.

trials had not been conducted on healthy participants.[433] Activists further objected to the lack of long-term insurance against adverse events, inadequate care for participants who seroconvert during the trial, and the lack of community involvement in the design of the trial.[434]

In February 2005, a similar trial was suspended by the Ministry of Public Health in Cameroon.[435] Major concerns that were raised included the quality of care given to participants during the trial and the quality of care that might be available after the trial had been concluded.[436] After a documentary programme on the trial aired on French television, the trial was suspended pending an independent inquiry by the Ministry of Public Health in Cameroon. The inquiry recommended that the trial recommence after certain conditions had been met. However, in July 2005, Family Health International, the organisers of the trial, announced that the trial would not continue as the suspension lasted too long to allow the trial to continue.[437]

In March 2005, Family Health International announced that the Nigerian arm of the Tenofovir trial would be abbreviated. It claimed to be closing the trial voluntarily because of 'logistical difficulties'. In conjunction with external, independent data and a safety monitoring committee, Family Health International states that the study team 'was unable to comply with the required operational and laboratory procedures'.[438]

ii) The ethical dilemma

A number of additional concerns have been raised about the ethics in these trials. Activists contend that, with the primary outcome being HIV infection, the counselling in the prevention of infection might be inadequate.[439] Trial participants have been requested by the trial sponsors to reduce the number of partners they had sex with during the trial. As the participants are impoverished sex workers, who depend for their livelihood on prostitution, this request was regarded as being rather unrealistic, and, arguably, unethical.[440]

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433 As above.
434 As above.
435 As above.
436 As above.
437 As above.
438 n 429 above, 1404.
439 As above.
440 As above.

In Cameroon, participants had been provided with male condoms as a proven prevention strategy. Activists argued that as women are not in a position to decide on safe sex, female condoms should have been provided.[441] Advocacy groups for sex workers claim that enrolling sex workers in trials is wrong as they are a vulnerable group and would not be given the intervention if it should prove beneficial.[442] They quote the trials of nonoxynol-9, which was found to contribute to increase the risk of genital ulceration, and HIV infection, as an example of trials which heighten the risk factor among participants from this community.[443]

iii) Commentary

The controversy outlined above highlights the importance of establishing the standard of care that will be available after a trial. Local research ethics committees should ensure that research is not undertaken in the developing world in order to avoid more rigorous ethical standards relating to care in developed countries.[444] In addition, the media attention and protests by NGOs demonstrate the important role that these play in raising awareness and mobilising public opinion against unethical trials. That these trials were indeed discontinued after ethical questions were raised is a measure of increased awareness about the potential for unethical practices during clinical research as a result of the controvercy surrounding the Ugandan vertical transmission trials.

d) The male circumcision HIV-transmission trials, Orange Farm, South Africa

i) Overview

Although previous studies had indicated that male circumcision may reduce the risk of HIV transmission, this was based on mere chance observation. A study by Auvert *et al* was conducted to confirm the causal relationship between circumcision and HIV prevention,[445] in the area of Orange Farm, near Johannesburg, between 2002 and 2004. The study enrolled 3272 men. At the beginning of the trial 1617 of these men were medically circumcised.

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441 As above.
442 As above.
443 As above.
444 See below.
445 Auvert *et al* (2005) 2 *PLos Med* e298.

The men were tested for HIV at the beginning of the trial, and follow-up visits were scheduled at three, twelve and 21 months. The investigators were not told the HIV status of participants, but the participants were given the option of finding out their status (at a nearby voluntary counselling and testing (VCT) centre).

After the twelve-month follow-up visit, an interim data analysis showed that twenty of the HIV negative men in the intervention group (which were circumcised) had become HIV positive, compared to 49 men in the control group who had become HIV positive. Hence, circumcision was shown to reduce the risk of acquiring HIV by about 60 per cent.

ii) The ethical dilemma

All the men who were circumcised appeared to have given valid informed consent to participation in the trial (which, of course, involved consent to circumcision). In her analysis of the ethical nature of the trial, Keymanthri Moodley comments upon two issues: the inclusion of HIV positive men in the trial, and the non-disclosure of HIV status to trial participants by the investigators.[446]

iii) Commentary

At the termination of the trial it was discovered that 146 HIV positive men were randomised at the beginning of the trial and a further 69 men had sero-converted during the trial.[447] The investigators were thus blinded to the HIV positive status of 215 men over an eighteen-month period.[448] During this period, the men remained undiagnosed and untreated. What is more, they could have infected their partners during this period.[449]

Moodley comments that, because research in South Africa is often conducted at the same site at which health care is provided to the community, it is impossible to conduct research without providing care for illnesses related to the study and even for other conditions.[450] Because the researchers were blinded to the status of the participants, those participants who were HIV positive went without care for

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446 Moodley (2006) Responses to Auvert *et al PoLS Med* <http://0-medicine.plosjournals.org.innopac.up.ac.za/perlserv/request=index-html?request=read-response&doi=10.1371/journal.pmed.0020298#r1053> (30 November 2006).

447 As above.

448 As above. The men were offered VCT, but at a VTC clinic, not as part of the trial.

449 As above.

450 As above.

eighteen months, even though ARV treatment became available at public health care sites while the study was still in progress.

Moodley additionally raises concerns about the publication of the trial in *PLos Medicine* after it had been rejected by *The Lancet*,[451] and the fact that the trial had been approved by two RECs; a French REC and the REC of the University of the Witwatersrand.

As it is expected that research displaying questionable ethics should not be published, and that RECs should take more care in approving trials which may cause harm to participants, Moodley concludes that, 'clearly, this landmark trial has raised many ethical questions and has emphasised the importance of conducting research that is both scientifically and ethically robust'.[452]

The survey of violations and ethical problems raised by clinical research in Africa is concluded by these four cases. The discussion below is more general in nature, and provides an overview of ethical concerns relevant to clinical research in Africa.

4.3 Ethical concerns relevant to clinical research in Africa

Clinical research ethics and practices in the developing world fall loosely into questions surrounding two main issues – issues which relate to the use of research participants (exploitation and informed consent are relevant here) and issues surrounding the distribution of risks and benefit, or distributive justice. These issues are introduced below. Note that the discussion is not meant to be exhaustive, but that it is rather meant as a brief outline of the relevant issues.[453]

The question that is at the centre of the controversy surrounding the placebo-controlled trials of shorter AZT regimens that were undertaken in developing countries - should research participants in the developing world be treated differently from those in the developed world? - is re-examined in this section with Africa as the focus.

At the outset it clear that developing countries cannot be viewed as a homogenous group – they vary in terms of infrastructure, the general levels of literacy and education of the population, levels of health care provision, the burden

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451 Because of the ethical issues raised by the inclusion of HIV positive men in the trial with the associated issues related to lack of treatment

452 Moodley (n 446 above).

453 For more on issues related to exploitation in research, see Macklin (n 405 above) for an excellent account of the controversies.

of disease borne by the population and social and cultural views on health and research. In view of this, it is more accurate to refer to 'least developed', 'less developed' and 'more developed' countries instead of 'developing' countries. Further, countries that are traditionally regarded as 'developed' and that are relatively economically advanced, may contain poorer communities who do not have the same access to resources.[454] The discussion below is general, but endeavours to incorporate an understanding of these differences.

The term 'developing', itself, is contested. La Nauze offers a critique of the terminology that reveals a level of confusion concerning the economic and political applications of the term.[455] He remarks that the terms 'underdeveloped', 'developed', 'First world', 'Third world' continue to be used to define countries and peoples and that these descriptions arose in the immediate post-war period at a time of decolonisation and political realignment:[456]

> Largely based around economic models involving the transfer of Western ideas and practices, it was thought that development would raise the 'Third world' (and I use the words advisedly) towards the West's level of achievement. This would occur through growth in industrialization and thereby increase the size of the economy. A 'trickle down' of these economic benefits would then lead to better conditions for the poor. The idea of development, however, was often confused with modernization as there was a desire by the dominant Western policy-makers to align development with their own strategic and policy interest. Thus the world became defined in terms of us and them, developed and underdeveloped, rich and poor, traditional and modern, and so on.

An ethical concern that is of paramount importance to clinical research in Africa and elsewhere is that of obtaining the informed consent of participants in clinical trials. Local circumstances, such as poverty, cultural differences, the position of women in society and a lack of literacy in scientific matters, are impediments to obtaining a valid informed consent from research participants. This issue is not be discussed here, as it is dealt with extensively in Chapter 5 which focuses specifically on issues related to informed consent in HIV vaccine trials in South Africa.

4.3.1 The burden of disease in sub-Saharan Africa, and particularly southern Africa

Despite the fact that only eleven per cent of the world's population lives in sub-Saharan Africa, the region carries a disproportionate burden of HIV/AIDS – more

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454 See Dickens (1997) 16 *Med and L* 187.
455 La Nauze (2002) 30 *Clinical and Experimental Ophthalmology* 66 – 67.
456 As above.

than 66.6 per cent of all people living with HIV/AIDS live here.[457] UNAIDS estimates that in 2006, 2.1 million people in Africa died of the disease.[458] In this region, the epidemic is showing no signs of slowing down, with southern Africa the hardest hit.[459] The people of the region urgently need clinical research that will produce the results which will alleviate the burden of disease it carries.

Disease has had a dramatic effect on the life-expectancy of the people living in sub-Saharan Africa. While most people born in the developed world have a life expectancy of 70 years or greater, those born in sub-Saharan Africa have a life-expectancy of less than 55, even as low as 40 years.[460] This is not only due to HIV/AIDS, but also to the incidence of diseases such as TB, hepatitis, malaria and diarrhoea.

Not only do people in sub-Saharan Africa carry a heavier burden of disease, but they also have fewer resources available to spend on health care. Because of other priorities, in part, developing countries devote a smaller proportion of their GDP to health care.[461] For example, whereas the United States of America spends $3 724 per year per person on health, Uganda spends $44, Sierra Leone $31 and Somalia $11 per person per year.[462]

The following tables reflect the core health indicators of selected countries in sub-Saharan Africa (Angola, Benin, Botswana, Burundi, Congo, Eritrea, Ethiopia, Ghana, Kenya, Lesotho, Malawi, Mali, Mozambique, Namibia, Nigeria, Senegal, South Africa, Swaziland, Tanzania, Uganda, Zambia, Zimbabwe). Brazil, Canada and India have been included for the purposes of comparison.[463]

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457 UNAIDS (2006) *AIDS epidemic update* 6. 58% of them are women. Also see para 3.3.4 of ch 2.

458 As above. These figures can be compared to those of the developed world. In North America, Western and Central Europe, for example, 1.9 million people are living with HIV/AIDS, and 65 000 people have acquired the disease during 2005.

459 As above, 3. Also see ch 2 above.

460 See below. Also see ch 1 above.

461 As above, 20. See ch 5 below and Table A below.

462 Nuffield Council on Bioethics (2002) *The ethics of research related to healthcare in developing countries* 20.

463 Information in both tables from WHO (2006) *World Health Statistics 2006*. Note that HIV prevalence rates are included for the sake of completeness (see para 3.3.4 of ch 2 for more recent UNAIDS statistics).

	Life expectancy at birth (years)	% HIV prevalence rate adults 15-49	Infant mortality rate (per 1000 live births)	TB prevalence rate per 100 000 of population	Physicians per 1 000 of population
Angola	38(M) 42(F)	3.9	154	310	0.08
Benin	52(M) 53(F)	1.9	90	142.3	0.04
Botswana	40(M) 40(F)	37.3	75	553	0.40
Burundi	42(M) 47(F)	6.0	114	563.7	0.03
Congo	53(M) 55(F)	4.9	79	464.5	0.20
Eritrea	58(M) 62(F)	2.7	52	437.2	0.05
Ethiopia	49(M) 51(F)	4.4	110	533.2	0.03
Ghana	56(M) 58(F)	3.1	68	376.1	0.15
Kenya	51(M) 50(F)	6.7	78	888.4	0.14
Lesotho	39(M) 44(F)	28.9	55	544	0.05
Malawi	41(M) 41(F)	14.2	109	501	0.02
Mali	44(M) 47(F)	1.9	121	577.9	0.08
Mozambique	44(M) 46(F)	12.2	102	635	0.03
Namibia	52(M) 55(F)	21.3	42	586	0.30
Nigeria	45(M) 46(F)	5.4	103	531.3	0.28
Senegal	54(M) 57(F)	0.8	78	451.3	0.06
South Africa	47(M) 49(F)	21.5	54	670	0.77
Swaziland	36(M) 39(F)	38.8	102	1120	0.16
Uganda	48(M) 51(F)	4.1	81	646.4	0.08
Tanzania	47(M) 49(F)	8.8	78	478.6	0.02
Zambia	40(M) 40(F)	16.5	104	707	0.12
Zimbabwe	37(M) 34(F)	24.6	78	673	0.16
Brazil	67(M) 74(F)	0.7	32	76.7	1.15
Canada	78(M) 83(F)	0.3	5	4	2.14
India	61(M) 63(F)	0.9	62	312.2	0.60

Table A: Male (M) and female (F) life expectancy at birth (expressed in years) (2004); HIV prevalence rate in adults 15 – 49 (2003); infant mortality rate (per 1000 live births) (2004); TB prevalence rate per 1000 of population (expressed as a percentage) (2004); and the number of physicians per 1000 of the population (2000 – 2005). The date of the statistic is in brackets.

The information speaks for itself; overall the healthcare situation in sub-Saharan Africa is in a parlous state. The infant morality rate per 1 000 live births is at least twenty times higher in some sub-Saharan African countries than it is in Brazil, Canada and India.

TB is a serious problem in sub-Saharan Africa: in Kenya, South Africa and Swaziland, the TB prevalence percentage per 1 000 of the population is 888, 670 and 1120 respectively, compared to 4 in Canada.

People living in southern Africa experience a lack of access to health care personnel. Whereas in Canada and Brazil there are more than two and more than

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These are the same countries that are included in the study of constitutional provisions of countries in Africa (para 3.3 of ch 4 below).

one physicians per 1000 of their populations, Malawi, for example, has 0.02, Mozambique 0.03, and Lesotho only 0.05.

The following table displays additional health care indicators for these countries:

	Nurses per 1000 of population	**Adult literacy rate (%)**	**% ARV coverage**	**Total expenditure on health as % of GDP**[464]
Angola	1.15	66.8	6	2.8
Benin	0.84	33.6	33	4.4
Botswana	2.65	78.9	85	5.6
Burundi	0.19	58.9	14	3.1
Congo	0.96	82.8	17	2.0
Eritrea	0.58	Not available	5	4.4
Ethiopia	0.21	41.5	7	5
Ghana	0.92	54.1	7	4.5
Kenya	1.14	73.6	24.3	4.3
Lesotho	0.62	81.4	14	5.2
Malawi	0.59	64.1	20	9.3
Mali	0.49	19.0	31	4.8
Mozambique	0.21	46.5	9	4.7
Namibia	3.06	85.0	71	6.4
Nigeria	1.70	66.8	6	5.0
Senegal	0.32	39.3	47	5.1
South Africa	4.08	83.4	21	8.4
Swaziland	6.30	79.2	31	5.8
Uganda	0.61	68.9	51	7.3
Tanzania	0.37	69.4	7	4.3
Zambia	1.74	67.9	26	5.4
Zimbabwe	0.72	79.0	8	7.9
Brazil	3.84	88.4	83	7.6
Canada	9.95	...	>75	9.9
India	0.80	61	7	4.8

Table B: Nurses per 1000 of population (2000–2005); adult literacy rate as a percentage; ARV coverage as a percentage (December 2005); and total expenditure on health care as a percentage of the country's GDP (2003). The date of the statistics is in brackets.

Again, the position in sub-Saharan Africa is deplorable. The region has many fewer nurses than Canada. Significantly, countries in sub-Saharan Africa spend less on health care as a percentage of their GDP – Angola 2.8 per cent, Burundi 3.1 per cent and Mozambique less than 5 per cent (South Africa and Malawi are exceptions).

In sub-Saharan Africa, a heavy burden of disease is combined with a lack of access to health care. Other factors, such as low levels of education, high levels of poverty, poor nutrition and the lack of readily available clean water, inadequate sanitation, civil wars and disintegrating infrastructure, play a role in increasing the already

heavy burden of disease carried by these countries.[465] Benatar places these considerations in a wider context:[466]

> Africans must clearly take some responsibility for the state of their continent since post-colonial independence. Poor governance, corruption, internal exploitation, nepotism, tribalism, authoritarianism, military rule and overpopulation through patriarchal attitudes and disempowerment of women have all contributed to this sad state. However, to be fair, these shortcomings must be seen in the context of powerful external disruptive forces acting over several centuries to impede progress in Africa.

With regards to this heavy burden of disease, health care research is essential in sub-Saharan Africa. However, research is under-funded in the region, as it is in other developing countries.[467] The Nuffield Council on bioethics[468] quotes a 1990 report by the Commission on health research for development[469] to the effect of the vast gap between health needs and research expenditures.[470] The WHO's *ad hoc* Committee on health research refers to the difference as the 10/90 disequilibrium[471] - of the 50 – 60 billion US dollars that each year is spent world-wide on health care-related research, only 10 per cent is spent on the health problems of 90 per cent of the world's population.[472]

Developing countries, generally, lack the resources to carry out health care research by themselves, and spend their limited resources on primary care rather than on research:[473]

> Despite the great need for research to determine the most effective interventions in developing countries, the indigenous capacity to conduct the research is severely limited. The lack of appropriate infrastructures, expertise and resources are major constraints. Externally supported research that does not address this issue of development of capacity in research may greatly limit the long-term value of research.

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464 Gross Domestic Product.

465 As above, 21.

466 Benatar 'The HIV/AIDS pandemic: a sign of instability in a complex global system' in Van Niekerk and Kopelman (eds) (2005) 75.

467 As above, 83.

468 The Nuffield Council on Bioethics was established by the Trustees of the Nuffield Foundation in 1991 to identify, examine and report on the ethical questions raised by recent advances in biological and medical research. Since 1994, if has been funded jointly by the Nuffield Foundation, the Medical Research Council and The Wellcome Trust <http://www.nuffieldbioethics.org/go/print/aboutus/page_2.html> (15 January 2007).

469 CRD (1990) *Health research: Essential link to equity in development.*

470 *The ethics of research related to healthcare in developing countries* (n 462 above) 22.

471 As above.

472 As above.

473 As above, 22.

Developing countries in sub-Saharan Africa and elsewhere, to a large extent, rely on research sponsored by developed countries. Considering high levels of poverty, social inequality and human rights violations, it is patently obvious that in this climate there exist endless possibilities for the exploitation of research participants.[474]

4.3.2 Exploitation

A criticism of clinical research in developing countries is that it is exploitative.[475] Not only the participants enrolled in research in developing countries are exploited, so too are their communities who support and bear the burdens of research. In 1997, in the wake of the controversy surrounding the short-duration perinatal HIV transmission trials in developing countries, Lurie and Wolfe described the potential exploitation of research participants:[476]

> Residents of impoverished, post-colonial countries, the majority of whom are people of colour, must be protected from potential exploitation in research. Otherwise, the abominable state of health care in these countries can be used to justify studies that could never pass ethical muster in the sponsoring country.

The potential for exploitation in clinical research is heightened in developing countries where there is a lack of access to health care and other resources. Consequently, Africa should not be chosen as a setting for research merely because of the 'convenience' of the setting and the vulnerability of its inhabitants.[477]

What should researchers and sponsors do to ensure that participants in clinical research in Africa are not exploited?

Much of the debate is about the acceptable standard of care that should be provided to research participants in developing countries,[478] as was seen in the controversy over the HIV vertical transmission trials in Uganda,[479] and revolves upon the question whether the new intervention or drug that is being tested should be measured against the standard of care of the host or that of the developing country.[480]

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474 It is also self-evident that, despite the prevailing circumstances, research sponsored by developed countries and carried out in developing countries need not, by definition, be exploitative.

475 Macklin (n 405 above) chs 1, 3 and 4; Resnik (2003) 24 *Theoretical Med* 233.

476 Lurie and Wolfe (n 333 above) 853.

477 Barry (1988) 319 *New Engl J Med* 1085.

478 See eg Geller *et al* (2004) *Intl J Gynecology and Obstetrics* 268.

479 See para 4.2.2 above.

480 Macklin (n 405 above) 38 – 65; Geller 268.

Ethicists distinguish between universal and local standards of care.[481] A universal standard of care reflects the best standard of care available in the world; usually, the standard of care available in developed countries. A local standard of care is the level or standard of care available in a specific region. For example, the universal standard of care to prevent perinatal transmission of HIV may be Nevirapine, yet the local standard of care in Somalia does not exist or is a course of vitamin A.

Because of the obligation to provide members of a control group in a randomised placebo-controlled clinical trial with the best proven treatment, in other words, the existing standard of care, the content of the term 'standard of care' becomes very important. It is cheaper on the basis of how the term is defined for a research sponsor company to conduct a clinical trial on a new drug to prevent perinatal transmission of HIV in Somalia than it will be to conduct the same trial in the UK. Equivalency trials[482] not only take longer than placebo-controlled trials and, consequently, cost more money, but, in the UK, researchers will have to provide Nevirapine to thousands of volunteers in the control group as that is the standard of care.

It is not always feasible to deliver the universal standard of care. In the case of developing countries, alternatives often have to be sought to make a treatment easier to administer, or more affordable, but, this reality should not excuse the exploitation of those who are vulnerable in order that cheaper or speedier results may be obtained in a clinical trial.

Geller *et al* remark that the CIOMS Guidelines have recently introduced a new nuance into the debate on 'standard of care'.[483] The CIOMS guidelines call for the 'highest attainable and *sustainable* therapeutic method'; their comment on this development is:[484]

> Sustainable refers to the level of treatment that one can reasonably expect to be continued in the host country after research has been completed. As such, sustainability often serves as a constraint on the highest attainable therapeutic

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481 Article II 3 Declaration of Helsinki originally referred to 'best proven diagnostic and therapeutic method' (1996 revision), but now reads (2000 revision): 'In any biomedical research protocol every patient-subject *including those from the control group*, if any, should be assured that he or she will not be denied access to the best proven diagnostic, prophylactic or therapeutic method *that would otherwise be available to him or her*.' (My emphasis.)

482 Where the control group is given the best proven treatment, in this case Nevirapine; the treatment group is given the new (experimental) treatment.

483 Geller (n 478 above) 268.

484 As above.

> method, particularly if the host country cannot maintain the considered therapy after study completion.

The last word in the standard of care debate goes to Ruth Macklin. She writes:[485]

> The main reason why I reject the typical "standard of care" argument is that it is the lowest-common-denominator basis for determining ethical obligations. If the principle of beneficence has any relevance to the conduct of research, it requires researchers to *maximize benefits* as well as to minimize harms. Since the research subjects themselves are surely among those who should be counted in seeking to maximise benefits, it follows that providing a higher standard of care during the research, when that is feasible, is ethically preferable to providing the minimal standard dictated by background conditions in the country or region.

A related issue is the level of care that is provided to research participants and their community, not only during the clinical trial but also at its conclusion.[486] A trial participant who responds well to the treatment that was tested may deteriorate if that treatment is withdrawn at the end of the clinical trial. What is at stake is a claim that sponsors of research have a responsibility to share the benefits of their research with participants. In this regard, the Declaration of Helsinki requires that:[487]

> [a]t the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified in the study.

As is always possible, the term 'assured of access' is open to interpretation, as is the case with CIOMS Guideline 15:

> As a general rule, the sponsoring agency should agree in advance of the research that any product developed through such research will be made reasonably available to the inhabitants of the host community or country at the completion of successful testing.

Again, the words 'made reasonably available' are open to interpretation – and could mean anything from 'provided for free' to 'marketed in the country in question'.

Paragraph 9.3.5 of the Clinical Trials Working Group of the South African Department of Health's Good practice guidelines[488] directs:

> Where a patient has a therapeutic response to a study drug, that patient should be offered ongoing treatment. In designing studies, consideration should be given to the costs of long term provision of study drugs and of clinical monitoring, including the costs of medical staff.

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485 Macklin (n 405 above) 38 – 39. Original emphasis.

486 For a detailed discussion on this topic, see Dickens 'Research ethics and HIV/AIDS' (1997) *Med and L* 187 – 19 and Macklin (n 405 above) 36 - 65.

487 Guideline 30.

488 See above, para 3.3.3.

Crouch and Arras criticise the requirement of offering ongoing treatment,[489] arguing that it is unreasonable to expect those funding research to commit themselves in advance to making available a treatment with only a hypothetical chance of succeeding, with hypothetical costs and benefits.[490]

The question as to whether the wider community should be provided with the study drug or intervention if that drug or intervention is successful is also controversial. Even the definition of 'community' is contentious – as is pointed out above, a 'community' could be those who took part in the clinical trial, that is, the treatment and control group, or the entire village, province or country.

Researchers have a responsibility towards their participants, expressly, if harm is caused by their research. Guideline 13 of the CIOMS Guidelines requires:

> Research subjects who suffer physical injury as a result of their participation are entitled to such financial and other assistance as would compensate them equitably for any temporary or permanent impairment or disability. In the case of death their dependants are entitled to material compensation. The right to compensation may not be waived.

Ideally, research conducted in Africa should match the health-care priorities of the host[491] developing country.[492] The example of the research into Burkitt's lymphoma in Africa seems egregious. Burkitt's lymphoma is a tumour that accounts for half of all childhood cancers in Africa,[493] but affects only two in every 100 000 African children per year, and is a very rare cause of death when compared to malaria which in some areas account for up to 20 per cent of childhood deaths.[494] Research into the disease would be considered a luxury in most African countries and not a priority. Yet Burkitt's lymphoma has been researched extensively in Africa by sponsoring countries.[495]

In order to obviate this situation, the Nuffield Council on Bioethics recommends:[496]

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489 Crouch and Arras *Hastings Center Report* (1998) 26 – 34.

490 As above, 29.

491 The country in which the research is conducted is referred to as the 'host' country in the literature. The developed country sponsoring the research is the 'sponsoring' country.

492 Barry (n 477 above) 1085. See also CIOMS Guideline 8.

493 *The ethics of research related to healthcare in developing countries* (n 461 above) 31.

494 As above. Unlike HIV/AIDS, malaria and other illnesses that kill countless more children.

495 29.

496 30.

> that when research funded by external sponsors is proposed which fall outside the national priorities for research into healthcare set by a host country, those proposing the research be required to justify the choice of research topic to the appropriate research ethics committee in both the host and sponsoring countries.

Research is considered non-exploitative only if the developed, sponsoring nation, as well as the developing nation, benefits, more or less equally.

Sponsors of clinical trials mostly offer participants a form of inducement to take part in clinical research. The inducement ranges from cash payments, access to free medical care during the trial, free medication, reimbursements for transport to and from trial sites, meals on days that participants have to visit a trial site and so on. In poor communities, even the promise of a free trip into town to visit the trial doctor is a rare opportunity; to shop, visit family members and see friends.

In communities where there is great poverty and deprivation, inducements may, by their nature, be exploitative. Trial participants agree to take part in research solely to access the benefits. In this way they may be exposed to a risk they might otherwise have found unacceptable. In the case of significant risk attached to participation in a clinical trial, researchers in African countries should be careful not to exploit the needs of the host community for medical care or food inducing them to enrol in research. If there is no other access to medical care, seriously ill people and their families may agree to take part in risky experimentation because they have no choice and so be exploited. In this case the research is not ethically justified:[497]

> What appears a horizontal relation of difference among equals may in fact be a vertical distinction of power. Developed countries may have the power of prestige, inducement, wealth or authority to persuade dependant populations in developing countries, at nation, group or individual levels, to accept participation in research studies that pose risks to their physical integrity, emotional health or, for instance, confidentiality. Poverty and related powerlessness leave individuals and groups vulnerable to exploitation and easy inducement to accept disproportionate risks of research participation.

This idea is revisited in chapter 6.

4.3.3 Distributive justice

'Distributive justice', defined as the fair, equitable, and appropriate distribution of goods governed by justifiable norms and values that structure the terms of social

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497 Dickens 196. This idea is reassessed in chs 5 and 6 below.

cooperation,[498] entails a fair and equitable distribution of all rights and responsibilities in society.[499]

The just distribution of benefits and burdens has long engaged the attention of philosophy. Each theory, discussed in paragraph 2 above, has answered the question of how to fairly distribute goods and burdens in society differently. Utilitarianism aims to maximise public utility as a universal principle; communitarian theories, on the other hand, stress traditions of justice that have evolved in different communities.[500] The purpose of the enquiry in this thesis is not to enlarge the philosophical debate, but to understand the practical implications of the principle for clinical research.[501]

In the arena of clinical research, distributive justice determines that there should be fair access to research, which, necessarily, incorporates fair access to participation in, and the benefits of, research.[502] In keeping with the principle of distributive justice, the Declaration of Helsinki requires that participants not be exposed to unnecessary risk and that the risk should be in proportion to the potential benefits of the research.[503] Notions of distributive justice, further, embody the wish that the burdens and benefits of research be fairly distributed among individuals, communities and countries. Ideally, an individual, group, community or country cannot be expected to bear a disproportionate share in the burden of research, nor should they gain a disproportionate share in the benefits of research.

The relevance of the demand for distributive justice in research in Africa is clear: research participants in Africa need access to the benefits created by research but should not be expected to carry a disproportionate share in the burden of research.

Because Africans carry the greater burden in terms of HIV/AIDS, it is viewed as acceptable that they bear a greater share of the risk in research in the field. Clearly, the research into HIV/AIDS and its treatment should relate to African circumstances, for example, research into the efficacy of a vaccine for HIV that does not focus on strains of the virus most prevalent in Africa will not be justified.

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498 Beauchamp and Childress 226; Barry 1085.
499 Beauchamp and Childress 226.
500 230.
501 See Walzer (1983) 3 – 28 for an interesting philosophical (communitarian?) view on the distribution of goods in society.
502 n 497, 227.
503 Art I.4 Declaration of Helsinki.

Similarly, research that results in a drug that is highly successful in treating the disease, but which is only affordable in developed countries, in terms of the demands of the distributive justice principle, is unjustifiable and amounts to exploitation of the research participants. Annas and Grodin's comments are pertinent in this regard:[504]

> Unless the intervention being tested will actually be made available to the impoverished populations that are being used as research subjects, developed countries are simply exploiting them in order to quickly use the knowledge gained from the clinical trials for the developed countries' own benefit. If the research reveals regimens of equal efficacy at less cost, these regimens will surely be implemented in the developed world. If the research reveals the regimens to be less efficacious, these results will be added to the scientific literature, and the developed world will not conduct these studies.

In the case of HIV vaccine trials to find an effective preventive vaccine against HIV, it is submitted that an efficacious vaccine should be made available to the communities who participated in clinical trails to develop it. Macklin uses the example of the AIDSVAX vaccine, where its developer, VaxGen, had promised to make it available to the Thai volunteers who received a placebo during clinical trials.[505] She remarks that such a commitment is in strict compliance of the Declaration of Helsinki. VaxGen also committed themselves to a tiered pricing of the vaccine, which could have increased the likelihood that a successful product eventually could have been available in Thailand.[506] Unfortunately, the AIDSVAX vaccine proved ineffective.[507]

The abuse of research discussed previously[508] illustrates the consequences of ignoring the principle of distributive justice.

4.4 Conclusion

The preceding pages examined the way in which ethical theories and guidelines have been employed to protect the interests of research participants in HIV/AIDS-related clinical research in Africa. This examination sets the scene for a more detailed discussion in Chapter 5 of preventive HIV vaccine efficacy trails in South Africa.

The overview of the failures of ethical guidelines to safeguard research participants in the rest of the world, at the beginning of the chapter, highlights that,

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504 Annas and Grodin (1998) 88 *American J Public Health* 561.
505 Macklin (n 405 above) 257.
506 As above.
507 See para 4 of ch 2 above.
508 Paras 4.2.1 (a) – (c) above.

although ethical guidelines existed, abuses still occurred. The discussion of the influence of the HIV/AIDS epidemic on the ethics of clinical research emphasises the shift from a situation previously in which the medical and scientific community viewed the role of research participants as passive, to one in which they are regarded as agents as well as autonomous beneficiaries of the products of research.

The account of the much-publicised ethical dilemma that arose over the use of a placebo in the AZT trials to prevent MTCT of HIV in Uganda demonstrates that despite the ethical guidelines, interpretation and implementation remain controversial areas and abuses still occur. Sometimes pharmaceutical companies use the urgency of the situation to justify unethical research, as is shown in the discussion of the Trovan trial in Nigeria.

Finally, the examination has shown research participants in developing countries to be especially vulnerable, which introduces the ethical concerns relevant to the discussion of the ethics of preventive HIV vaccine efficacy trials in Chapter 5 below.

5 CONCLUSION

Clinical research on human participants is subject to a superfluity of ethical guidelines. The Chapter explores the origins and nature of the ethical principles that form the foundation of the protection of human research participants in clinical research. The scope of core ethical principles, namely autonomy, beneficence (including nonmaleficence) and justice, as they are embodied in various international and domestic documents, is presented.

The protection afforded by international and national ethics documents is investigated. Although, at fist glance, such protection appears to be extensive, the survey of past non-compliance presented in paragraph 4.2.1 demonstrates that in practice, ethical guidelines do not usually function in preventing abuse.

This failure may be attributed to two causes:[509]

First, ethical guidelines are only that – guidelines – they do not have the force of law, and, therefore, cannot be enforced in the same way that law may be enforced. In the case of transgression, fierce ethical debate may follow, but little else can be done unless publicity drives government to act. Though the editor of the *New England Journal of Medicine*, Marcia Angell, regards the HIV perinatal

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509 For a more extensive discussion on the failures of ethical guidelines to protect the interest of research participants, see pare 4.1 of ch 6 below.

transmission trials[510] as unethical, she published the results in the journal. To a large extent, observance of ethical guidelines depends on the sanction of various professional bodies and research funding agencies. Other than a refusal to fund or publish unethical research, there is little to guard against such research.

Second, ethical principles such as autonomy, beneficence and justice are too general, too vague and ambiguous, to be of much value in specific practical circumstances. The same could be said about legislation. Legislation, however, is given content by interpretation in the courts, whereas ethical principles, on the whole, are rarely litigated.[511] The perinatal HIV transmission trials again serve as a case in point. During the debate on the ethics of these trials, both camps used similar ethical principles in support of their arguments.[512] As well, there was no institution or body that was able to finally determine who the 'winner' in the debate was; no court could give an authoritative interpretation of the relevant principles and the disputed practice.

The chapter analyses the ethical dilemma that was presented in the controversy over the placebo-controlled trials of AZT to prevent MTCT of HIV in Uganda.[513] This analysis not only points to the non-binding nature and inherent

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510 See para 4.2.2 above.

511 There are exceptions where ethical principles were litigated in court. See ch 5 below.

512 See Angell (n 336 above) 847; Lurie and Wolfe (n 333 above) 853; Varmus and Satcher (n 357 above) 1003.

513 The chapter presents only a few examples of unethical research conducted in Africa. Subsequent to the controversy over the ethics of the MTCT trials in developing countries, the *Lancet* in 1999 and the *New England Journal of Medicine* in 2000 published the results of yet other clinical trials (also in Uganda) where the ethics of the investigators are questionable. I refer to the clinical trials of Quinn *et al* that was described in 'Viral load and heterosexual transmission of human immunodeficiency virus type 1' (2000) *New Engl J Med* 921 – 929 and Wawer *et al* 'Control of sexually transmitted diseases for AIDS prevention in Uganda: A randomised community trial' in (1999) *The Lancet* 525 – 535. During the first of the trials, rural Ugandan villagers (who included a number of pregnant women) were studied to determine the risk factors associated with heterosexual transmission of HIV and whether sexually transmitted diseases, such as syphilis and gonorrhoea, increased the risk of transmission of the virus. Villagers in the treatment group were given antibiotics to treat and reduce the incidence of these diseases; in the control group they were given no antibiotics. In the second trial the investigators wanted to study the link between viral load and HIV transmission and the influence of circumcision on transmission of the virus. Couples in which one partner was HIV-positive and the other negative were studied during the trial. Not only were the participants not given any treatments, but, even though both partners were often seen by the investigators, no information was given on safe sex practices. More importantly, the HIV-negative partner was not informed of the status of the positive partner. Participants who were found to suffer from other sexually transmitted diseases were left to seek treatment elsewhere. The abuses described in the Tenofir clinical trials in Cameroon and Nigeria (see para 4.2.2 above and Akoa (2005) 15

ambiguity of principles and ethical guidelines, it highlights some of the priorities of health care provisioning and research in a developing country, such as finding easy and affordable alternatives to complicated or expensive HIV treatment regimens. It further emphasises the disparity that exists in health care provision between developed and developing countries or between resource rich and resource-poor settings. Other contentious issues arising out of clinical trials in Africa are commented upon in further examples.

The question of whether research participants in HIV and AIDS-related clinical research in sub-Saharan Africa should be afforded special protection is the final issue that has been raised. Poverty, social inequality, a lack of resources and a heavy burden of disease make health and HIV-related research in sub-Saharan Africa an imperative, but they are the cause of the situation being fraught with the potential for the abuse of research participants.

The chapter does not offer an extensive critique of principlism in bioethical discourse, such as that presented by feminist and also communitarian theorists. Such a critique forms the substance of some of the conclusions reached in chapters 5 and 6 below and will therefore be dealt with in those chapters.

The next chapter examines human rights as an alternative system in the protection of participants in HIV-related clinical research in Africa, especially seen in the light of the defects in the system of bioethics currently used. The foundation for a more detailed discussion in chapter 5 on preventive HIV vaccine efficacy trials in South Africa is established.

Interights bulletin 66 – 68) are another case in point. Also see Angell 'Investigators' responsibilities for human subjects in developing countries' (2000) *New Engl J Med* 967 – 968.

CHAPTER 4

HUMAN RIGHTS IN CLINICAL RESEARCH IN SUB-SAHARAN AFRICA: AN ALTERNATIVE TO ETHICS?

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7 Conclusion

1 INTRODUCTION

Chapter 3 examined non-binding ethical guidelines, whereas this chapter explores human rights law as an alternative means for the protection of participants in clinical research in Africa. Human rights law is examined as a system consisting of both international human rights law and national human rights law; each, in turn, composed of binding regulations and so-called 'soft law'.

First, the origin and nature of human rights are explored; a philosophical background to the development of the notion of human rights is given; and arguments relating to the universality or relativity of human rights are outlined. The effects of the forces of globalisation on the international research endeavour are investigated, as well as the interaction between national and international human rights law.

Second, national human rights systems in African countries are scrutinised for specific human rights provisions relating to the protection of participants in clinical research in sub-Saharan Africa. Particular attention is paid to the South African Bill of Rights.

Third, the development and impact of the United Nations' Charter-based and treaty-based systems are explored; three regional systems are outlined; and the African system is discussed in greater detail. Fourth, a critical examination of the protection which international and regional human rights documents and instruments offer participants in clinical research in Africa is presented. Finally, international human rights documents are situated in a South African context. Sections 39(1), 231, 232 and 233 of the Constitution are detailed, and the status of specific international human rights instruments in South Africa is charted.

The focus of this chapter is on HIV-related clinical research in general, and it mentions preventive HIV vaccine efficacy trials only in passing. The foundation for the discussion in chapter 5, which deals specifically with informed consent in HIV vaccine efficacy trials in South Africa, is still being laid.

The focus in the chapter is on clinical research in *sub-Saharan* Africa and not the African continent because sub-Saharan Africa is hit hardest by the HIV epidemic - two thirds or almost 64 per cent of all adults and children living with HIV/AIDS globally are in sub-Saharan Africa, amounting to almost 25 million people.[1] In comparison, Africa north of the Sahara reflects scant evidence of an epidemic.[2] With exception of Sudan,[3] national adult HIV prevalence in the countries of North Africa and on the Red Sea is low, not exceeding 0.1 per cent.[4]

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1 UNAIDS (2006) *AIDS epidemic update* 15.

2 As above.

3 In Sudan, national adult HIV prevalence rate was an estimated 1.6% in 2005. The epidemic is most severe in the country's southern areas (which are flanked by countries with comparatively high HIV prevalence) (UNAIDS 48).

4 UNAIDS (n 1 above) 48.

Moreover, almost nine in ten children (younger than 15 years) living with HIV are in sub-Saharan Africa.[5] An estimated 2.7 million people in the region are newly infected with HIV, and 2.0 million adults and children have died of AIDS.[6] Three-quarters of all women (15 years and older) living with HIV are in sub-Saharan Africa.

These statistics illustrate that it is not a single 'African' epidemic; HIV prevalence rates vary significantly between and within the regions and countries in Africa.[7]

An examination of human rights law as an alternative system for the protection of participants in clinical research in sub-Saharan Africa follows below.

2 HUMAN RIGHTS LAW

2.1 Introduction

Although a great deal of attention is paid in the literature to ethical guidelines governing clinical trials involving human subjects, only limited work has been done on the human rights of trial participants.[8] In the past, violations of the interests of participants in clinical research by trial administrators were viewed as violations of universal (biomedical) ethical principles and not as violations of the human rights of trial participants.[9] This view is to be expected, as clinical research is in the domain of the medical profession and medical professionals who, although well-versed in medical ethics, are relatively unfamiliar with human rights discourse.

In contrast to the traditional approach, this chapter places HIV-related clinical research in Africa within the context of human rights discourse. In the following section, the origins and development of the idea of human rights are explored.

2.2 Conceptual framework

There is an extensive philosophical literature on the definition and nature of rights; for example, the so-called choice or will theories of rights; or alternatively, interest or

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5 As above, 15.

6 As above.

7 As above.

8 In the work of Jonathan Mann alone, who was the head of the WHO's Global plan on AIDS (now the UN joint programme on AIDS or UNAIDS), is there a focus on the link between health and human rights and their value in ensuring human well-being. See eg Mann *et al* (eds) (1999) *Health and human rights: A reader*.

9 See for example, the debate regarding the supposed unethical nature of the short-duration AZT trials in Africa, discussed in ch 3 above.

benefit theories of rights.[10] However, most authors agree on the definition that rights are the *justified claims* of individuals and groups against one another or society.[11] Such justified claims may refer to the right holder being *entitled* to something, thus placing a correlative duty on another person or state; they may refer to *immunity* from having one's legal status altered; they may refer to a *privilege* to do something; and they may also refer to a *power* to create a legal relationship.[12]

The existence of a right presupposes a set of rules under which that right is justified – whether these are legal rules, moral rules, institutional or religious rules.[13] Legal rights, therefore, are claims based upon legal rules.[14]

To have rights enables one to determine what other persons (or the state) should or should not do.[15] In accounting for the moral foundations of liberalism, Joseph Raz determines that rights are 'grounds for holding others to be subject to duties'.[16]

Generally speaking, rights are not absolute.[17] Rights may be limited by other people's rights as individuals or by the interests of society in general. Rights are '*prima facie* claims' which may yield to other claims.[18]

Human rights are a specific type or subspecies of rights. Human rights are born out of the idea that, as human beings, we possess intrinsic rights[19] which are

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10 This thesis is primarily concerned with a specific type of rights – human rights – consequently no account of these theories is given. For more on the different theories of rights, see for example Jones (1994) *Rights*; Freeden (1991) *Rights*; Nelson (2005) 31 *Social Theory and Practice* 359; Kramer *et al* (1998) *A debate over rights: Philosophical enquiries*; Sumner (1987) *The moral foundation of rights* (ch 5); Lyons 'Utility and rights' in Waldron (ed) (1984) *Theories of rights* and Wellman (1985) *A theory of rights: Persons under laws, institutions and morals*.

11 See eg Brown 'Universal human rights: A critique' in Dunne and Wheeler (1999) 105; Beauchamp and Childress (2001) 357. This idea of rights as claims is not universally held - see eg Nelson (n 10 above) 362 – 365.

12 Shestack (1998) 20 *Human Rights Q* 203.

13 Brown in Dunne and Wheeler (n 11 above) 105; Shestack (n 12 above) 203; Beauchamp and Childress (n 11 above) 357.

14 As above.

15 Beauchamp and Childress 357.

16 Raz (1984) 4 *Oxford J Legal Studies* 5.

17 As above.

18 As above.

19 The intrinsic nature of human rights is much disputed. Michael Ignatieff, for example, argues that the Holocaust demonstrates that human rights can have no foundation whatever in natural human moral attributes, since that event negates or explodes the myth of natural human pity or solidarity as being either innate or universally distributed. There can thus be no intrinsic or 'natural' moral attributes among human beings (see Ignatieff (2001) *Human rights as politics and idolatry* 80 - 81).

held to be self-evident.[20] In other words, the idea of human rights emphasises that, simply because we are human beings, there are certain things that should never be done to us, and certain things that should be done to and for us. The idea is not new, and is traceable back at least to the writings of philosophers of the 16th and 17th century.[21]

Human rights have been defined as 'universal moral rights' or 'generally accepted principles of fairness and justice' or 'universal rights that belong to all people simply because they are human beings'.[22] It is claimed, currently, that that human rights are the *only* universally recognised system of values.[23]

Descriptive definitions characterise human rights as the 'sum of civil, political, economic, social cultural and collective rights laid down in international and regional human rights instruments, and in the constitutions of states',[24] or as the 'only universally recognised value system under present international law comprising elements of liberalism, democracy, popular participation, social justice, the rule of law and good governance'.[25]

From these definitions, it can be observed that the concept of human rights is open to varying interpretation. One view holds that human rights are inherent in humankind by virtue of its members being human; the other view is that human rights are concerned primarily with the relationship between the individual - or groups of individuals - and the state. In this view, the individual or group is seen as, potentially, the victim of the state's exercise of authority. In liberal democracies the individual is the ultimate 'owner' of human rights, and the protection of human rights takes the form of a 'bill of rights' which may be invoked against the will of the state or group within a state. Jerome Shestack writes as follows about some of the definitional difficulties inherent in the term 'human rights':[26]

> Some scholars identify human rights as those that are 'important', 'moral', and 'universal'. It is comforting to adorn human rights with those characteristics; but, such attributes themselves contain ambiguities. For example, when one says a right is 'important' enough to be a *human* right, one may be speaking of one or more of the following qualities: (1) intrinsic value; (2) instrumental value; (3) value to the

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20 Self-evident in the sense that they are human beings have rights simply because they are human - in other words independent of 'varying social circumstances and degrees of merit' (Shestack 203).

21 Discussed in para 2.3 below.

22 Jerome Shestack defines human rights as 'a set of moral principles [of which the] justification lies in the province of moral philosophy' (202).

23 Nowak (2003) 1.

24 As above.

25 As above.

26 Shestack (n 12 above) 203.

> scheme of rights; (4) importance in not being outweighed by other considerations; or (5) importance as structural support for the system of the good life. 'Universal' and 'moral' are perhaps even more complicated words. What makes certain rights universal, moral, and important, and who decides?

In the section below the philosophical nature and origin of the idea of human rights are traced in an attempt to provide an answer to a few of Shestack's questions.

2.3 Philosophical background

The contemporary concern with the protection of human rights was born out of a widespread sense of horror at the devastation caused by World War II. The human rights enumerated in the Universal Declaration on Human Rights[27] were intended to address and to redress in some form the atrocities the National Socialist government in Germany committed against the Jewish people during World War II, as well as the crimes of the Japanese Imperial government.[28] The hope was that these rights should serve as a protection for future generations against a repetition of such barbaric behaviour on the part of any state.

However, the post-war era is certainly not the first occasion that reference has been made to human rights, or, to rights that attach to human beings by the mere fact that they are human. Throughout the centuries, the basis of what is now known as human rights has been established among various religions, cultures and peoples. Nowak points out that the value system manifested in human rights is not specifically Western in nature, and that it may be found among all major cultures[29] and religions of the world.[30]

In the Age of the Enlightenment in Europe and in accordance with the theory of natural law, there is a formal realisation that individuals are not objects, but subjects, with rights against society.[31] This shift in focus places individuals at the centre of legal and social systems.[32]

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27 See para 3.1.1 below.

28 Twiss (2004) 32 *J Religious Ethics* 42.

29 In an article on her theory of capabilities and human rights, Martha Nussbaum attempts to identify a range of 'central elements of truly human functioning that can command a broad cross-cultural consensus'. These elements, she argues, permit us to understand why diverse cultures accept human rights norms (See Nussbaum (1997) 66 *Fordham L Rev* 292 – 297).

30 Nowak 9. The moral values underlying human rights may be found in all religions of the world. See Nowak 9 for an interesting outline of the 'golden rule' or moral commandment to be found in all religions. See Shestack (n 12 above) 205 – 206 for his idea that, in a religious context, every human being is considered sacred.

31 Nowak (n 23 above) 9.

32 As above.

In their search for a law that was higher than positive law, the philosophers of the Enlightenment drew on theorists such as Sophocles, Aristotle, the stoics and thinkers of the Greek Hellenistic period. For these philosophers, natural law embodied those 'elementary principles of justice' which were 'right reason', that is, in accordance with nature and never-ending.[33]

The idea of 'natural law' also is not entirely new.[34] George Annas points out that in Sophocles' play, *Antigone*, written over 2400 years ago, there is mention of a higher, universal law to which all humans are held accountable.[35] Antigone justifies her defiance of the king on the basis of this higher, unwritten, moral law: 'Nor did I think your edict had such force that you, a mere mortal, could override the gods, the great unwritten, unshakable traditions'.[36]

Finnis ascribes the basis of the idea of natural law to:[37]

> (i) [a] set of basic practical principles which indicate the basic forms of human flourishing as goods to be pursued and realised, and which are in one way or another used by everyone who considers what to do [and] (ii) a set of basic methodological requirements of practical reasonableness ... which distinguish sound from unsound practical thinking, and which, when brought to bear provide the criteria [which enable us] to formulate (iii) a set of general moral standards.

Enlightenment thought also resulted in a shift in perception with regard to the state and its legitimacy.[38] The state is no longer legitimised by divine order; 'God's anointed King' is 'dethroned' as head of state and the individual as legal subject replaces the individual as legal object. Some interpretations of the social contract caused a shift in understanding, so that the existence of the state is justified solely by the need to protect the natural rights of the individual.[39]

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33 Shestack (n 12 above) 206.

34 Ideas about the source of natural law have varied through the centuries – it has been ascribed to the different gods and to human reason and respect for human dignity. The Nuremberg trials of war criminals rested on the premise that there exists a higher law of humanity and that violators of that law may be tried for their actions.

35 Annas in Gostin (ed) (2002) 99.

36 As above. Shestack points out that, with the decline of feudalism, modern secular theories of natural law emerged, such as those of Grotius and Pufendorf. These theorists detached natural law from religion, laying the foundation for a secular, rationalistic version of natural law (Shestack 206 – 207).

37 Finnis (1980) 23.

38 As above.

39 As above.

The natural rights of the individual are rights inherent in the individual, such as the right to life, property, security and liberty.[40] Natural law thinkers of as varied dispositions as John Locke, Thomas Paine and Jean-Jacques Rousseau, argued that natural rights were the inalienable fundamental freedoms and basic rights of every individual against the unrestricted power of the state.[41]

John Locke imagined the existence of human beings in a state of nature as being a state of freedom and equality, in which they are able to determine their actions and in which no one is subject to the will of another.[42] To escape the hazards of the state of nature Locke's men and women enter into a 'social contract',[43] by which they agree to set up a community and form a political state.[44] In setting up a political authority they retain their natural rights to life, liberty and property.[45] Government's obligation to protect the natural rights of its subjects is the sole source for the validity of its actions.[46] John Locke writes: 'the great and chief end, therefore, of men uniting into commonwealths, and putting themselves under government, is the preservation of their property – that is, their lives, liberties and estates.'[47]

Natural rights theory provided the 'philosophic impetus' for revolution during the late 18th century.[48] Shestack sums up the contribution of natural rights theory to human rights:[49]

> [Natural rights theory] affords an appeal from the realities of naked power to a higher authority that is asserted for the protection of human rights. It identifies with and provides security for human freedom and equality, from which other human rights easily flow. It also provides properties of security and support for a human rights system, both domestically and internationally.

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40 As above. Nowak points out that the schools of thought upon which the concept of human rights of the Enlightenment was founded were those of political liberalism and democracy.

41 Nowak (n 23 above) 9.

42 Shestack (n 12 above) 207.

43 Shestack 207.

44 As above.

45 As above.

46 As above.

47 Locke (1690) *Two treaties of government*. Opposed to this version of natural rights is legal positivism, a doctrine which replaces natural theory during most of the 19th century and 20th century. Legal positivism denies the existence of a *priori* sources of law. For the positivist theorist, all authority stems from the state and its officials. The source of law is to be found only in the enactments of the system of law. Positivism separated the legal system from the ethical and moral foundations of society; no matter how immoral a law may appear to be, it should be obeyed without question, for the law is all there is. See Shestack 209 – 210.

48 Shestack 207.

49 Shestack 208.

> From a philosophical viewpoint, the critical problem that natural rights doctrine faced is how to determine the norms that are able to be considered as part of the law of nature and therefore inalienable, or at least *prima facie* inalienable.

The critical problem Shestack proposes is the central criticism of natural law: the rights considered to be 'natural' by natural law may differ from theorist to theorist, or situation to situation.[50]

The notion of human rights outlined in natural law has close links to the philosophical theory of liberalism or liberal individualism. Liberal individualism indicates a space in which the individual pursues his or her own personal objects.[51] The individual must fulfil himself or herself without interference by the state, church or society.[52]

Central to liberalism is the protection of the basic liberties and interests of the individual. In the essay 'On Liberty' (1859), John Start Mill writes as follows:

> The object of this essay is to assert one very simple principle, as to govern absolutely the dealings of society with the individual in the way of compulsion and control, whether the means used be physical force in the form of legal penalties or the moral coercion of public opinion. That principle is that the sole end for which mankind are warranted, individually or collectively, in interfering with the liberty of action of any of their number is self-protection. That the only purpose for which power can by rightfully exercised over any member of a civilised community, against his will, is to prevent harm to others ... Over himself, over his own body and mind, the individual is sovereign.

The liberal idea of human rights refers to what are sometimes called first generation civil and political rights, freedom of speech, religion, conscience and so on, which require the state to refrain from interfering in the freedoms of the individual. These are the core human rights of the Age of Enlightenment and constitute the substance of the achievements by the French and American Revolutions.[53]

In contrast, in the Russian and in other 'socialist' revolutions, precedence is claimed for economic and social rights.[54] Socialists argue that there is no necessary separation between the state, society and the individual.[55] Men and women in their

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50 Shestack points out that, because of this and other difficulties, natural rights theory became unpopular, only to experience a renaissance during the aftermath of World War II (208).

51 Beauchamp and Childress (n 11 above) 356.

52 Nowak 10.

53 Nowak (n 23 above) 10.

54 Nowak 11.

55 As above.

view are not autonomous individuals with rights derived either from a divine or an inherent nature, but are 'specie beings'.[56] Shestack comments as follows:[57]

> The Marxist system of rights has often been referred to as 'parental', with the authoritarian political body providing the sole guidance in value choice. The creation of such a 'specie being' is a type of paternalism that not only ignores transcendental reason, but negates individuality. In practice, pursuit of the prior claims of society as reflected in the interests of the Communist state has resulted in systematic suppression of individual civil and political rights.

In Marxian terms the philosophical basis for the natural law approach is idealist and 'ahistoric'; human rights are neither inalienable nor natural.[58] The notion of individual rights is an illusory product of bourgeois individualism.[59] The state alone grants rights and their exercise is 'contingent on the fulfilment of obligations to society and to the state'.[60]

In contrast to liberal 'negative' freedom, the socialist state enforces 'positive' access to economic and social rights. The Constitution of the Union of the Socialist Soviet Republics of 1936 included an elaborate catalogue of economic, social and cultural rights.[61]

The division into Western and Socialist ideologies, including human rights, continued throughout most of the 20th century. Nowak writes:[62]

> The conflicting ideologies of the classical human rights concept in the West and the socialist human rights concept in the East, ie of the first two generations, proved a considerable hindrance to human rights and their philosophical and political development right up to the end of the Cold War.

Apart from contributing to the development of a notion of so-called second generation rights, as Shestack remarks, on an international level Marxist concepts were incompatible with the functioning of an international system of human rights:[63]

> The prior claim of a Communist society does not recognise overruling by international norms ... Communist states repeatedly asserted in international *fora* that their alleged abuse of human rights was a matter of exclusive *domestic* jurisdiction, not just as a matter of protecting sovereignty or avoiding the embarrassment of international examination, but the assertions reflected communist theory of the unlimited role of the state to decide what is good for the specie beings.

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56 Shestack (n 12 above) 210.
57 Shestack 211.
58 As above.
59 As above.
60 As above.
61 Nowak 13.
62 Nowak 12.
63 Shestack (n 12 above) 211. Original emphasis.

In the aftermath of World War II there was a renewed concern that principles of morality should be established to protect humanity from a repetition of such events.[64] This concern revived the interest in natural law and natural rights theory, and was reflected in human rights instruments of the time. Phrases, such as 'inherent dignity',[65] 'inalienable rights of all members of the human family' and '[a]ll human beings are born free and equal in dignity', from the Universal Declaration of Human Rights,[66] assert the basic tenets of natural law and natural rights theories – that human beings are born free, autonomous, equal and possess inherent dignity.[67] These rights are seen as 'core' rights, from which all the other elements of a complete system of human rights can evolve.[68]

During the sixty or so years which follow World War II and the Universal Declaration of Human Rights, different theories of human rights have attempted to define the content of, and justification for, a system of human rights. For some, natural rights theories were deficient and outmoded in the late 20th century. John Rawls's theory of rights based on justice, as he expounds it in *A Theory of Justice*, for example, establishes principles of justice that provide 'a way of assigning rights and duties in the basic institutions of society'.[69] Rawls explains:[70]

> [e]ach person possesses an inviolability founded on justice that even the welfare of society as a whole cannot override ... Therefore in a just society the liberties of equal citizenship are taken as settled; the rights secured by justice are not subject to political bargaining or to the calculus of social interests.

A further contribution to the understanding of the origins of human rights are theories that see human rights as a reaction to injustice. Edmund Cahn's theory of 'justice' is such a theory. He writes, '"[j]ustice" ... means the active process of remedying or preventing what would arouse the sense of injustice.'[71] The need to right a wrong, according to Cahn, has the capacity to produce action, and from that need a set of rights arises.[72]

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64 Shestack points out that the horror and revulsion against Nazism coalesced with the rejection of a positivist interpretation 'where the individual counted for nothing' (215). See also Brown (n 4 above) 106 – 108 for a discussion of positivism as opposed to natural law as the philosophical foundation of human rights law.

65 Universal Declaration of Human Rights.

66 See para 3.2.1 below.

67 See Shestack 216 – 217.

68 Shestack 217.

69 Shestack 218.

70 Rawls (1971) 3 – 4.

71 Cahn (1949) 13 – 14.

72 Shestack (n 12 above) 224.

The sociological school[73] of jurisprudence contributes the notion of human rights as a system which is aimed at 'obtaining a just equilibrium of interests among prevailing moral sentiments and the social and economic conditions of time and place'.[74] Consequently, help for the unemployed, the handicapped and the underprivileged exert demands upon contemporary society that cannot be provided for by a system limited to civil and political rights.[75]

Philosophers have constructed theories about the moral basis of a comprehensive system of human rights based on utility,[76] dignity,[77] religion[78] and equality of respect and concern.[79] Although some theorists attempt to justify the existence of a system of human rights on an external set of norms or values, others are more pragmatic, as well as those who are described as 'intuitive',[80] holding that human rights grow out of the lessons we learn from history and from the social knowledge accumulated over time, independent of any specific philosophical theory or system of values. Jacques Maritain writes about:[81]

> the natural operation of spontaneous reason, pre-scientific and pre-philosophic ... at every stage conditioned by the acquisitions, the constraints, the structure and evolution of the social group ... a kind of plant-like formation and growth of moral knowledge and feeling ... independent of philosophical systems and their rational justifications ... where the principal part has been played by the lessons of history and by the kind of practical apprehension.

The thesis does not aim to provide an exhaustive philosophical overview of contemporary and post-modern theories about the origin, content, nature and

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73 Shestack regards the term 'school' to be a misnomer as the 'school' has developed from a number of disparate theories 'all trying to line up the law with the facts of human life in society' (211).

74 Shestack 212.

75 As above.

76 See Shestack 213 – 215.

77 Some human rights theorists have tried to construct a comprehensive system of human rights on a value-policy orientated approach focussed on the protection of human dignity. For philosophers such as Myres McDougal, the ultimate goal is a 'world community in which a democratic distribution of values is encouraged and promoted, all available resources are utilized to the maximum, and the protection of human dignity is regarded as the paramount objective of social policy' (Shestack 226).

78 See eg Perry (1998) *The idea of human rights: Four enquiries* 11 – 41.

79 Such as the theories of Ronald Dworkin. Dworkin postulates a premise that all governments should treat their citizens with equal concern and respect. According to him, no basis for any valid discourse on rights and claims exists in the absence of such a premise (Shestack 226).

80 See Twiss' use of the term to denote theorists who use a kind of 'moral intuitism' to argue that human rights need no explicit justification (Twiss (n 28 above) 60 – 61).

81 Maritain 'Introduction' in UNESCO (1948) *Human rights: Comments and Interpretations* i – ix, iv.

justification for the existence of human rights.[82] The aim is merely to indicate the theoretical foundations that shape the beginnings of an international human rights system in the late 1940s. The discussion concludes with a debate on an issue in contemporary human rights theory that is especially relevant to HIV-related clinical trials in Africa: Is there a place for a notion of cultural relativism in an international system of human rights?

2.4 Cultural relativism or universal human rights?

The concept of human rights, at its centre, has the basic assumption that human rights are universal, that is, that they apply to everyone, everywhere. The Vienna Conference in 1993 proclaimed that the 'universal nature of human rights is beyond question'.[83] If human beings have rights by virtue of their common humanity it can only be because there are general moral standards that are universal in application.[84] 'All human rights for all' refers to the indivisibility and interdependence of human rights,[85] economic, social and cultural rights are equivalent to civil and political rights and should have the same protection. Thus, the right to non-interference for individuals and groups and a right to positive state action are of equal significance.[86] Human rights are, in principle, applicable to all people whatever their class, race, religion or any other attribute.[87]

The debate raised by cultural relativism has its beginnings in the 20th century divisions with regard to different generations of rights, but gained impetus by claims in the developing world that the developed world uses human rights to pursue neo-liberal and neo-colonial policies.[88] Human rights norms impose a world political view upon peoples who have their own cultural and moral principles.[89]

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82 For a lucid exposition of these theories see Shestack (n 12 above) 215 – 226 and Twiss (n 28 above) 56 – 65.
It is also important to remember that there are many critics who express reservations about human rights - in this regard, see generally Kennedy 'The international human rights movement: Part of the problem?' (2002) 15 *Harvard Human Rights L J* 101.

83 Vienna Declaration and Programme of Action, adopted by the World Conference on Human Rights, 24 June 1993, UN Doc A/Conf 157/24 (Part 1), 13 October 1993.

84 See Brown (n 11 above) 106 – 108.

85 Nowak 14.

86 As above.

87 As above.

88 Twiss 57. See generally Renteln (1990) *International human rights: Universalism versus relativism* and Brown in Dunne and Wheeler (n 11 above); Donnelly 'Cultural relativism and universal human rights' (1984) 6 *Human Rights Q* 400.

89 They have argued for the separate, independent value of all cultures. During the 19th century, Western colonisers viewed the colonised peoples of the world and their cultures as barbaric and primitive. In reaction to this, the concept of cultural

Cultural relativism is essentially an anthropological and sociological concept and is loosely based on a theory of moral relativism[90], in which it is claimed that, because different cultures are widely disparate in terms of morality, customs, motivations and preferences, no human rights principles can be said to be self-evident, applicable equally to all peoples, at all times and in all geographic locations.[91] No human right is absolute, instead the society in which one is raised determines the way one views the behaviour of others, and customs are morally equivalent and equally valid, determined by time and place, and in the judgment of one's cultural peers.[92]

Shestack summarises the debate:[93]

> A universal moral philosophy affirms principles that protect universal, individual human rights of liberty, freedom, equality, and justice everywhere, giving them a nontranscient, nonlegal foundation. The relativists defend a cultural conditioning that supposedly reflects a set of wants and goods that members of disparate cultural groups share (and that may include various human rights goods), but are not wants and goods arrived at through individual choices or preserved for individuals in the community as a matter of right.

Cultural relativist arguments have been perverted in the justification of human rights abuses. Political elites reject universal human rights norms as a form of Western cultural imperialism exerted upon local culture. Cultural relativism has served to justify abuses of the right to freedom of speech[94] as well as the suppression of women through cultural practices, such as female genital mutilation in which their physical integrity is violated.

The United Nations, the supposed defender of the universal nature of human rights, adopts the relativist argument with regard to cultural practices. Thus, two UN

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relativism was posited at the end of colonialism to assert that all cultures are equally valid, and that no culture is superior to another. Cultural relativism was given a moral or ethical stance by anthropologists and sociologists – they argue that all cultures are morally equal and that universalist values (such as human rights) are dead (Shestack (n 12 above) 229 - 230).

90 There exists different 'schools' of relativism, such as cultural relativism, ethnic relativism and moral relativism. These schools cannot be seen as a homogenous group, neither can the theorists in each school be seen as holding the same relativist theory. The discussion above is therefore very broad.

91 Shestack 228.

92 As above. Shestack writes: 'To suggest that fundamental human rights may be overridden or adjusted in light of cultural practices is to challenge the underlying moral justification of a universal system of human rights, reflecting the autonomous individual nature of the human being' (Shestack (n 12 above) 228).

93 Shestack 230.

94 The most notable example is President Robert Mugabe of Zimbabwe who considers freedom of speech (or freedom of the press) as an example of Western imperialism.

Special Rapporteurs remarked in the case of a Mali woman who had been given a prison sentence in France for practicing female genital mutilation:[95]

> ... the importance attached to certain traditional practices in some communities must be taken into account ... [The Rapporteurs] firmly and unequivocally condemned all practices that violate individuals' physical integrity ... [but] felt nevertheless that punishments and sentences *based on value judgments* could sometimes be counter-productive and encourage communities to close ranks and cling to practices which ... are the *only means they have of expressing their cultural identity*. Such practices *should not be condemned* in the courts *except as a last resort* when education, information and the proposal of alternative rites ... have not been successful.

These arguments fly in the face of facts. First, most - if not all - cultures display basic universal assumptions about morality.[96] For example, all cultures demonstrate a concern for the value of human life; all oppose crimes, such as murder and rape; all cultures value truth, goodness and justice within groups.[97] For example, Abdullahi An-Na'im points out that the adage 'do unto others as you would want them to do onto you', is present in most societies.[98]

Second, cultural relativism presents culture as static, ignoring changes over time and that cultures accommodate varying individual responses to its norms.[99] Values that may be true for a certain culture at a certain time do change, and within individual cultures, there are clashes over the nature and identity of that culture. An-Na'im recognises that culture itself is not a homogenous or a monolithic institution, and that different versions of local cultures exist apart from the official state-sanctioned one.[100]

Third, change brought about by technology and communication prompt many societies to incorporate values other than those considered 'traditional' into their culture.[101] The role of globalisation in this respect cannot be underestimated.

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95 Observation by UN Special Rapporteur on Violence against Women and the Special Rapporteur on Traditional practices affecting the Health of Women and the Girl Child UN Doc E/CN.4/Sub.2/1999, para 75. (My emphasis.)

96 In this regard, see Yasuaki 'Towards an intercivilizational approach to human rights' in Bauer and Bell (eds) (1999) *East Asian challenges for human rights* 103 – 123; Bielefeldt 'Muslim voices in the human rights debate' (1995) 17 *Human Rights Q* 587 and Engle 'From scepticism to embrace: Human rights and the American Anthropological Association from 1947 – 1999' (2001) 23 *Human Rights Q* 536 – 539.

97 Shestack (n 12 above) 231; Finnis (n 37 above) 83 – 84.

98 An-Na'im 'Islam, Islamic law and the dilemma of cultural legitimacy for international human rights' in Welch and Laery (eds) (1990) 31.

99 Shestack 232.

100 An-Na'im (n 98 above) 36 – 49. Also see An-Na'im (2006) 27 *Third World Q* 785.

101 As above.

Recently, different cultural contexts have been used to identify instead possible shared reasons for a normative agreement on the creation and existence of (universal) human rights:[102]

> It is a fact that globalisation has enhanced cross-cultural contact, awareness, and exchanges about worldviews, moral, political, and religious systems and about diverse patterns of reasoning and justification throughout the world ... In all of these settings, one encounters explicit attempts, for example, to relate cultural moral categories to human rights norms, to identify and negotiate interpretations of these norms, to scrutinise cultural, social, and political traditions for their human rights implications, and even to articulate new social visions combining aspects of different traditions in a manner supportive of the priority interests represented by human rights.

Finally, the relativist argument, in many ways, seems moot. Shestack argues that:[103]

> ... another approach still exists that, in part, renders moot the conflict between universalist and relativist theory. This approach consists of appreciation of what has transpired in international law. Even as theorists have continued to quarrel with each other, fundamental human rights principles have become universal by virtue of their entry into international law as *jus cogens*, customary law, or by convention. In other words, the relativist argument has been overtaken by the fact that human rights have become hegemonic and therefore universal by *fiat* ... the broad acceptance by many nations across the globe of the principal human rights treaties can be taken, at least on the legal level if not yet in practice, as a triumph of universalism over relativism.

What 'has transpired in international law' – in Shestack's words - is a pragmatic international consensus that human rights are a largely self-sufficient and legally binding compact among the different states in the world that needs no further justification in terms of its universality, its acceptance among different cultures, or its ability to transcend different cultural norms.[104]

Fareda Banda remarks as follows about the ability of universal human rights law norms to bring about change in cultural practices which deny women their humanity:[105]

> 'Law' is not to be accepted uncritically. However, an engagement, filtering and implementation of law using feminist tools of analysis can yield positive results for women. Ultimately what matters is not whether we attach the labels 'relativist' or 'universalist', 'northern' or 'southern', but that all change feeds into the goal of according women worldwide their full humanity.

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102 Twiss (n 28 above) 59.

103 Shestack (n 12 above) 233.

104 See generally in this regard Twiss (n 28 above) 59 – 60, who argues that philosophical inquiries into the origins of human rights in natural law are a waste of time as we have a pragmatic agreement among states to acknowledge human rights norms as a self-sufficient system, no matter what their theoretical justification may be.

105 Banda (2003) 17 *Intl J L, Policy and Family* 19.

2.5 The impact of globalisation

Martin Wolf describes globalisation as the 'integration of economic activities, across borders, through markets'.[106] This integration entails the free movement of goods, services, labour and capital, thereby creating a single market.[107] An-Na'im offers an understanding of globalisation as an 'increasing assimilation of economies through international integration of investment, production, and consumption that is driven by market values'.[108] Benatar's more comprehensive definition, declares globalisation to be a 'complex and ambiguous concept with social and ecological manifestations that reflect a long, interwoven economic and political history in which peoples, economies, cultures and political processes have been subject to international influences'.[109]

Globalisation brings both positive and negative consequences: advances in science and technology, enhanced economic growth, freedom and prosperity for many; but also a widening gap between rich and poor within countries as well as globally.[110] Rejectionists claim that globalisation is the spring only of more poverty and greater exploitation.[111] Globalisation functions to reduce barriers to economic activity with little regard to social justice or environmental and public health.[112] For example, in African states as elsewhere, trade liberalisation policies result in the loss of jobs because trade agreements allowing entry to cheaper imports are detrimental to the profits of local manufacturers. Countries, such as in sub-Saharan Africa, 'remain on the periphery of these trends towards progress and economic dynamism'.[113]

Clinical research shares in the multiplication of the forces and effects of globalisation. The research enterprise is international; international collaborative research is the order of the day.[114] Multi-national corporations engage in clinical

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106 Wolf (2004) 14.

107 As above.

108 An-Na'im (2003) 'Politics of Religion and Morality of Globalization', unpublished paper, available at <http://www.sess.smu.edu.sg/events/Paper/Abdhu.pdf> (31 January 2007) 3. For a detailed discussion on the meaning of the concept of globalisation, which is outside the scope of this thesis, see Bartelson 'Three concepts of globalization' (2000) 15 *Intl Sociology* 180.

109 Benatar 'The HIV/AIDS pandemic: A sign of instability in a complex global system' in Van Niekerk and Koplelman (eds) (2005) 72.

110 As above.

111 See eg Went (2000) *Globalization: Neoliberal challenge, radical response.*

112 An-Na'im (n 108 above) 3.

113 Alonso 'Globalization, civil society, and the multilateral system' in Eade and Lightering (eds) (2001) 87.

114 See para 2.2.4 of ch 5 below.

research across the globe, and, increasingly, turn to Africa in search of research participants. Tony Barnett and Alan Whiteside comment on the outcome.

> Investment, cost and productivity and realisation of profit are spread across a world of space through complex networks of finance and organisation, and through decades of time. Cause and effect are often so widely separated through time that it is difficult or impossible to locate responsibility. The same is true of losses and costs associated with the impact of HIV/AIDS.[115]

In a globalised world corporate responsibility is more difficult to monitor, and raises the possibility of exploitation.[116]

A greater emphasis on ideologies such as international human rights law is a by-product of globalisation; the limitations on state sovereignty enhance the chances for supra-national enforcement of international human rights standards. But, is a system of international human rights law better able to protect the interests of clinical research participants in sub-Saharan Africa than bioethics? This enquiry is a major concern in the rest of the chapter.

2.6 Human rights and bioethics

This chapter argues for an approach to the protection of the rights of trial participants in clinical HIV-related research in Africa that is based on human rights rather than on clinical or bioethics.[117] The following paragraphs evaluate the differences and similarities between these systems.

At the outset it is indicated that an approach which argues that there is a place for human rights in the protection of the rights of trial participants in clinical research, rather than the traditional approach which relies on clinical or research ethics, is not widely supported by either the scientific community or by bioethicists.

Critics of a human rights approach to what has traditionally been the field of medical or bioethics claim that human rights discourse cannot cope with the complex moral issues involved in clinical research. They base the claim on the argument that the language of rights is too 'crude and ineffective' to deal effectively with the task of ethical reasoning. David Benatar, a philosopher and bioethicist, writes as follows:[118]

> Morality is a complex matter. This complexity cannot be managed completely with only the concept of rights – and *a fortiori* with only the concept of *human* rights. A health and human rights approach is unable to discover a non-natural right, such as a right arising from a promise or from membership in a medical insurance scheme.

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115 Barnett and Whiteside (2002) 353.
116 See para 2.3.3 of ch 5 below.
117 The approach based on clinical or research ethics is discussed in ch 3.
118 Benatar (2006) 32 *J Med Ethics* 19.

> Even if the notion of human rights were extended to include not only natural rights possessed by humans but also non-natural rights possessed by humans, the human rights approach would still be unable adequately to approach important issues in medicine. For example, it could not take account of the interests of those animals on which medical experimentation is conducted ... Using only the language of rights to grapple with every moral issue is analogous to treating every sickness with the same medication (or class of medication) or it is like trying to speak by using only nouns. It is crude and ineffective.

Benatar's argument is contestable, not least because of its false analogies. A few aspects of the argument are dealt with below.

First, human rights theory does not claim that human rights take the place of ethical or moral reasoning. Ethics, ethical reasoning, morality, moral reasoning and human rights are not equivalents. Human rights are a codification of a small measure of humankind's ideas about morality and morally good actions. Yet, human rights are a 'set of moral principles of which the justification lies in the province of moral philosophy'.[119] Philosophical human rights discourse grapples with the same 'complex moral issues' as does ethics or even bioethics. The strength of human rights lies in the fact that it consists of moral values or principles that are universally held; which have been tried and tested by history; and about which there is a certain amount of international consensus.

Second, Benatar seems to equate human rights and natural rights, as he writes '[e]ven if the notion of human rights were extended to include not only natural rights possessed by humans but non-natural rights ...'. This statement displays an inadequate understanding of the history of human rights. The renaissance of natural rights theory in the 20th century has been responsible for the revival of interest in human rights, but, as was shown above,[120] human rights are not the same as natural rights. Natural rights are the philosophical antecedents of contemporary human rights.

Third, Benatar's objection to natural/human rights that they do not include so-called 'non-natural rights', or rights 'such as a right arising from a promise or from membership in a medical insurance scheme' is unfounded. A promise is not the basis for the existence of a right, natural or unnatural.[121] Promises belong in the sphere of morality and ethics. In any case, membership of a medical scheme does

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119 Shestack (n 12 above) 202.

120 See para 2.3 above.

121 The legal term 'legitimate expectation' is the closest the law comes to enforcing promises.

not rest within the field of clinical - or bioethics – it falls into the ambit of the law of contract or insurance law.

The (human) right of access to social security or health care, may, in certain circumstances, arguably include a (human) right of access to membership of a medical scheme, for example, in the case of a HIV-positive person who is denied membership of a medical scheme because of her status. Such a person may rely on human rights to equality, access to health care and social security to enforce her right.

Lastly, proponents of human rights cannot claim the applicability of human rights to animals; they are *human* rights, after all. Using the situation of animals in experimentation as an example of an 'important issue[] in medicine' that is not covered by natural/human rights, does not strengthen the biomedical argument, but plays on human sensibilities.

The paragraphs that follow illustrate that the 'language of [human] rights' is not 'crude and ineffective', but is, instead, valuable in protecting the rights of participants in clinical research.

Clinical research ethics and human rights are, essentially, products of the spirit and philosophy of the mid-20th century. To a large extent, both arose as a response to humankind's horror at the events of World War II and the atrocities committed by National Socialism and Japanese Imperialism. In the words of George Annas: 'World War II was the crucible in which both human rights and bioethics were forged, and they have been related by blood ever since'.[122]

The Nuremberg Code, written in 1946 as the final part of the judgment delivered in the Nuremberg trials, contains the first comprehensive set of guidelines on how to conduct ethical research on humans.[123] The Nuremberg Code is a consequence of the outrage that was felt at the conduct of doctors under National Socialism in Germany, who, in the guise of science, performed cruel and inhuman medical experiments on German and non-German nationals, including Jewish and 'asocial' people during the Second World War. In the first part of the Nuremberg Code, reference is made to the fact that 'the record clearly shows the commission of war crimes and crimes against humanity ...'.[124] George Annas remarks, '... I believe

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122 Annas (2004) *J L, Med & Ethics* 659.

123 See para 3.1.1 in ch 3 above.

124 Part I Nuremberg Code 'Proof as to War Crimes and Crimes against Humanity'.

it is accurate to conclude that the [Nuremberg] Trial itself marked the birth of American bioethics'.[125]

Similarly, the Universal Declaration of Human Rights is the first comprehensive human rights document to be adopted by an international organisation.[126] It is considered by many to be a milestone in humankind's struggle for the recognition of human rights and the struggle for freedom and human dignity. The Universal Declaration of Human Rights too was adopted after the Second World War in the realisation that international co-operation is needed to protect individuals against abuses of state power. Its preamble reads: 'disregard and contempt for human rights have resulted in barbarous acts which have outraged the conscience of mankind ...'[127]

The Nuremberg Code and the Universal Declaration of Human Rights are thus reactive in nature – both are products of outrage and anger. In Edmund Cahn's words '"[j]ustice" ... means the active process of remedying or preventing what would arouse the sense of injustice'.[128] These two documents are memorative, they epitomise 'lest we forget'.

As well as a shared historical background, clinical research ethics and human rights have a common purpose: broadly, they aim to protect the individual or groups of individuals from harm. In the case of clinical research ethics, such harm may come from abuses by scientists or researchers in a clinical research setting; in the case of human rights, such harm may arise from state action or the actions of other individuals or groups of individuals within a state.

Despite the shared objective to protect individuals or groups from harm, each system has its own focus: ethical principles governing research with human subjects aim at regulating the relationship between researchers and research participants; as apposed to principles regulating the relationship between the individual and the state or the relationship between individuals in a state. Clinical research ethics or bioethics apply to a very specific, narrowly defined situation only, whereas human rights potentially apply to a wide or broadly defined range of situations. Specific human rights conventions which deal with specific human rights topics, for example, the Convention against Torture, are, of course, narrower in their focus.

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125 Annas (n 122 above) 658.
126 See para 3.2.1 (b) below.
127 Preamble Universal Declaration of Human Rights.
128 Cahn (n 71 above) 13 – 14.

The difference outlined above has implications for the way in which the different documents are drafted and worded. Clinical research ethics documents are specific in their content and phrasing, human rights documents tend to be more general. For example, clinical research ethics codes contain phrases giving specific instructions, such as '[t]he subjects should be volunteers – either healthy persons or patients from whom the experimental design is not related to the patient's illness'.[129] Human rights documents tend, on the other hand, to contain general phrases, such as '[e]very individual shall have the right to enjoy the best attainable state of physical and mental health'.[130] Both articles require interpretation to determine their application to a given situation, but the human rights section certainly requires a more extensive interpretation in order to discover the meaning of the value judgment implicit in 'best attainable state of health'.

Despite the necessity to be more precise and exact in phrasing, ethical guidelines are severely criticised for, in general, being too vague and ambiguous. Human rights, it is true, are phrased in yet more general terms, however, human rights are given content by their interpretation in courts or other tribunals, with the consequence that it is not a serious failing as is the case with ethical guidelines which are not litigated.

As a rule, human rights and clinical research ethics both operate in situations of unequal power. Most bioethicists, however, deny theirs is a relationship of unequal power.[131]

> The word *power* is essentially absent from the vocabulary that scholars of medical ethics have constructed for their discipline and that has been accepted by almost everyone who does work in the field or tries to apply medical-ethical insights to the clinical context.

The potential victims of abuse in a human rights situation are vastly less powerful than their abusers – whether government, private individuals or multinational corporations – but, generally, are reasonably well-informed about their human rights through the media and education programmes. Because they have been educated about their human rights, they are generally conscious of any infringement of these rights.

Clinical research subjects are less well-informed about the scientific and clinical issues involved in research. In settings where there are significant levels of

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129 Art III.2 Declaration of Helsinki.
130 Art 16(1) African Charter of Human and Peoples' Rights.
131 Brody (1992) 12.

illiteracy the situation is exacerbated. Furthermore, in settings in which there are high levels of poverty, and where research is a means to access treatment, the potential for exploitation is greatest. Research initiatives seldom are accompanied by large-scale programmes aimed at educating research subjects about the nature and implications of the research for themselves and their communities.

Ethical principles governing clinical research on human subjects often deal with subjects in different countries, in multiple sites, and truly are international in their application, whereas human rights law primarily deals with citizens of a single state. States enter into multilateral agreements with other states, committing themselves to respecting human rights, but, in reality, it is of slight concern to them whether or not the other parties actually adhere to this aspect in relation to their citizens. It is a true case that many states ratify human rights treaties merely to receive aid. In addition, even when a human rights convention is litigated, often this is done first at the domestic level due to the requirement in many treaties that domestic remedies should be exhausted. Many domestic constitutions contain bills of rights, so that human rights are generally litigated first within the domestic courts of a specific state by citizens of a specific state.

A crucial difference between the two systems lies in the nature of each: one system consists of non-legal, non-binding ethical *principles*; the other of legally binding *rights*. It is true that human rights and ethical principles, equally, are systems which embody society's moral values, moral norms or its 'common morality',[132] and it is also true that human rights *contain* principles of ethics, but the values and norms in each system are codified very differently - as principles in the one and rights in the other.

Implicit in this difference between principles and rights, lies another crucial distinction between the two systems in terms of the enforcement mechanisms devised to monitor a system of non-binding principles as apposed to a system of legally binding rights.

In the case of ethical guidelines governing clinical research on human subjects, compliance with and enforcement of the system rely on professional sanction and other non-legal means. It is assumed that researchers are 'ethical' people who will uphold the guidelines of clinical research. Because of the non-legal nature, to a large extent, observance of ethical guidelines depends on the sanction of various professional bodies and research funding agencies. Other than a refusal

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132 See para 2.2 above, as well as para 2.2 of ch 3 above.

to fund or a refusal to publish unethical research, there is little to guard against unethical research conducted by unscrupulous agencies.

In respect of human rights, collective monitoring and implementation mechanisms are in place. These monitoring systems are sophisticated and well-developed. International organisations, such as the United Nations, assume a duty to protect human rights. Similar institutions have been introduced at a regional level as well, and in some regional systems they include a court in which international human rights are litigated and enforceable against violators.[133] At the domestic level, many states have promulgated constitutions which include justiciable bills of rights, making human rights immediately enforceable in a domestic court of law.[134]

2.7 A rights-based approach to clinical research

Much of this chapter is an argument in favour of human rights as an alternative strategy in protecting the interests of participants in clinical HIV-related research. The nature of such a human rights or rights-based approach is examined below.

A 'rights-based' approach is based or founded on *rights*, instead of policy, ethical reasoning or principles of goodness. A rights-based approach usually is seen as the counterpoint for a policy-based approach[135] or a needs-based approach.[136]

Rights are enforceable claims;[137] they are supported by a legal system that considers rights as enforceable or justiciable against other persons or entities in a setting such as a court of law. Specifically, a rights-based approach, in the context

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133 See paras 3.3.2 and 3.3.4 below.

134 See paras 5.1 – 5.2 below.

135 In a policy-based approach, the executive has the discretion whether to act or not; in a rights-based approach there is a legal obligation upon the executive to act in a certain way. Policy-makers usually have the freedom to determine the content and the extent of their policies, they may even determine when it is convenient (for them) to implement their policies. They can decide who the beneficiaries are, how they will allocate resources (eg whether they will support HIV/AIDS-related research financially) and who will be bound by their policies. The provision in the past of anti-retrovirals in South Africa to only a limited number of research sites is an example of the exercise of government discretion.

136 A needs-based approach focuses on securing resources for delivery of services to particular groups, where a greater need exists. Once again this approach depends upon executive discretion, in the sense that making available resources for special needs or priorities is an executive decision and depends on the perception of the executive of the need. Needs may be met by charitable institutions, whereas rights are based on legal obligations.

137 See para 2.2 above.

of this discussion, deals with the legal system established by the international system of human rights, with its binding human rights law instruments.[138]

Frans Viljoen characterises a rights-based approach as follows:[139]

> Rights-based approaches convert needs into justiciable rights. These 'rights' may come in the form of constitutional provisions or national legislation. Violation of, or non-compliance with, these rights gives rise to a claim for redress that may be asserted before a court or other tribunal. Rights thus form the basis for governmental accountability.

Viljoen stresses that, while needs-driven programmes or policies depend on an *ad hoc* exercise of discretion, rights place an obligation on a duty-bearer (mostly governments), creating an expectation of compliance and deliver accountability on the basis of a clear obligation.[140]

In the context of clinical research, a rights-based approach goes further than prescribing ways of acting morally or ethically towards research participants. A rights-based approach provides a justiciable, legal framework by means of which a reliance on ethical conduct or morality is converted into a legal claim. A right-based approach to clinical HIV-related research participation locates the needs of participants in such research within a human rights context, enabling access to a mechanism for claiming and asserting their rights.

In a rights-based approach, the ethical obligation to treat participants in clinical research in a certain way becomes a legal imperative that may be enforced in a court of law if the need arises. For example, a moral or ethical principle, based on an ethical guideline which ensures that research participants give informed consent to participation in research, or that they are given fair access to the products of research, under a rights-based approach becomes a legally enforceable right to informed consent in clinical research and a legally enforceable right of access to the products of clinical research.

There are further, non-legal, consequences in a rights-based approach. Human rights may be used to question the *status quo*, the established way in which things are done.[141] In the previous chapter an illustration was offered of how PLWHA have been able to change the protracted process of drug licensing;[142] by

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138 Such as binding treaties as well as decisions of international human rights organs and judicial or quasi-judicial bodies. They are contrasted with non-binding policy statements, declarations, ethical guidelines and the like.

139 Viljoen (2005) 15 *Interights Bulletin* 47.

140 As above.

141 Viljoen (n 139 above) 47.

142 See para 4.2.1(c) of ch 3 above.

framing their demands in the language of rights, PLWHA in the United States successfully achieved a fast-track in the licensing of anti-HIV medication and speedier access to certain drugs. Viljoen speculates that a rights-based approach, as an alternative way of seeing and thinking about experience, extends outside the courtroom; that human rights discourse is 'a language of moral authority that may be used in many ways, such as lobbying for reform or mobilising and strengthening social movements'.[143] He develops this claim to propose that as justiciable rights raised in court or even as a basis for social conflict, rights which have the effect of destabilising aspects of the *status quo*,[144] result in governments being made accountable by means of an assessment of performance and delivery.[145]

A rights-based approach not only has the power to hold governments and other persons or entities accountable for the violation of clinical research participants' rights, it establishes a standard against which government action may be measured in estimating whether it has fulfilled its obligations.

Talking about rights, of itself, is proposed as a vehicle for 'increasing the accountability of government organisations to their citizens and consequently increasing the likelihood that policy measures will be implemented in practice'.[146] Government action will be tested against human rights standards and inaction monitored. In stipulating an internationally agreed set of norms backed by international law, human rights provides a firmer foundation upon which people have a claim on governments, holding them accountable in the performance of a duty to enhance access in the realisation of human rights.

More broadly, engaging with a rights-based approach is an opportunity to reflect on general issues in research ethics and the practice of international research, including the internal dynamic as well as the obligations of those engaged in international HIV-related research towards clinical research participants. Thus, it is a framework for reflection that politicises international HIV-related clinical research sponsorship and participation.

From the discussion above, six ways can be observed in which a rights-based approach relates to HIV-related clinical research.

- As a set of normative principles to guide the way in which HIV-related research participation is carried out.

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143 Viljoen (n 139 above) 47 – 48
144 As above.
145 As above.
146 Ferguson (1999) 23.

- As a justiciable framework which converts ethical conduct or morality into legal claims, and locates the needs of participants in HIV-related clinical research in a human rights context, offering a mechanism for claiming and asserting rights.
- As a means of questioning the *status quo*.
- As a standard against which government action in the fulfilment of their obligations may be measured, in other words, as a means of judging state performance.
- As a way of making government organisations more accountable to their citizens and, consequently, to increase the likelihood that policy measures will be implemented in practice.
- As an opportunity for a broader reflection on the power dynamic of international research and on questions in research ethics.

Self-evidently, the goal of HIV-related clinical research is the promotion of human health and human well-being. Human rights define and advance human well-being; a rights-based approach to HIV-related research participation delivers a conceptual and a practical framework by which to assess the process.

2.8 Different levels of protection: National and international human rights law

The protection afforded by human rights law functions at different levels. The first line of 'defence' against a human rights violation is at the national level (also called the domestic or municipal level). At this level human rights law takes the form of a domestic bill of rights, a human rights act or human rights provisions included in a constitution, as well a international human rights law that has been 'domesticated'. The next line of 'defence' is at the regional level.[147] Different states in a region or continent adhere to the same system of human rights protection, usually based upon a founding document embodying human rights values.[148] The final line of 'defence' against human rights violations is at the global or UN level. States across the globe adhere to human rights norms contained in different international human rights documents and treaties.

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147 Some authors talk also of a sub-regional level. This is human rights at the level of the sub-region, such as SADC, which is primarily an economic organisation but which includes human rights concerns.

148 See para 4 below.

There is thus a division between 'national' or 'municipal' human rights law, and international (regional or global) human rights law. This division is rather artificial, as the national and international systems apply simultaneously. However, international law does not 'replace' national law: the person whose rights were violated needs first to look for redress at the national level. Only in instances where no remedy is available or possible at the national level, may the person turn to the international (regional or global) level.[149] The international level of protection therefore functions as a 'safety net', to catch victims of human rights violations who fall through the cracks of the national level.

At the national level it is the state which is responsible for the implementation of human rights norms. A state may have its own bill of rights, either standing on its own or embedded in a constitution, which it has to comply with and give effect to, and the state also has to 'domesticate' international human rights treaties and declarations. At the regional or global levels it is a regional or global organisation which is responsible for the implementation of human rights norms.

The existence of international human rights law is a product of the erosion of state sovereignty. When becoming a state party to a human rights treaty, states voluntarily relinquish their own sovereignty: they agree that an independent regional or global body may supervise their compliance with the provisions of that treaty and take steps to interfere if it is deemed necessary.[150] Some treaties allow for individual complaints against states by their nationals for human rights violations.

The 'domestication' of international human rights law in the domestic human rights system is discussed in detail below.[151]

2.9 Conclusion

In this section the origins and development of the idea of human rights were explored in order to introduce the thesis developed in this chapter – that human rights may be used effectively to protect the interests of participants in clinical HIV-related research in Africa.

It was pointed out that human rights discourse is about the use of terms such as 'right', '*prima facie* claims', 'justiciability', 'universal moral rights', 'justice', and so

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149 Known as the principle of subsidiarity – international human rights law is subsidiary to national human rights law.

150 Such interference may take the form of political, military or humanitarian action.

151 See para 6 below.

on, and that human rights are a particular type, or subspecies, of rights. Various definitions of human rights were offered, and some writers have claimed that human rights is the *only* universally recognised system of values.

The philosophical background of human rights was traced, and the merits of a universal system of human rights beyond theories of cultural relativism have been explored. The impact of globalisation upon the international research enterprise was considered. A human rights approach was contrasted with bioethics, and it has been asserted that, because of their enforceable nature, human rights directly benefit participants in clinical research. A distinction is drawn between 'national' and 'international' human rights law, and human rights protection at the regional and global levels is sketched.

George Annas, in pleading for the acceptance of the importance of human rights discourse by bioethicists, comments:[152]

> While bioethics has aspired to be a universal language, the only language that can be said to have attained that status, as tentative as it is, is the language of human rights.

At a point later in chapter 4 the issue raised by George Annas is developed. In the following paragraphs, specific human rights provisions in domestic bills of rights relevant to clinical research in sub-Saharan Africa are inspected.

3 NATIONAL HUMAN RIGHTS NORMS

3.1 Introduction

This section examines specific human rights provisions in domestic constitutions relevant to the protection against the abuse of clinical research participants in HIV-related research Africa. As indicated in the introduction to this chapter, the investigation is limited to countries in *sub-Saharan* Africa because of the comparatively low prevalence of HIV/AIDS in countries north of the Sahara.[153]

Not every country in sub-Saharan Africa is included: the survey is limited to 22 countries selected from each region (north, south, central, east and west). Most countries situated in southern Africa, where the HIV prevalence rate is the highest, are included. Sudan has been omitted as its constitution has been suspended in the wake of the civil war.

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152 Annas (n 122 above) 661.

153 See para 1 above, and para 3.3 of ch 2 above.

The investigation centres in human rights provisions in the constitutions of the following countries (in alphabetical order): Angola; Benin; Botswana; Burundi; Congo; Eritrea; Ethiopia; Ghana; Kenya; Lesotho; Malawi; Mali; Mozambique; Namibia; Nigeria; Senegal; South Africa; Swaziland; United Republic of Tanzania; Uganda; Zambia; and Zimbabwe. (Also refer to paragraph 4.3.1 of chapter 3 for tables presenting the core health indicators of these countries.)

The survey investigates the following:

- Whether a provision specifically mentioning clinical research is contained in the country's constitution.
- Whether the constitution guarantees freedom from torture and other inhuman and degrading treatment which could be used to defend participants in clinical research against abuses of their person.
- Whether the right to physical integrity is guaranteed by the constitution (for similar reasons as above).
- Whether the right to dignity is guaranteed (clinical research undertaken without the informed consent of a participant may be regarded as a violation of dignity).
- Whether the constitution contains a provision guaranteeing equality, which could be used to ensure that the rights of research participants who are, or are perceived to be, HIV positive are protected; as well as a clause ensuring the equality of minority groups taking part in research and who are prone to stigma and discrimination, such as MSM, WSW, sex workers and IDUs.
- Whether the constitution guarantees the individual's privacy.
- Whether the constitution guarantees women and children's rights which may be violated during clinical trial participation.
- Whether the right to health care or access to health care is guaranteed by the constitution, giving an indication of whether clinical research will be seen by research participants as an opportunity to gain access to heath care that is not otherwise available.

3.2 Specific human rights provisions in domestic bills of rights (relevant to clinical research in sub-Saharan Africa)

3.2.1 Angola

Part II of the Constitutional Law of the Republic of Angola[154] sets out 'fundamental rights and duties'. Several provisions are relevant to clinical research, but Part II does not make direct reference to clinical research.

Article 18 of the Angolan Constitution ensures the equality of all Angolan citizens. The list of prohibited grounds of discrimination includes 'color, race, ethnic group, sex, place of birth, religion, ideology, level of education or economic or social status'. Article 20 obliges the state to respect and protect the human person and human dignity.[155]

Article 47(1) of the Angolan Constitution is significant. It guarantees that the state will promote the measures needed to ensure the rights of citizens to medical and health care.[156] Although clinical research is not mentioned explicitly, the article could be interpreted as supporting measures undertaken by the Angolan government that encourage research which promotes medical and health care, such as HIV-related clinical research.

Part II, article 23 reads: '[n]o citizen may be subjected to torture or any other cruel, inhuman or degrading treatment or punishment'. The provision in the Angolan Constitution is identical to article 5 of the Universal Declaration, and article 7 of ICCPR.[157] Unlike the corresponding article in the ICCPR, however, the Angolan Constitution does not contain an additional sentence prohibiting medical experimentation without informed consent. Further, the provision contains an internal qualifier – 'citizens' alone are entitled to the right. These limitations apart, it is submitted that article 23 of the Angolan Constitution can be called upon to protect the rights of research participants in Angola, as well as the rights already mentioned.

Children's rights are protected.[158] Women's rights are protected only within the context of the family, in which women and men are held to have equal rights.[159]

3.2.2 Benin

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154 Constitutional Law of the Republic of Angola, adopted 25 August 1992; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/Angola%20Constitution(rev).doc> (31 January 2007).

155 Arts 18 and 20 Constitutional Law of the Republic of Angola.

156 As above, art 47.

157 See para 4.3.1 of ch 5 below.

158 Art 30 Constitutional Law of the Republic of Angola.

159 Arts 18 and 29(2) Constitutional Law of the Republic of Angola.

Title II of the Constitution of the Republic of Benin[160] contains provisions dealing with the 'rights and duties of the individual'. Several provisions are relevant to clinical research, but Title II does not refer directly to clinical research.

Article 8 guarantees the sacred and inviolable nature of the human being. Article 15 reads: 'Each individual has the right to life, liberty, security and the integrity of his person'. This article may be enforceable against clinical research which threatens or violates the life or integrity of the person.

Article 18 reads: '[n]o one shall be submitted to torture, nor to maltreatment, nor to cruel, inhumane or degrading treatment'. Note 'no one': unlike a similar provision in the Angolan Constitution, the Benin provision is applicable to all persons within Benin territory, not only to citizens of Benin. Article 19 prohibits acts of torture and inhuman or degrading treatment carried out by someone in an official capacity.

Article 26 guarantees equality before the law, and the list of prohibited grounds of discrimination are: origin, race, sex, religion, political opinion and social position. Women and men are regarded equal under the law.[161] A duty is placed upon the state to protect the family, especially the mother and child.

3.2.3 Botswana

Chapter II of the Constitution of Botswana[162] contains a bill of rights. Several provisions are relevant to clinical research, but chapter II does not make direct reference to clinical research.

Article 3 protects the fundamental rights and freedoms of the individual, whatever her 'race, place of origin, political opinions, colour, creed or sex'. Art 7(1) reads: '[n]o person shall be subjected to torture or to inhuman or degrading punishment or other treatment'. It is submitted that this provision can be called upon to protect participants of clinical research in Botswana.

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160 Constitution of the Republic of Benin, adopted 2 December 1990; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/BeninC(englishsummary)(rev).doc> (31 January 2006).
Interestingly, the Benin Constitution incorporates the human rights guaranteed by the African Charter in its bill of rights (see art 7 Constitution of the Republic of Benin).

161 Art 26 Constitution of the Republic of Benin.

162 Constitution of Botswana, adopted in 1966, last amended in 1999; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/Botswana(summary)(rev).doc> (31 January 2007).

The individual's right to privacy is protected, and no search of her person may be carried out without her permission.[163] However, the right to privacy is limited by, amongst others, anything that is 'reasonably required in the interests of public health'.[164] No special mention is made of women's or children's rights in the Botswana Constitution.

3.2.4 Burundi

The Constitution of the Republic of Burundi[165] contains human rights provisions which are relevant to the position of research participants, but the Constitution does not mention clinical research specifically.

Article 15 prohibits arbitrary treatment; article 19 explicitly prohibits discrimination against people living with HIV or AIDS; article 25 ensures confidentiality of personal communications; article 33 concerns participation in public life (which could be interpreted to mean participation in a public good, such as clinical research); and article 35 relates to child health and well-being.

Article 17 is of special significance to clinical research as it guarantees the right to life, security of the person and physical integrity.

3.2.5 Congo

The Constitution of the Republic of the Congo[166] contains a bill of rights in Title II, 'rights and fundamental liberties'. Although no reference is made to clinical research, the Constitution of the Congo does contain provisions which are relevant to participation in clinical research.

Equality is guaranteed, and the prohibited grounds of discrimination are 'origin, social or material situation, racial, ethnic, gender, education, language, religion, philosophy or place of residence'.[167] Privacy is guaranteed[168] as is the

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163 Art 8 Constitution of Botswana. However, the right to privacy is limited by, amongst others, anything that is 'reasonably required in the interests of public health'.

164 This article may be relied upon by proponents of mandatory or 'opt out' HIV testing in public hospitals in Botswana.

165 Constitution of Burundi, 2004; available at <http://democratie.francophonie.org/article.php3?id_article=368&id_rubrique=94> (31 January 2007).

166 Constitution of the Republic of the Congo, 1992; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/CongoC%20(english%20summary)(rev).doc> (31 January 2007).

167 Art 8 Constitution of the Republic of the Congo.

168 Art 14 Constitution of the Republic of the Congo. This provision may be limited to privacy of the home.

secrecy of correspondence.[169] The state guarantees the public's health[170] and the rights of the mother and child within the family are guaranteed.[171]

The situation of children and adolescents participating in HIV-related research may be covered by article 34. Although initially not intended for this purpose, article 34 may be used to prevent the exploitation of children and adolescents in such research. Article 34 determines that the state must protect children and adolescents from 'economic exploitation'.[172] Clinical research of an exploitative nature in which children and adolescents are enrolled is thus prohibited.[173]

3.2.6 Eritrea

Chapter 3 of the Constitution of Eritrea[174] contains provisions on human rights, entitled 'Fundamental Rights, Freedoms and Duties'. Several provisions are relevant to clinical research, but Chapter 3 does not refer directly to clinical research.

Article 14 prohibits discrimination on a range of listed grounds. They are: 'race, ethnic origin, language, colour, gender, religion, disability, age, political view, or social or economic status'. Discrimination based on what is referred to as 'other improper factors' is also prohibited. Article 18 protects the individual's privacy.

The right to human dignity is protected in article 16. Article 16(2) reads, '[n]o person shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment'. A verbatim copy of art 5 of the Universal Declaration and article 7 of the ICCPR, this article could be read as prohibiting clinical research in Eritrea which constitutes 'cruel, inhuman or degrading treatment or punishment'. It is submitted that clinical research without proper informed consent, clinical research which is exploitative and clinical research which is not responsive to the needs of the community at the very least, are 'degrading'.

Article 21 provides every citizen with the right to equal access to publicly-funded social services and states that the state shall endeavour to make available to all citizens health, education, cultural and other social services. Women are

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169 Art 20 Constitution of the Republic of the Congo.

170 Art 30 Constitution of the Republic of the Congo.

171 Art 31: 'The state has the obligation to assist the family in its mission as guardian of the morality and the traditional values recognised by the community. The rights of the mother and the child are guaranteed'.

172 Art 34 Constitution of the Republic of the Congo.

173 See para 2.3.3 of ch 5 below.

174 Constitution of Eritrea, adopted by the Constituent Assembly on 23 May 1997; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/EritreaC.pdf> (31 January 2007).

protected in the 'Democratic Principles', of which article 7 protects against participation in 'any act that violates the human rights of women or limits or otherwise thwarts their role and participation is prohibited'.

3.2.7 Ethiopia

Chapter 3 of the Constitution of the Federal Republic of Ethiopia[175] sets out fundamental rights and freedoms; several provisions are relevant to the situation of clinical research participants in Ethiopia.

Article 14 protects the individual's 'inviolable and inalienable right to life, the security of [the] person and liberty'. Article 15 protects the right to life and article 16 protects the rights of every person against 'bodily harm'. Under certain conditions, clinical research could constitute 'bodily harm', and the provision may be called upon in an action against perpetrators of research which causes harm.

Article 18 reads: 'Everyone has the right to protection against cruel, inhuman or degrading treatment or punishment'. This article mirrors the protection in the Universal Declaration and in the ICCPR, and could be interpreted to include violations by researchers in clinical research.

A general equality provision is contained in article 25, and the prohibited grounds of discrimination are 'race, nation, nationality, or other social origin, colour, sex, language, religion, political or other opinion, property, birth or other status'. It is not a closed list, and the words 'other grounds' might cover 'real or perceived HIV status'. Article 25 would protect participants in HIV-related clinical research from being discriminated against based on their real or perceived status.

Article 35 prohibits harmful customs and elaborates rights with respect to the transfer of property to women and women's inheritance. Article 36 guarantees children's rights. Article 41 states that every Ethiopian has the right to equal access to publicly-funded social services and that the state must allocate ever-increasing resources to provide to the public health, education and social services.

3.2.8 Ghana

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175 The Constitution of the Federal Democratic Republic of Ethiopia; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/EthiopiaC(rev).doc> (31 January 2007).

The Constitution of the Republic of Ghana[176] contains human rights provisions in Chapter 5. Several provisions are relevant to clinical research, but Chapter 5 does not refer directly to clinical research.

Article 12(2) ensures the rights and freedoms in the Constitution to everyone, regardless of 'race, place of origin, political opinion, colour, religion, creed or gender'. Article 15 guarantees the individual's dignity. Article 15(2) reads:

> No person shall, whether or not he is arrested, restricted or retained, be subjected to -
>
> (a) torture or other cruel, inhuman or degrading treatment or punishment;
> (b) any other condition that detracts or is likely to detract from his dignity and worth as a human being.

This utility of this provision in protecting participants in HIV-related research is self-evident.

Article 17 prohibits discrimination on the grounds of 'race, place of origin, political opinions, colour, gender, occupation, religion or creed'. Article 27(1) ensures special care to mothers before, during and after child-birth, and article 27(3) ensures equal training and opportunities for women. Children's rights are protected in article 28. Article 28(3), which reads, '[a] child shall not be subjected to torture or other cruel, inhuman or degrading treatment or punishment', is especially important.

3.2.9 Kenya

The Constitution of Kenya[177] contains human rights provisions that are relevant to the situation of clinical research participants. Chapter 5 is entitled 'protection of fundamental rights and freedoms of the individual'.

Article 74 prohibits 'inhumane treatment' but appears to limit such treatment to 'forced labour'. Article 76 guarantees privacy and reads: 'Except with his own consent, no person shall be subjected to the search of his person or his property or the entry by others on his premises'.[178]

Article 82 prohibits discrimination based upon 'race, tribe, place of origin or residence or other local connexion, political opinions, colour, creed or sex whereby

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176 Constitution of the Republic of Ghana, 1991; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/GhanaC.pdf> (31 January 2007).

177 Constitution of Kenya, adopted in 1963 and amended in 1999; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/KenyaC(rev).doc> (31 January 2007).

178 Art 76(1) Constitution of Kenya.

persons of one such description are subjected to disabilities or restrictions to which persons of another such description are not made subject or are accorded privileges or advantages which are not accorded to persons of another such description'.[179] The provision includes an internal limitations clause, restricting the general right on the basis of marriage, adoption, burial, devolution of property upon death and so on.[180]

An amendment to the constitution which has been proposed would add health status as a protected ground.[181] Also, women are afforded greater protection in the new amendment,[182] and specific provisions dealing with children have been included.

3.2.10 Lesotho

The Constitution of Lesotho[183] in Chapter 2 contains fundamental rights and freedoms which are relevant to the protection of research participants. No direct reference is made to clinical research.

Article 8 guarantees freedom from inhumane treatment. Article 8(1) reads: 'No person shall be subjected to torture or to inhuman or degrading punishment or other treatment'. Article 11 guarantees privacy of the person, and article 8 guarantees freedom from discrimination. The prohibited grounds are:[184]

> race, colour, sex, language, religion, political or other opinion, national or social origin, property, birth or other status whereby persons of one such description are subjected to disabilities or restrictions to which persons of another such description are not made subject or are accorded privileges or advantages which are not accorded to persons of another such description.

Because this is not a closed list, it is conceivable that perceived or actual HIV status may be 'read into' the provision, giving research participants protection against discrimination during HIV-related clinical research. However, the rights in article 8 are subject to an internal limitations clause in sub-article 4, which includes 'adoption, marriage, divorce, burial, devolution of property on death or other like matters which is the personal law of persons of that description; or for the application of the

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179 Art 89 Constitution of Kenya.
180 Art 89(4)(b) Constitution of Kenya.
181 The Proposed New Constitution of Kenya 2005 art 37.
182 As above, art 38.
183 Constitution of Lesotho, adopted in 1993, amended 1996, 1997, 1998 and 2001; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/LesothoC(summary)(rev).doc> (31 January 2007).
184 Art 8(3) Constitution of Lesotho.

customary law of Lesotho with respect to any matter in the case of persons who, under that law, are subject to that law'.[185]

In Chapter III of the Lesotho Constitution, principles of state policy are set out. Article 27 reads:

> Lesotho shall adopt policies aimed at ensuring the highest attainable standard of physical and mental health for its citizens, including policies designed to -
> (a) provide for the reduction of stillbirth rate and of infant mortality and for the healthy development of the child;
> (b) improve environmental and industrial hygiene;
> (c) provide for the prevention, treatment and control of epidemic, endemic, occupational and other diseases;
> (d) create conditions which would assure to all, medical service and medical attention in the event of sickness; and
> (e) improve public health.

From the wording of the article and the fact that it is not contained in the chapter on fundamental rights but as a 'directive of state policy'[186] it is clear that article 27 is not immediately enforceable against the Lesotho state. However, the provision may be used to argue that the state should put in place policies and frameworks which facilitate clinical HIV-related research and protect the rights of participants in such research.

3.2.11 Malawi

The Constitution of the Republic of Malawi[187] contains human rights provisions in Chapter IV relating to the situation of clinical research participants. The Constitution of the Republic of Malawi specifically refers to clinical research.

The right to life is guaranteed in article 16. Article 19 guarantees the human dignity of the person. Article 19(3) dictates that '[n]o person shall be subject to torture of any kind or to cruel, inhuman or degrading treatment or punishment'. This provision is similar to that in other constitutions, however, the Constitution of Malawi goes further. In article 19(5) the following prohibition is added: '[n]o person shall be subjected to medical or scientific experimentation without his or her consent'. The Malawian Constitution is a departure from the norm in taking

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185 Art 4(b) and (c) Constitution of Lesotho.

186 So-called 'directive principles of state policy') and 'fundamental objectives of state policy' (see the Constitution of Nigeria below) are not justiciable human rights. Rather, they serve as a guide to the executive or legislature in the exercise of their functions. They are often used by the judiciary as a guide to the interpretation of the Constitution and other laws.

187 The Constitution of the Republic of Malawi, entered into force on 18 May 1994; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/MalawiC.pdf> (31 January 2007).

cognisance of clinical research and guaranteeing the right not to be subjected to medical experimentation without consent. Although not precisely the same, the wording of article 19 mirrors the prohibition on research without consent in article 7 of the ICCPR.

Article 20(1) prohibits discrimination on the grounds of 'race, colour, sex, language, religion, political or other opinion, nationality, ethnic or social origin, disability, property, birth or other status'. 'Other status' may be interpreted to include HIV status. The right to privacy is guaranteed in article 21. Children's and women's rights are protected by the Malawian Constitution.[188]

3.2.12 Mali

The Constitution of the Republic of Mali[189] in Title I contains provisions on human rights that are relevant to the situation of clinical research participants.

Article 1 guarantees human dignity which is regarded as 'sacred and inviolable'. The article further provides that '[e]ach individual has the right to life, liberty, and the security and integrity of his person'. Discrimination based on the grounds of 'social origin, color, language, race, sex, religion, or political opinion' is prohibited. Article 6 guarantees privacy.

Article 3 reads: 'No one will be put to torture, nor to inhumane, cruel, degrading, or humiliating treatment' and is especially significant. The article provides further that anyone found guilty of such an act, 'either on his own initiative, or by another's command', is punishable at law'.

Health care is to 'constitute some of the social rights'.[190] Women's and children's rights are not singled out for mention.

3.2.13 Mozambique

The new Mozambican Constitution[191] came into effect in 2005. Article 35 guarantees equality:[192]

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188 Arts 23 and 24 Constitution of Malawi.

189 Constitution of the Republic of Mali, adopted in 1992; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/MaliC(rev).doc> (31 January 2007).

190 Art 17 Constitution of the Republic of Mali.

191 Constitution of Mozambique 2005; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/Mozambique.doc> (31 January 2007).

192 Art 35 Constitution of Mozambique.

> All citizens are equal before the law, and they shall enjoy the same rights, and shall be subject to the same duties regardless of colour, race, sex, ethnic origin, place of birth, religion, educational level, social position, the marital status of their parents, their profession or their political preference.

Article 40 guarantees everyone the right to life and physical and moral integrity. Article 41 guarantees the protection of privacy. Article 45(e) states that everyone has a duty to their community to defend and promote health. It is submitted that participation in clinical research with the aim of defending and promoting health could be such a duty.

Article 47 protects children's rights. Article 89 of the Mozambican Constitution guarantees all citizens the right to medical and health care, but within the terms of the law.

3.2.14 Namibia

The Constitution of Namibia[193] contains a bill of rights in chapter 3, setting out the protection of the fundamental rights and freedoms of all persons in Namibia. Several of the provisions in the Constitution are relevant to the protection of clinical research participants though clinical research is not mentioned specifically.

Articles 8, 10 and 13 of the Constitution are of particular interest. Article 8(1) ensures that 'the dignity of all persons shall be inviolable'; article 10 ensures equality. The grounds of prohibited discrimination in article 10 are 'sex, race, colour, ethnic origin, religion, creed or social or economic status'. Article 13 protects the right to privacy and article 15 protects children's rights.

3.2.15 Nigeria

The Constitution of the Federal Republic of Nigeria[194] does not contain a bill of rights as such, but rather 'fundamental objectives of state policy',[195] the provisions of which could be relevant in the protection of HIV-related clinical research participants.

Article 15(2) prohibits discrimination on the grounds of 'place of origin, sex, religion, status, ethnic or linguistic association or ties'. Article 17(3)(d) declares that

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193 Constitution of Namibia, adopted in February 1990, amended on 24 December 1998; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/NamibiaC(rev).doc> (31 January 2007).

194 Constitution of the Federal Republic of Nigeria, entered into force on 29 May 1999; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/NigeriaC(rev).doc> (31 January 2007).

195 See n 186.

the state 'shall ensure that there are adequate medical and health facilities' for all persons. Article 21 places a duty on the state to 'protect, preserve and promote the Nigerian cultures which enhance human dignity and are consistent with the fundamental objectives as provided in this Chapter; *and encourage development of technological and scientific studies which enhance cultural values*'.[196] It is doubtful whether this is a reference specifically to HIV-related clinical research.

3.2.16 Senegal

The Constitution of the Republic of Senegal[197] in Title II contains provisions relating to 'public liberties and the person'. Clinical research is not mentioned specifically.

> Article 7 reads:
>
> The human person is sacred. The human person is inviolable. The state shall have the obligation to respect it and to protect it. Every individual has the right to life, to freedom, to security, the free development of his or her personality, to corporal integrity, and especially to protection against physical mutilation.

The right of privacy is guaranteed in article 14, and the rights of 'wives' to marital property and to 'worldly goods' in article 19.

3.2.17 South Africa

The South African Constitution[198] contains a bill of rights in chapter 2. Apart from a specific provision on informed consent in clinical research in section 12(2)(c), discussed in detail later,[199] the South African Constitution provides in section 9 for the right to equality; in section 10 for the right to human dignity; in section 11 for the right to life; and in section 14 for the right to privacy.

The Constitution also guarantees the right of access to health care services in section 27: '[e]veryone has the right to have access to health care services, including reproductive health care'. Furthermore, the state must take 'reasonable legislative and other measures, within available resources, to achieve the progressive realisation of each of these rights'.

Children's rights are guaranteed in section 28, as well as their right to 'basic health care services'.

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196 My emphasis.

197 Constitution of the Republic of Senegal, adopted on 7 January 2001 and available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/SenegalC%20(english%20summary)(rev).doc> (31 January 2007).

198 Constitution of the Republic of South Africa 1996.

199 See para 4.4.2 of ch 5 below.

3.2.18 Swaziland

Chapter III of the 2005 Constitution of the Kingdom of Swaziland guarantees the fundamental human rights and freedoms of the individual.[200] A number of rights in Chapter III are relevant in the protection of participants in HIV-related clinical research.

Personal liberty is guaranteed in section 16(1): 'A person shall not be deprived of personal liberty save as may be authorised by law'. Article 18 guarantees the dignity of the individual. Article 18(2) states that '[a] person shall not be subjected to torture or to inhuman or degrading treatment or punishment'. Reflecting as it does the provisions of the Universal Declaration and the ICCPR, article 18(2) could be relied as a remedy by research participants in Swaziland who have been subjected to inhuman or degrading treatment.

Section 20 guarantees all persons the right to equality before the law: 'All persons are equal before and under the law', specifically, no one is to be 'discriminated against on the grounds of gender ... or disability'.[201] Section 22 guarantees the right against arbitrary searches: '[a] person shall not be subjected ... to the search of the person' except when 'reasonably required in the interests of' fundamental social objectives such as the promotion of 'public order, public morality ... public health'.[202] Children's rights are protected alongside those of mothers in section 27: 'Motherhood and childhood are entitled to special care and assistance by society and the State.'[203]

There is no provision specifically dealing with the protection of participants in clinical research in the Swaziland Constitution.

3.2.20 Tanzania

Part III of the Constitution of the United Republic of Tanzania[204] contains several human rights provisions relevant to the protection of participants in clinical research, but does not mention clinical research specifically.

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200 Constitution of the Kingdom of Swaziland, 2005; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/Swaziland.doc> (31 January 2007).

201 Art 20(1)(2) Constitution of the Kingdom of Swaziland, 2005.

202 Art 22(1)(a) and 22(2)(a) Constitution of the Kingdom of Swaziland, 2005.

203 Art 27(4) Constitution of the Kingdom of Swaziland, 2005.

204 Constitution of the United Republic of Tanzania, 1998, incorporates and consolidates all amendments made in the Constitution since its enactment by the Constituent Assembly in 1977 up to 1998; available at

Section 12 guarantees equality and states that all persons are born free and are equal. Everyone is entitled to the recognition and respect of their dignity. Section 13 prohibits discrimination on the grounds of 'nationality, tribe, place of origin, political opinion, colour, religion or station in life'. Section 14 guarantees the right to life and the right to protection of life by the society in accordance with law. Section 16 guarantees the right to respect of the person and privacy.

3.2.21 Uganda

The Constitution of the Republic of Uganda[205] includes a number of rights and entitlements that affect people participating in clinical research, though there is no specific reference to clinical research. Equality and freedom from discrimination are guaranteed in section 21. Article 22 protects the right to life, article 27 the right to privacy and article 33 women's rights. Amongst others, laws, cultures, customs or traditions which are against the dignity, welfare or interest of women or which undermine their status are prohibited.[206] Article 34 protects children's rights.

3.2.22 Zambia

The Zambian Constitution[207] guarantees human rights, but clinical research is not referred to specifically. The right to life in article 12 and article 17 protects the privacy of the person. Article 15 prohibits 'torture, or to inhuman or degrading punishment or other like treatment'.

Zambia currently has as well a draft Constitution which guarantees human rights. Article 39 of the draft Constitution prohibits discrimination based on race, sex, pregnancy, health, marital, ethnic, tribe, social or economic status, origin, colour, age, disability, religion, conscience, believe, future, language or birth.[208] Article 39 prohibits discrimination based on race, sex, pregnancy, health, marital,

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<http://www.chr.up.ac.za/hr_docs/constitutions/docs/TanzaniaC.pdf> 31 January 2007).

205 The Constitution of the Republic of Uganda, 1995; available at < http://www.chr.up.ac.za/hr_docs/constitutions/docs/UgandaC(rev).doc> (31 January 2007).

206 Art 33(6) Constitution of the Republic of Uganda, 1995.

207 Constitution of Zambia, as amended by Act 18 of 1996; available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/ZambiaC(rev).doc> (31 January 2007).

208 Draft Constitution of Zambia Cap 1.

ethnic, tribe, social or economic status, origin, colour, age, disability, religion, conscience, belief, torture, language or birth.[209]

Article 40 guarantees equal treatment for men and women. Article 40 further prohibits any law, culture, customs or traditions that undermine the dignity, welfare, interest or status of women or men.[210]

3.2.23 Zimbabwe

The Constitution of the Republic of Zimbabwe[211] contains a 'declaration of rights' in Chapter 3. Although clinical research is not mentioned, several of the rights in the Constitution of Zimbabwe apply to the situation of clinical trial participants.

Article 12 protects the right to life, and article 15 protects the individual's freedom from inhuman treatment. Article 15(1) determines that '[n]o person shall be subjected to torture or to inhuman or degrading punishment or other such treatment'; which is relevant to the situation of HIV vaccine trial participants.

Article 17 protects privacy; article 23 prohibits discrimination based on race, tribe, place of origin, political opinions, colour, creed or gender. Real or perceived HIV status is not mentioned, neither are the rights of persons who belong to minority groups subject to stigmatisation and discrimination, such as MSM, WSW, sex workers and IDUs.

3.3 Conclusion

This section delineated specific human rights provisions in domestic constitutions of selected sub-Saharan African countries which may be referred to in seeking to protect clinical research participants. The following conclusions are drawn.

First, all the countries contain provisions guaranteeing human rights in their constitutions and all the constitutions surveyed include at least some provisions relevant to providing protection for research participants. For example, the right to equality is guaranteed in the constitutions of 21 of the 22 countries; the right to human dignity in the constitutions of ten countries; and the right to privacy in the

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209 Draft Constitution of Zambia Cap 1.

210 Art 40(2) Draft Constitution of Zambia.

211 Constitution of the Republic of Zimbabwe, as amended to no 16 of 20 April 2000 (amendments in terms of Act 5 of 2000 (Amendment 16) are at sections 16, 16A (Land Acquisition) and 108A (Anti-Corruption Commission)); available at <http://www.chr.up.ac.za/hr_docs/constitutions/docs/ZimbabweC(rev).doc> (31 January 2007).

constitutions of sixteen countries. Many of the constitutions guarantee children's and women' rights as well.

Second, of special significance in guarding against possible abuses of clinical research participants, the right to freedom from torture and other degrading and inhuman treatment or punishment is declared in twelve of the 22 constitutions surveyed and the right to physical integrity or security of the person is guaranteed in the constitutions of six countries.

Third, only two of the constitutions surveyed – those of Malawi and South Africa - contain a provision which makes specific reference to clinical research. This omission may be ascribed to a number of reasons which are explored in a different context below.[212]

Fourth, of the 22 sub-Saharan African countries, six potentially protect the rights of persons living with HIV/AIDS or perceived to be living with HIV/AIDS.[213] The Constitution of Burundi explicitly protects people living with HIV/AIDS against discrimination. The rights of groups especially vulnerable to HIV infection and abuse in the research process, such as sex workers, MSM, IDUs and prisoners or detainees, are not mentioned in any of the constitutions (although the South Africa's constitution prohibits discrimination based upon 'sexual orientation' and some of the others prohibit discrimination based upon 'social status'). South Africa and Swaziland grant detainees the right of access to health care.

Finally, nine of the 22 constitutions guarantee a form of health care or access to health care either as a right or as a directive principle of state policy. The Eritrean Constitution provides that 'the state shall endeavour to make available to all citizens health, education, cultural and other social services,[214] and the South African Constitution provides for the 'progressive realisation' of health care.[215]

It is not in the purview of the survey to include information on the *implementation* of the constitutional provisions. Factors, such as a dysfunctional state and judiciary, civil war, corruption, poverty, illiteracy and a lack of effective access to the law,

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212 See para 4.5 of ch 5 below.

213 Here open-ended constitutional provisions on equality, such as those including the words 'other status', were taken to indicate a possibility of 'reading in' the protection of people living with HIV/AIDS, or people perceived to be living with HIV/AIDS. This study surveys only constitutional provisions, no account is given of protections provided by other legislation in force in those countries.

214 Art 21 Constitution of Eritrea.

215 Art 27 Constitution of the Republic of South Africa 1996.

compromise the force of human rights provisions guaranteed in a country's constitution. All that is intended is to demonstrate that in national constitutions there are provisions that could be called upon in protecting participants in HIV-related clinical research in Africa.

International human rights systems and instruments are now the focus.

4 INTERNATIONAL HUMAN RIGHTS SYSTEMS

4.1 Introduction

In the following section, international and regional systems for the protection of human rights are described.

First the United Nations (UN) system is described, and Charter and treaty-based instruments are outlined. Then follows an analysis of the three regional systems for the protection of human rights, including the African system which is discussed in relative detail. In the case of each system the implementation mechanisms are presented.

International human rights law divides into so-called 'hard' law and 'soft' law. Treaties and other binding instruments, known as 'hard law', are arrived at by agreement or consensus; whereas declarations, resolutions and other such instruments are known as 'soft' law because of their non-binding nature. This distinction has become of less value as 'soft law', despite its non-binding nature, has grown in importance as a source of international human rights law.

Soft law may not confer binding legal obligations upon states, but it is not without force and effect. For example, the Universal Declaration of Human Rights, technically, is not legally binding, however, many of the provisions have evolved into rules of customary law, and as such, are binding under international law.[216] Again, 'general comments' 'resolutions' and 'recommendations' of different treaty bodies do not generate binding obligations upon states, but they provide an authoritative interpretation of treaties and sometimes are lent a 'binding' nature when they are enforced through political rather than legal measures.

Chinkin asserts that the distinction between hard and soft law represents a false dichotomy;[217] he claims there exists a wide diversity in the instruments which

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216 See paras 4, 5 and 6 of ch 5 below.

217 See Chinkin (1989) 38 *The Intl and Comp L Q* 850.

compose so-called soft law, so that the generic term is a misleading simplification.[218] Soft law instruments vary in form, language, subject matter, participants, addresses, purposes and monitoring procedures. There is an inherent contradiction in the concept; the term 'law', which by its very nature is actionable, is combined with 'soft', designating something which is not enforceable.

Kenneth Abbott and Duncan Snidal argue that international actors deliberately choose soft law as being superior to hard law in institutional arrangements.[219] Soft law often is selected as a precursor to the 'harder' legalisation of obligations, but also is preferred in and of itself because it offers many of the advantages of hard law, while avoiding some of the cost. 'Soft' law has the advantage of being less challenging of state sovereignty and its obligations, therefore, are more acceptable to states.[220] Further, it allows state actors to become accustomed to the impact of commitments over time. Because soft law does not require all the formalities of hard law, it is accomplished in a less complicated and time-consuming manner.[221] Moreover, soft law facilitates compromise and cooperation between actors with different interests and values, different time horizons and different degrees of power.[222]

In the discussion below the focus falls primarily on hard law in the form of binding international human rights law, but occasionally soft law is mentioned.

4.2 The UN system

4.2.1 The Charter-based system

Dating back to the late 1940s, the international system for the protection of human rights is the oldest system. Traditionally, international law has governed the relationships between the different nations of the world.[223] States alone were the subjects of international law, and had rights under international law.[224] After World War I this narrow definition was broadened to include certain international

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218 As above.
219 Abbott and Snidal (2000) 54 *Intl Organization* 423.
220 As above.
221 Chinkin (n 217 above) 860.
222 As above.
223 Nowak (n 23 above) 16; Buergenthal (1995) 2.
224 Nowak 16 – 17; Buergenthal 2.

organisations; as yet individuals were not considered the bearers of international law rights.[225]

Today, individual human beings, as individuals, are considered to have internationally guaranteed human rights, and no longer need to belong to a particular state to claim these rights.[226] Whereas violations of human rights, in the past, were regarded as the 'internal affairs' of sovereign states, the atrocities committed during World War II strengthened the realisation that international co-operation was needed to protect individuals against abuses of state power.[227]

a) The UN Charter

Following a multi-national conference held in San Francisco, in the USA, the UN was formed in 1945 as a successor to the League of Nations.[228] The UN was intended to function as a permanent peace-keeping organisation.[229] The Preamble of the UN Charter sets out its purpose as relieving 'succeeding generations of the scourge of war', through maintaining international peace and security.[230]

The UN Charter did not provide the nations of the world with a comprehensive human rights system, but did lay the 'legal and conceptual foundation for the development of contemporary international human rights law'.[231] Article 1(3) of the UN Charter reaffirms the worth of human beings and describes the aims of the UN as follows (note that no reference is made to *protecting* human rights):[232]

> To achieve international co-operation in solving international problems of an economic, social, cultural, or humanitarian character, and in promoting and encouraging respect for human rights and for fundamental freedoms for all without distinction as to race, sex, language, or religion.

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225 As above.

226 Buergenthal (n 223 above) 19.

227 Nowak 17; Gostin and Lazzarini (1997) 2.

228 Nowak 73.

229 Nowak (n 23 above) 73; Annas in Gostin (n 35 above) 100. At present the UN's membership compromises all the countries of the world, except Nauru, a Pacific island state. Switzerland joined in 2002, after original refusing to join because of its wish to remain neutral.

230 Art 1 UN Charter.

231 Buergenthal (n 223 above) 23.

232 Nowak comments that for years, the UN took the 'promoting' aspects of its duties literally – the Human Rights Commission considered actions that went beyond mere promotion of human rights as 'inadmissible interferences with the domestic jurisdiction of states in accordance with art 2(7) of the UN Charter' (Nowak 73).

Articles 55 and 56 of the Charter outline the basic obligations of UN member states and the organisation.[233] The mandate is broad, but in reality confers very limited power upon the UN and its members.[234] The charge is to 'promote' respect for human rights. Also, articles 2(1) and 2(7) of the Charter reinforce the sovereignty of states, and stress the idea of non-intervention.[235]

Despite the limitations, the UN Charter has had a significant impact on international human rights law.[236] The UN Charter facilitates the acceptance of the notion that human rights are an international matter.[237] Nowak writes:[238]

> While to this day there is no international court of human rights that would compel states to meet their treaty obligations by internationally binding judgments, the significance of this universal codification process as the foundation of a world order rooted in the principles of the rule of law, democracy and human rights must not be underestimated.

The obligation of member states to co-operate in the promotion of human rights has ensured that the UN has the legal authority to define and codify these rights.[239] This promotional mandate, indirectly, has resulted in all the UN instruments for the protection of human rights.[240]

The obligation upon member states to promote human rights has enabled the UN over the years to adopt or create various Charter-based institutions to ensure member states' compliance, such as article 68 of the Charter that requires the Economic and Social Council of the UN to set up commissions for the protection of

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233 Art 55 reads: With a view to the creation of conditions of stability and well-being which are necessary for the peaceful and friendly relations among nations based on respect for the principle of equal rights and self-determination of peoples, the United Nations shall promote:
a) Higher standards of living, full employment, and conditions of economic and social progress and development;
b) Solutions of international economic, social, health, and related problems; and international cultural and educational cooperation; and
c) Universal respect for, and observance of, human rights and fundamental freedoms for all without distinction as to race, sex, language, or religion.
Art 56 reads: 'All members pledge themselves to take joint and separate action in co-operation with the Organisation for the achievement of the purposes set forth in Article 55'.

234 Buergenthal 24.

235 As above.

236 Buergenthal 25.

237 As above.

238 Nowak 73.

239 Buergenthal (n 223 above) 27.

240 As above.

human rights. [241] Resolutions of UN organs have also interpreted and elaborated upon certain provisions of the Charter.[242]

b) The Universal Declaration of Human Rights

Already at the San Francisco Conference proposals were made for the adoption of a human rights instrument.[243] These proposals were acted upon at the first meeting of the UN, which instructed the newly-created Commission on Human Rights to draft an international bill of rights.[244]

The Commission on Human Rights decided that first it should draft a declaration, and then proceed to creating legally binding documents in the form of draft treaties.[245] The Universal Declaration of Human Rights (Universal Declaration) was adopted by the UN General Assembly in December 1948.[246]

The Universal Declaration is the first comprehensive human rights document adopted by an international organisation[247] and it is considered a milestone in humankind's struggle for the recognition of human rights and the struggle for freedom and human dignity.[248]

Nowak comments on the fact that the Human Rights Commission in such a short space of time was able to get the international community to agree to adopt the Universal Declaration of Human Rights. He ascribes this success to the personal commitment of the individual delegates of the Human Rights Commission and to the fact that the international community of the 1940s was small, although ideological differences divided it.[249]

The Universal Declaration contains two classes or categories of rights. These are mostly civil and political rights and fewer economic, social and cultural rights. Civil and political rights in the Universal Declaration include the right to life, to liberty, to freedom of speech and religion, the prohibition on slavery and torture, of special relevance to the present study the right against inhuman and degrading

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241 For example, working groups on specific issues; rapporteurs for the different countries and supervisory committees that monitor compliance with the different treaties.

242 Eg *Reparation Case* ICJ Rep (1939) 174; *Voting Procedure Case* ICJ Rep (1955) 67; *International Status of South West Africa Case* ICJ Rep (1966) 6.

243 Nowak (n 23 above) 75.

244 Nowak 75; Buergenthal 29.

245 As above.

246 Buergenthal 29.

247 Buergenthal 29 – 30.

248 Buergenthal 30.

249 Nowak 75 – 76.

treatment,[250] the right to own property, the right to privacy and the right to a fair trial.

Economic, social and cultural rights included in the Charter are the right to social security, to protection against unemployment, to equal pay for equal work, to rest and leisure, the right to freely participate in the cultural life of the community, to education and to a standard of living adequate for the health and well-being of himself and of his family.

The rights listed above are not absolute; the Universal Declaration permits states to enact laws which limit the exercise of these rights provided their sole purpose is to secure 'due recognition and respect for the rights and freedoms of others ...'[251] Article 30, on the other hand, ensures that a government cannot violate the Universal Declaration by enacting legislation aimed at denying any of the rights in the Universal Declaration.

The Universal Declaration has no force in law as it is not a treaty. Its purpose is to promote a 'common understanding' of the human rights in it.[252] However, despite not having the force of law, the Universal Declaration has become a normative instrument that creates, at least, some obligations on the member states.[253] At the present time, some provisions of the Universal Declaration are recognised to be part of the body of customary international law[254] that may be called upon as the standard for human rights implementation.[255] The Universal Declaration has become the embodiment of what the international community means by the term 'human rights', and is an 'authoritative interpretation' of the term.[256] The Universal Declaration:[257]

> [a]s an authoritative listing of human rights, has become a basic component of international customary law, binding all states, not only members of the United Nations.

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250 See para 4.3.1 of ch 5 below.
251 Art 29(2) Universal Declaration.
252 Preamble Universal Declaration.
253 Buergenthal 33; see para 4.3.1 of ch 5 below.
254 See eg Alfredsson *et al* (eds) (1999) *The Universal Declaration of Human Rights – A common standard of achievement*; Beahr *et al* (eds) *Innovation and inspiration: Fifty Years of the Universal Declaration of Human Rights*; Heyns and Viljoen (2002) *The impact of the United Nations Human Rights Treaties on the Domestic Level*.
Not all scholars agree on whether the Universal Declaration of Human Rights has attained the status of customary international law. See para 5.2.3 below.
255 See para 4.3.1 of ch 5 below; Nowak 76; Buergenthal 34 – 35.
256 Nowak (n 23 above) 76, Buergenthal (n 223 above) 35.
257 Sohn (1982) 32 *American University L Rev* 16 – 17, quoted in Buergenthal 37.

The possibility of some sections of the Universal Declaration constituting customary international law is discussed below.[258]

4.2.2 The treaty-based system

a) The International Covenant on Civil and Political Rights and the Optional Protocol on the Convention on Civil and Political Rights

Background

Upon completion of the Universal Declaration, the Human Rights Committee set out to draft a legally binding treaty on human rights. There was to be a single treaty, containing, as is the case with the Universal Declaration, both civil and political rights and socio-economic rights.[259] Upon the insistence of the Western states, however, the treaty was divided into two – each contains a separate 'generation' of rights.[260]

On 16 December 1966 the International Covenant on Civil and Political Rights (ICCPR) was adopted by the UN General Assembly and opened for signature.[261] Only after ten years had sufficient states ratified both it and the International Covenant on Economic, Social and Cultural rights to bring them into operation.[262]

Because it is a treaty, the ICCPR bestows binding legal obligations on member states.[263] Non-compliance with the human rights enumerated in the ICCPR thus becomes a matter for international concern.[264]

Substantive provisions

The ICCPR is similar in substance to the European and American Conventions on Human Rights, but goes further in scope than these conventions.[265] Apart from many classic civil and political rights, it includes the right to self-determination of peoples and children's rights, as well as minority rights.[266]

The human rights that are guaranteed are not limitless. The ICCPR permits state parties to limit their exercise and protection of human rights. For example,

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258 See para 4.4 below, as well as para 4.3.1 of ch 5 below.
259 Nowak 78.
260 Nowak 78. Nowak explains that this decision was resisted by socialist states, who stressed the interdependence and indivisibility of human rights, while the West argued that 2nd generation rights are only 'programmatic' rights which are not immediately enforceable and which could therefore not be made justiciable.
261 GA Res 2200A (XXI) of 16 December 1966. Nowak 80; Buergenthal 38 - 39.
262 Nowak 79; Buergenthal 38.
263 Beurgethal 38.
264 As above.
265 Nowak 79.
266 As above.

article 18 guarantees freedom of religion, and asserts that 'freedom to manifest one's religion or beliefs may be subject only to such limitations as are prescribed by law and are necessary to protect public safety, order, health, or morals or the fundamental rights and freedoms of others.'[267]

For a limitation of the rights guaranteed to be considered legitimate, a government has to address five criteria spelled out in the Siracusa principles adopted by the UN Economic and Social Council.[268] They are:[269]

- The proposed restriction has to be provided for and implemented *in accordance with the law*.
- The restriction has to be directed towards a *legitimate objective of general interest*, such as preventing transmission of HIV.
- It must be *strictly necessary* to achieve the objective in question.
- *No less intrusive and restrictive means* should be available to reach this objective.
- It cannot be *unreasonable or discriminatory* in its application.

The government that wants to restrict rights has a burden to prove adherence to the principles enumerated above. Any restriction on the rights of participants in clinical research in Africa, therefore, will have to meet these criteria.

Art 2(1) sets out the obligations of state parties to the ICCPR. State parties undertake to respect and ensure that all individuals enjoy the rights enumerated in ICCPR. Art 2(2) requires all states to adopt measures to give effect to the rights in the ICCPR. An immediate obligation is thus imposed on state parties to the ICCPR.[270]

Article 7 of ICCPR reads '[n]o one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment'. This article is of peculiar

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267 Art 18.

268 ECOSOC (1985) *The Siracusa principles on the limitation and derogation provisions in the international covenant on civil and political rights*; available at <http://portal.unesco.org/shs/en/ev.php-URL_ID=5078&URL_DO=DO_TOPIC&URL_SECTION=201.html> (30 November 2006).

269 As above; my emphasis.

270 Unlike the Covenant on Economic, Social and Cultural Rights, which merely obliges states to progressively implement the rights.

importance to this study, since it adds '[i]n particular, no one shall be subjected without his free consent to medical or scientific experimentation'.[271]

Procedures for implementation

The 18 member Human Rights Committee established by the ICCPR was to ensure that state parties comply with their obligations under the ICCPR.[272] The Human Rights Committee was responsible for administering the reporting system of states,[273] as well as the individual and inter-state complaints system.[274] The Human Rights Council was established in April 2006 to replace the Human Rights Committee.[275]

State parties are required to submit reports on the measures they have taken to give effect to the rights in the ICCPR.[276]

The ICCPR also allows an inter-state complaints system where one state party may complain about human rights violations committed by another state party.[277]

'Special procedures' is the general name given to the mechanisms established by the Commission on Human Rights to address either specific country situations or thematic issues in all parts of the world.[278] Currently, there are 28 thematic and 13 country mandates in place.[279] The Office of the High Commissioner for Human Rights provides these mechanisms with personnel and logistical assistance to aid them in the discharge of their mandates.

The UN Commission on Human Rights has appointed a Special Rapporteur to examine questions relevant to torture.[280] The mandate of the Special Rapporteur covers all countries, irrespective of whether a state has ratified the Convention against Torture and Other Cruel, Inhuman or Degrading Treatment or Punishment.[281]

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271 See para 4.3.2 below.
272 Nowak (n 23 above) 80; Buergenthal (n 223 above) 43.
273 In terms of art 40 – it is mandatory.
274 In terms of art 41 – there have been no cases to date, Nowak 80.
275 UN A/Res/60/251.
276 Art 40(1).
277 Arts 41 & 42. States parties had to have made an optional declaration which recognises the jurisdiction of the Human Rights Committee to receive such complaints.
278 See <http://www.ohchr.org/english/bodies/chr/special/index.htm> (31 January 2006).
279 As above.
280 <http://www.ohchr.org/english/issues/torture/rapporteur/index.htm> (31 January 2007).
281 As above.

The mandate comprises three main activities: transmitting urgent appeals to states with regard to individuals reported to be at risk of torture, as well as communications on past alleged cases of torture; undertaking fact-finding country visits; and submitting annual reports on activities, the mandate and methods of work to the Human Rights Council and the General Assembly.[282] The Special Rapporteur does not require the exhaustion of domestic remedies to act.[283] The Rapporteur has not yet investigated an issue related to inhumane or degrading treatment during medical or scientific research, although this may fall within the Rapporteur's mandate.

The 1st Optional Protocol to the ICCPR, a separate treaty, supplementing the enforcement measures of the ICCPR,[284] entered into force in 1976. It allows individuals to claim violations of their human rights by state parties in the form of individual communications.[285] The Rules of Procedure[286] of the Human Rights Committee determines that the Human Rights Committee examines these complaints or communications in two stages – first, it decides on the admissibility of a complaint, and second it decides on the merits of the complaint.[287] The state that has been complained about in the individual complaint has six months within which to respond,[288] after which the Human Rights Committee reviews the submissions of the individual and the state party and makes a decision. However, many of the large number of individual complaints that have been received have been ruled inadmissible by the Committee due to non-exhaustion of domestic remedies.

A major problem with the ICCPR is that, unlike the European and Inter-American systems, it does not establish an international court of human rights.[289] The decisions of the Human Rights Committee are not legally binding, so that, in practice, it has become a quasi-judicial monitoring body for state reporting and individual complaints procedures.[290] At the UN there is not a body that enforces its decisions through political measures.[291]

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282 As above.
283 As above.
284 104 state parties, similar to procedure before European Court of Human Rights (Nowak 80).
285 Arts 1 and 2.
286 Rules of Procedure, Doc CCPR/C/3 Rev 3 (1994).
287 Rules 93 – 94 Rules of Procedure.
288 Art 4.
289 Nowak 79.
290 Nowak 80.
291 Nowak 81.

The 2nd Optional Protocol to the ICCPR entered into force in 1991. The objective of the Protocol is the abolition of the death penalty.[292]

b) International Covenant on Economic, Social and Cultural Rights

Background

The International Covenant on Economic, Social and Cultural Rights (ICESCR) recognises a wide range of second generation rights.[293] It was adopted by the UN General Assembly on 16 December 1966, and, ten years later, entered into force on 3 January 1976.[294]

Substantive provisions

The rights guaranteed in the ICESCR are not immediately enforceable. A state party undertakes only to 'take steps ... to the maximum of its available resources ... with a view to achieving the full realisation of the rights ...'[295] As Nowak points out, the wording of article 2(1) refers to 'obligations of conduct', rather than 'obligations of result'.[296]

Procedures for implementation

The monitoring body which supervises the implementation of this treaty is the Committee on Economic, Social and Cultural Rights.[297] The ICESCR has not established an individual or inter-state complaints mechanism, but it does require states to submit reports on what they have done to ensure the observance of the rights in the ICESCR.[298] There is a draft Optional Protocol to the ICESCR which proposes to allow for an individual complaints mechanism. The Human Rights

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292 Art 1 Second Optional Protocol to the ICCPR.

293 The right to work, the right to join trade unions, the right to strike, the right to social security, the right to protection of the family, maternity protection, protection of children and young people, the right to an adequate standard of living, the right to health, the right to education and participation in cultural life, etc.
Of importance to the present study is art 2(1) which refers to international assistance and co-operation of a technical nature, implying an obligation on developed countries to help ensure the worldwide realisation of these 2nd generation rights. This provision has implications for international co-operation in clinical testing.

294 GA Res 2200A(XXI) of 16 December 1966; 147 states parties; Nowak 81.

295 Art 2(1)

296 Nowak 81. States are merely obliged to achieve progressive realisation of these rights.

297 Not provided for in the treaty, established by the ECOSOC, Res 1985/17); Nowak 82.

298 Art 16(1).

Commission has deliberated on this draft protocol for several years, but still it has not been adopted.[299]

c) Miscellaneous UN human rights treaties

Over the past decades the UN established a number of treaties which deal with specific types of human rights violations. These treaties include (the list is not exhaustive)[300] the Convention on the Elimination of all forms of Discrimination Against Women (CEDAW);[301] the Convention Against Torture and Other Cruel, Inhuman or Degrading Treatment or Punishment (CAT);[302] and the Convention on the Rights of the Child (CRC);[303] and the Convention on the Protection of the Rights of All Migrant Workers and Members of Their Families (CMW).[304] Each of these treaties establishes a treaty monitoring body (or 'committee') in the form of a supervisory quasi-judicial institution.

CEDAW and CRC will be discussed below as they are relevant to the present enquiry into the human rights of participants in clinical trials. The discussion is general[305] in preparation for a more detailed discussion of selected provisions in paragraph 5 below.

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299 Nowak 83. See also Arambulo (1999) *Strengthening the supervision of the International Covenant on Economic, Social and Cultural Rights: Theoretical and procedural aspects* and Craven (1995) *The International Covenant on Economic, Social and Cultural Rights: A perspective on its development.*

300 See Nowak 95 for a list of other UN treaties and the years they entered into force.

301 UN GA Res 34/180, UN Doc A/34/46; adopted 18 December 1979, entered into force 3 September 1981.

302 UN GA Res 39/46, UN Doc A/39/51; adopted on 10 December 1984 and entered into force on 26 June 1987. It has 133 state parties.

303 UN GA Res 44/25; adopted 20 November 1989, entered into force 2 September 1990. CRC has been ratified by almost every state in the world. The exceptions are Somalia and the USA.

304 UN GA Res 45/158; adopted in 1990, entered into force 1 July 2003.

305 For a more detailed discussion on CRC, see Hammarberg 'The United Nations Convention on the Rights of the Child – And how to make it work' (1990) 12 *Human Rights Q* 97; Viljoen 'Supra-national human rights instruments for the protection of children in Africa: The Convention on the Rights of the Child and the African Charter on the Rights and Welfare of the Child' (1998) 31 *Comp and Intl L J Southern Africa* 199; Detrick *A Commentary on the United Nations Convention on the Rights of the Child* (1999) 415; Van Bueren (1995) *The international law on the rights of the child.* For a more detailed discussion on CEDAW, see Cook (ed) (1994) *Human rights for women: National and international perspectives*; Charlesworth *et al* 'Feminist approaches to international law' (1991) 85 *American J Intl L* 613; Gallagher 'Ending the marginalisation: Strategies for incorporating women onto the United Nations human rights system' (1997) 19 *Human Rights Q* 283.

i) CEDAW

Background

There has been a considerable focus on the rights of women at the UN. A Special Rapporteur has been appointed for women, and various conventions on women's' issues are in existence.[306]

CEDAW entered into force in 1981, after its adoption in 1970.[307] The Preamble outlines reasons for the adoption of CEDAW - the impact of discrimination against women upon their human dignity and the dire situation of women who are poor.

> *Recalling* that discrimination against women violates the principles of equality of rights and respect for human dignity, is an obstacle to the participation of women on equal terms with men, in the political, social, economic and cultural life of their countries ...
>
> and
>
> *Concerned* that in situations of poverty women have the least access to food, health, education, training and opportunities for employment and other needs ...

The drafters of CEDAW demonstrated the realisation that legislation alone is unlikely to change perceptions about women and the position of women in society. Article 5 obliges states:

> to modify the social and cultural patterns of conduct of men and women, with a view to achieving the elimination of prejudices and customary and all other practices which are based on the idea of the inferiority or the superiority of either of the sexes ....
>
> to ensure that family education includes a proper understanding of maternity as a social function and the recognition of the common responsibility of men and women in the upbringing and development of their children ...

Substantive provisions

In article 1, 'discrimination against women' is defined as 'any distinction, exclusion or restriction made on the basis of sex' which results in the impairment of women's enjoyment of their human rights. Apart from this prohibition on discrimination, article 4 of CEDAW explicitly allows affirmative action for the purpose of benefiting women.

Other provisions of CEDAW deal with women's civil and political rights,[308] their social, economic and cultural rights[309] and marriage and family rights.[310]

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306 eg Convention on the Political Rights of Women and the Convention on the Consent to Marriage.

307 Nowak 87.

308 Arts 7 – 9 CEDAW.

Special provision is made with regard to trafficking in women[311] and the problems facing rural women.[312]

Of particular interest for the present investigation is article 12 of CEDAW. State parties are compelled to take 'all appropriate measures' to eliminate discrimination in the field of health care; to ensure 'access to health care services, including those related to family planning'.[313] Women should also be assured of appropriate services in connection with pregnancy, confinement and the post-natal period, 'granting free services where necessary'.[314]

Art 12 of CEDAW corresponds, in some aspects, with article 12 of the ICESCR which also deals with health. Both provisions ensure 'access' to health only, and, in the ICESCR, the right is qualified by 'steps to achieve the full realisation of this right'. However, the obligation on state parties in CEDAW to eliminate discrimination in health services is without qualification.

Implementation procedures

A 23-member Committee on the Elimination of Discrimination against Women monitor state parties in the fulfilment of their obligations under CEDAW to eliminate discrimination against women in all spheres of life.[315] The state reporting procedure is mandatory for all state parties.[316] Upon examining state reports, the Committee makes country-specific observations, as well as general recommendations.[317] There is no inter-state complaints procedure under CEDAW.[318]

Initially, the Committee simply examined state reports, but it has been instrumental in the adoption by the UN General Assembly in 1999 of an Optional Protocol to CEDAW which allows for an individual communications procedure and an enquiry procedure.[319] The Optional Protocol entered into force in December 2000.[320]

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309 Arts 10 – 14 CEDAW.
310 Art 16 CEDAW.
311 Art 6 CEDAW.
312 Art 14.
313 Art 12(1).
314 Art 12(2).
315 Nowak (n 23 above) 86 – 87.
316 Art 18 CEDAW.
317 Nowak 87.
318 As above. For a feminist critique of human rights which draws upon CEDAW, see Charlesworth *et al* 'Feminist approaches to international law' (1991) 85 *American J Intl L* 613.
319 Nowak 87 – 88.
320 GA Res 54/4 of 6 October 1999, entry into force on 22 February 2000. There are 51 states parties to the Optional Protocol.

ii) CRC

Background

CRC reflects a realisation that the specific needs and rights of children require specialised recognition and protection, and that the family is of utmost importance in this regard.[321]

> *Convinced* that the family, as the fundamental group of society and the natural environment for the growth and well-being of all its members and particularly children, should be afforded the necessary protection and assistance so that it can fully assume its responsibilities in the community,
>
> *Recognising* that the child, for the full and harmonious development of his or her personality, should grow up in a family environment, in an atmosphere of happiness, love and understanding ...

The importance of the child's culture and traditions is not neglected:[322]

> *Taking* due account of the importance of the traditions and cultural values of each people for the protection and harmonious development of the child ... .

Substantive provisions

CRC includes a comprehensive selection of civil and political and economic, social and cultural rights, as well as rights that are specific to children.[323] It is the first treaty to place the different generations of rights on an equal footing.[324]

Article 1 of CRC defines a 'child' as every human being below the age of 18 years. Article 2 guarantees every child the enjoyment of the rights in the Convention free from discrimination, and state parties have to ensure that enjoyment to children within their jurisdiction.

Article 3 of CRC provides that in all actions affecting the child the 'best interests of the child must be a primary consideration'. In other words, every decision taken regarding children must have their enhanced growth and development as the purpose, regardless of whether it is made by a private or a public institution, courts of law, administrative authorities or legislative bodies.

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321 Preamble CRC.

322 Preamble CRC.

323 For example, development of children's identity, rights against arbitrary separation from parents and to engage in play and recreational activities.

324 Nowak (n 23 above) 93. Civil and political rights are included in the same document with social, economic and cultural rights.

Article 4 obliges state parties to CRC to undertake all appropriate measures to implement the rights recognised in the CRC. The availability of resources limits social, economic and cultural rights.[325]

Among other rights included in CRC are the child's right to life and development;[326] access to information, which includes the encouragement of state parties to produce and disseminate children's books;[327] the primary responsibility of parents in bringing up their children;[328] the rights of disabled children;[329] the child's right to benefit from social security;[330] an adequate standard of living;[331] the right to education;[332] the right of children belonging to minorities to enjoy his or her culture, religion or language;[333] the right to rest and leisure;[334] and the right to be protected from economic exploitation.[335]

Of interest to the present study is article 24 which guarantees the child's right to the enjoyment of the highest attainable standard of health. Subsection 2 lists a number of steps to be taken by state parties to effect the realisation of this right. These are measures to diminish infant mortality;[336] the provision of medical assistance and health care to all;[337] to combat disease 'through the application of readily available technology';[338] appropriate pre- and post-natal health care for mothers[339]; education on health and accidents;[340] and 'the development of preventive health care'.[341]

Further, traditional practices prejudicial to the health of children are to be abolished.[342] This sub-section is directed at harmful cultural practices, such as

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325 Art 4 CRC.
326 Art 6 CRC.
327 Art 17 CRC.
328 Art 18 CRC.
329 Art 23 CRC.
330 Art 26 CRC.
331 Art 27 CRC.
332 Arts 28 – 19 CRC.
333 Art 30 CRC.
334 Art 31 CRC.
335 Art 32 CRC.
336 Art 24(2)(a).
337 Art 24(2)(b).
338 Art 24(2)(c).
339 Art 24(2)(d).
340 Art 24(2)(e).
341 Art 24(2)(f).
342 Art 24(3) CRC.

female genital mutilation.[343] Finally, state parties shall undertake steps which promote and encourage international co-operation with a view to progressively realising the rights recognised in section 24.[344]

Implementation procedures

The monitoring of state compliance with treaty obligations is carried out by the Committee on the Rights of the Child.[345] The Committee oversees a mandatory state reporting procedure in terms of article 44 of CRC. There is no provision for inter-state complaints or for individual communications.

The UN Committee on the Rights of the Child considers four principles fundamental to the CRC.[346] These four principles underpin the entire Convention. They are the prohibition of discrimination;[347] the right to participation of children;[348] the right to life and development of the child to the maximum extent;[349] and that the best interests of the child shall be a primary consideration in all actions concerning children.[350]

Two Optional Protocols to CRC have been adopted. Each focuses on a specific problem relating to children's human rights. They are the Optional Protocol on the Involvement of Children in Armed Conflicts,[351] and the Optional Protocol on the Sale of children, Child prostitution and Child pornography.[352]

4.3 The regional systems

4.3.1 Introduction

Regional systems for the protection of human rights are an important part of international human rights protection. After domestic remedies are exhausted, usually it is to the regional system that victims of human rights violations turn.

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343 See generally in this regard, Kaime 'The Convention on the Rights of the Child and the cultural legitimacy of children's rights in Africa: Some reflections' (2005) 5 *African Human Rights L J* 221.

344 Art 24(4) CRC.

345 Art 43 CRC.

346 Nowak (n 23 above) 93.

347 Art 3 CRC.

348 Art 12 CRC.

349 Art 6 CRC.

350 Art 3 CRC.

351 GA Res 54/263 of 25 May 2000, entry into force on 12 February 2002, 52 state parties.

352 GA Res 54/263 of 25 May 2000, entry into force on 18 January 2002, 51 state parties.

Consequently, the regional system is a rich source of human rights jurisprudence, to be drawn upon by judges in domestic jurisdictions.[353]

The following paragraphs outline the three regional systems for the protection of human rights; namely, the European system, the Inter-American system and the African system.[354] Because of its relevance to HIV-related clinical research in Africa, the African system is discussed in greater detail than the other two systems.

4.3.2 The European system

Background

The European system for the protection of human rights dates back to 1949.[355] The European system was established by a group of western European nations with the goal of preserving individual freedom and democracy.[356] The system is the oldest regional system, and, is also, arguably, the most effective in its enforcement of human rights.

The European system's human rights law is founded on the European Convention for the Protection of Human Rights and Fundamental Freedoms[357] and the European Social Charter.[358] The European Convention deals with civil and political rights; the Charter deals with economic and social rights. Each treaty establishes its own monitoring mechanism.

The European Convention was signed on 4 November 1950 and entered into force on 3 September 1953.[359] Although ratification of the Convention was not initially required of the members of the Council of Europe;[360] all existing members have ratified the Convention and the Council of Europe has subsequently made the ratification of the Convention a precondition to admission to the Council.[361]

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353 See ch 5 below.

354 For a schematic comparison of the three regional systems, see Heyns *et al* 'A schematic comparison of regional human rights systems: An update' (2005) 5 *African Human Rights L J* 308.

355 Nowak (n 23 above) 158; Buergenthal (n 223 above) 102.

356 As above.

357 It has 45 ratifications. From now on referred to as the 'European Convention'.

358 Buergenthal 102. The European Social Charter is from now on referred to as the 'Charter'.

359 Buergenthal 103.

360 Founded in 1949 by eleven western European states to promote human rights, the rule of law and pluralistic democracy (Nowak 158).

361 Buergenthal 103.

Substantive provisions

The Convention guarantees most of the traditional civil and political human rights. These include the right to life; the right not to be subjected to torture, inhuman or degrading punishment; freedom from slavery; the right to liberty and security of the person; due process of law; freedom of thought, conscience and religion and freedom of expression.

Article 13 of the European Convention stipulates that an 'effective remedy before a national court must be provided to anyone whose rights had been violated'. Also, 'everyone' within the 'jurisdiction' of the state parties is a bearer of the rights in the European Convention, regardless of their nationality.[362]

Several protocols have been appended to the European Convention, each adding to and expanding upon the rights guaranteed in the European Convention. For example, Protocol 1 deals with the right to own property, the right to education, and the right to free and secret elections at regular intervals; Protocol 6 abolishes the death penalty in member states.

Implementation procedures

The adoption in 1998 of the 11th Additional Protocol to the European Convention[363] dramatically changed the implementation mechanism of the European system.[364] Before the 11th Protocol, the European Convention had two mechanisms to ensure the observance of rights: the European Commission of Human Rights (European Commission) and the European Court of Human rights (European Court).[365] The process to bring a complaint before and after the adoption of the 11th Protocol is briefly outlined below.

The European Commission consisted of members equal in number to the 'high contracting parties' to the European Convention.[366] The European Court consisted of judges equal in number to that of the Members of the Council of Europe.[367] The judges served nine-year terms; in their individual capacities; they

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362 Art 1 European Convention.
363 Entering onto force on 1 November 1998 (Nowak 164).
364 Nowak 164.
365 The Committee of Ministers has a supervisory role in relation to overseeing the enforcement of rights (Buergenthal 106).
366 Buergenthal 107.
367 Art 38 European Convention; Buergenthal 107.

had to be of 'high moral character'; and 'possess the qualifications required for appointment to high judicial office or jurisconsults of recognised competence'.[368]

Strasbourg was the seat of the European Commission and Court, but is now the seat of the European Court.[369]

The rights guaranteed by the European Convention are enforced at a national (domestic) and an international level.[370] In a substantial number of member states, the European Convention enjoys the status of national law, and, thus, it may be invoked in the national courts[371] and it creates rights that are directly enforceable by individuals.[372] Only when domestic law does not remedy the violation may the victim turn to the European Court and Commission.[373]

The European Commission allowed for inter-state complaints. In ratifying the European Convention, states were deemed to have accepted the jurisdiction of the European Commission.[374] The requirement of exhausting domestic remedies applied to cases heard in front of the European Commission as well.[375]

Only a small number of inter-state complaints have been lodged with the European Commission.[376] Mostly, the complaints have been against states who have not acknowledged the right of individual's petitioning,[377] however, states have not been eager to lodge complaints against other states in case it is seen as an act of hostility.[378]

The European Commission could hear private petitions for violations of the Convention in terms of art 25 of the European Convention.[379] To be effective, a special declaration in terms of art 25(1) was required and was not automatic upon signing the European Convention. Most state parties accepted the Commission's jurisdiction to deal with private complaints.[380] Further, natural and juristic persons could approach the European Commission.[381]

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368 Art 38(3) European Convention.
369 The new Court also has its seat in Strassbourg.
370 Nowak 160.
371 Nowak 160; Buergenthal 108.
372 As above.
373 Art 26 European Convention; Buergenthal 109.
374 Art 24 European Convention, Buergenthal 110.
375 Arts 26 – 27 European Convention; Buergenthal 110.
376 Nowak 161; Buergenthal 111.
377 As above.
378 Buergenthal 112.
379 Buergenthal 112.
380 Buergenthal (n 223 above) 112.
381 As above.

Private petitions were examined in different stages by individual rapporteurs, committees or by the plenary Commission.[382] Upon their being received, individual complaints were assigned to a commission member designated as a rapporteur. The rapporteur prepared a report on the complaint's admissibility and decided whether to refer the matter to a committee or a chamber.[383]

A chamber dealt with cases 'which can be dealt with on the basis of established case law' or which raised no serious questions related to the application and interpretation of the European Convention.[384] Other complaints were dealt with by the plenary Commission.[385] On the other hand, inter-state complaints went directly from the rapporteur to the plenary Commission.[386]

Only about 10 to 15 per cent of cases have been declared admissible and have proceeded to a hearing by the Commission.[387] The Commission first investigated the facts of the case; it held interviews, received written submissions and examined witnesses.[388] During the process, the Commission sought at the same time to achieve a friendly settlement between the parties.[389] If a settlement was reached, it consisted of an agreement in terms of which the respondent state undertook to pay damages or make amends. This agreement or settlement did not include any admittance by the state that it had violated the convention.[390]

Cases that were not settled in this manner proceeded to the next stage in which the Commission drew up a report stating its opinion on whether the facts disclosed were a breach of the Convention.[391] The report was drafted in the form of a judicial opinion but was not a judgment;[392] and was then given to the Committee of Ministers, along with the Commission's recommendations.[393] The Commission and the parties then had three months within which to refer the case to the Court, failing

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382 Art 20 European Convention, as amended by Protocol 8.
383 Buergenthal 123.
384 Art 20(2) European Convention, Buergenthal 123.
385 Art 20(5) European Convention; Buergenthal 124.
386 As above.
387 Buergenthal 124.
388 Art 28(1)(a) European Convention.
389 Art 28(1)(b) European Convention; Buergenthal 125.
390 Buergenthal 126. This friendly settlement is then recorded in a report of the Commission (art 28(2) European Convention).
391 Buergenthal 126; art 28(2) European Convention.
392 As above. It is not a judgment as the Commission cannot formally decide the case.
393 Buergenthal 126; arts 31(2) and 31(3) European Convention.

which, the Committee of Ministers decided whether there had been a violation of the Convention.[394]

The Plenary Commission took the decision whether or not to refer a case to the Court. Until the entry into force of Protocol 9, individuals were unable to refer a case to court.[395]

If a case had not been referred to the Court within the three months time period, the Committee of Ministers decided whether there had been a violation of the Convention.[396] The Committee of Ministers consisted of the foreign ministers, or their deputies, for each member state of the Council of Europe, and it was, therefore, a political, rather than a judicial, body.[397]

A decision by the Committee of Ministers that there had been a violation of the Convention required a two-thirds majority vote, and the state parties to the dispute were allowed to vote.[398] The decision of the Committee of Ministers, in accordance with article 32, were binding upon the state parties to the Convention, and a time limit could be imposed upon states to comply with the decision of the Committee of Ministers.[399]

Article 54 of the European Convention declared the Committee of Ministers shall ensure the implementation of the Court's decision and 'shall supervise its execution' by means of two rules of its procedure: rule 1 which determines that a judgment of the Court shall be put on the Committee's agenda, and rule 2 by which the state concerned must indicate what it has done to comply with the decision of the Court.[400] If the state failed to comply with the order of the Court, the item was automatically placed on the Committee's agenda to be considered within six months.[401]

In 1998, after the adoption of the 11th Protocol, a single and permanent European Court was established to take over from the earlier Commission and Court.[402] Before this the Commission and Court had been staffed by voluntary part-

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394 Buergenthal 127; art 32 European Convention.
395 Buergenthal 127. This remains a problem for individuals from states who have not ratified this protocol.
396 Art 32(1) European Convention.
397 Buergenthal 128.
398 Buergenthal 128.
399 Buergenthal 130.
400 Buergenthal 131.
401 Buergenthal 131.
402 Nowak (n 23 above) 164.

time commissioners and judges, but now they have been replaced by full-time, permanent staff. [403]

The 11th Protocol deletes the clauses which make access to the Court optional, with the consequence that individual and inter-state complaints procedures before the new Court are compulsory for all states parties.[404] The role of the Committee of Ministers in the decision-making procedure was done away with, instead it oversees the execution of the Court's judgments at the domestic level, streamlining the process.[405]

The Court is the only body to decide on the admissibility and merit of complaints, and is able to deal with a far greater number of cases than before, including the steep rise in individual complaints.[406]

Nowak sums up the consequences following the adoption of a single Court as follows:[407] the length of proceedings is shortened; the judicial character of the system is strengthened; the adjudicative role of the Committee of Ministers has been abolished; the European Commission of Human Rights has been abolished; and the optional clauses concerning individual complaints and the jurisdiction of the Court have been removed.[408]

The European Court's caseload increased dramatically after the change brought about by the 11th Protocol. In 2004, the European Court delivered 21 191 decisions and 718 judgments; by the end of 2004, 78 000 applications were pending before the Court; and an astonishing 44 100 communications have been lodged.[409]

European Social Charter

Background

The European Social Charter was opened for signature in 1961 and entered into force on 26 February 1965.[410] The European Social Charter establishes a system for the protection of social, economic and cultural rights. Nowak remarks that the European community through the years paid lip service to the indivisibility and

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403 As above.
404 Nowak 164.
405 As above.
406 As above.
407 Nowak 165.
408 For a clear schematic exposition of the new procedure before the Court, see Nowak 172.
409 Heyns *et al* (n 354 above) 308 - 311.
410 Nowak 173; Buergenthal 151. It is established under the auspices of the Council of Europe.

interdependence of human rights; they have done little to change the inequality of the two classes or categories of rights.[411] The European Social Charter is still regarded as the 'little sister' of the better known European Convention.[412]

Substantive provisions

The European Social Charter includes 19 categories of rights, including the right to work, to bargain collectively and to fair remuneration. It recognises the right of the family to social, legal and economic protection, as well as the right to protection of health, to social security, and to social and medical assistance.[413]

Implementation procedures

The European Social Charter system establishes a reporting system to monitor state parties' compliance with the Charter and Protocol.[414] Two types of reports are necessary: the first, due every two years, addresses domestic implementation of the rights in the Charter;[415] the second deals with the status of the rights that the particular state did not accept upon ratifying the European Social Charter.[416] These reports are examined by different bodies of the Council of Europe.[417]

Additional protocols, extending the rights protected by the Social Charter, have been added. The first Additional Protocol of 1988, entered into force in 1992, but has been ratified by eleven states only.[418] This Protocol supplements the list of social and economic rights guaranteed, adding four further 'rights and principles'; namely, the right of workers to equal treatment and non-discrimination on the grounds of sex, the right to take part in the improvement of working conditions and the right of elderly persons to social protection.

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411 Nowak 173.
412 As above.
413 In accordance with art 20 of the European Charter, states parties are allowed to 'selectively' ratify the rights they want to be bound to – this is called an 'opting in' system or an '*a la carte*' ratification system.
414 Buergenthal 155.
415 Art 21 European Social Charter; Buergenthal 155.
416 Buergenthal 154.
417 Buergenthal 154.
418 Nowak 173.

A Protocol Amending the European Social Charter was signed in 1991. This Protocol has nineteen state parties.[419] A third protocol provides for a system of collective complaints and was adopted in 1995. It has ten state parties.[420]

The Revised European Social Charter entered into force in 1999. As well as adding rights to the Charter, the revision replaces the Committee of Independent Experts of the earlier Charter with a European Committee of Social Rights to assess state compliance with their obligations under the European Charter.[421] The Committee's conclusions still have to be submitted to a Council of Europe Government Committee and accepted in a Committee of Ministers by a two-thirds majority vote.[422]

The Revised European Social Charter co-exists with the original Charter.[423] It has been ratified by 19 of the 45 European Council members. The others continue to adhere to the original Charter of 1961.[424]

Several additional treaties, each with a specific focus on a specific problem or aspect of human rights protection, have been adopted under the European system. Among these are the European Convention for the Prevention of Torture,[425] the European Framework Convention for the Protection of National Minorities,[426] the European Charter for Regional and Minority Languages[427] and the European Convention on Human Rights and Biomedicine,[428] which is of particular importance to the present study.

European Convention on Human Rights and Biomedicine

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419 Nowak 173. This protocol was superseded by the Revised European Social Charter.

420 A collective complaints system differs from the individual complaints system in that it does not recognise individual complaints, but rather collective complaints through NGOs (Nowak 176).

421 Nowak 175.

422 Nowak 175.

423 Nowak 176.

424 Nowak 176. The unrevised Social Charter has 27 ratifications. For more on the European system for the protection of human rights, see Cameron (2002) *An introduction to the European Convention on Human Rights* (4th ed); Ovey *et al* (2002) *Jacobs and White: The European Convention on Human Rights.*

425 Opened for signature 26 November 1987 and entered into force on 1 February 1989. It has 44 states parties.

426 Opened for signature on 1 February 1995, entered into force on 1 February 1998. It has 35 states parties

427 Opened for signature on 5 November 1992, entered into force on 1 March 1998. It has 17 states parties.

428 Opened for signature on 4 April 1997, entered into force on 1 December 1999. It has 19 states parties.

The European Convention on Human Rights and Biomedicine (European Biomedicine Convention) is an 'open' convention, in the sense that it is open for signature to non-Council of Europe member states.[429] Nevertheless, no state outside of Europe has signed the Convention.

Nowak designates as challenges to human rights protection developments in biomedicine and biotechnology:[430]

> It is to be said though that it is not states which primarily threaten the dignity of human beings, but mostly private persons (in science, economy or private health care). Thus, the question for states and international organisations is not so much to what extent state interventions are to be prohibited, but whether in fact the positive state obligation to protect and ensure life, dignity and privacy of human beings today and in the future is sufficient protection against the interventions on the part of science and economy.

The European Biomedicine Convention applies the language of human rights to issues formerly regarded as purely within the ambit of medical and research ethics. For this reason it is a revolutionary document, which transforms principles of ethics into justiciable human rights norms.[431]

The European Biomedicine Convention guarantees a large number of substantive rights, some of which are viewed as novel formulations of rights that are already in existence, such as the principle of informed consent already contained in the right to human dignity and privacy.[432]

The general provisions of the Convention recognise the primacy of the human being, whose welfare takes precedence to the interests of science or of society.[433] Other rights in the European Biomedicine Convention include: equitable access to health care;[434] the right to the protection of human dignity, identity and integrity;[435] the principle that free and informed consent should be given to every health-related intervention;[436] the right to information;[437] issues related to scientific research;[438]

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429 Nowak 182. The idea was to extend the protection of the Convention as far as possible.

430 Nowak 179 – 180.

431 For more on the European Biomedicine Convention, see Rosenau 'Legal prerequisites for Clinical trials under the revised Declaration of Helsinki and the European Convention on Human Rights and Biomedicine' (2000) 7 *European J Health L* 105.

432 Nowak (n 23 above) 183.

433 Art 2 European Biomedicine Convention.

434 Art 4 European Biomedicine Convention.

435 Art 1 European Biomedicine Convention.

436 Art 5 European Biomedicine Convention.

437 Ch III European Biomedicine Convention.

438 Ch V European Biomedicine Convention.

prohibitions against genetic manipulation;[439] and a prohibition against the use of the human body or its parts for financial gain.[440] Article 27 states that national law granting more far-reaching protection is not affected by the European Biomedicine Convention, thus making the Convention a minimum standard of protection.

The European Biomedicine Convention is supplemented by two additional protocols, the Additional Protocol on the Prohibition of Cloning of Human Beings;[441] and the Additional Protocol on Transplantation of Organs and Tissues of Human Beings.[442]

Because there is no clause in the European Biomedicine Convention that makes provision for a specific treaty monitoring body, the international monitoring system of this treaty is considered particularly weak.[443] Reports by states parties are submitted only upon request by the Secretary-General of the Council of Europe, and not as a matter of course.[444] This state of affairs is regrettable, as the European Biomedicine Convention has the potential to make a significant contribution in the protection of human rights in biomedicine.

4.3.3 The Inter-American system

The Organization of American States[445] includes 35 member states in the Americas and was established in 1948.[446] The functions of the OAS are fulfilled by its General Assembly, the policy-making body of the OAS.[447] Each member state has one vote in the General Assembly.[448] The Permanent Council consists of the permanent representatives of the member states of the OAS, and functions as the OAS's decision-making body between sessions, as well as fulfilling various other functions.[449] Both the General Assembly and the Permanent Council have jurisdiction in matters relating to human rights.[450]

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439 Arts 11 – 13 European Biomedicine Convention.
440 Art 21 European Biomedicine Convention.
441 Opened for signature on 12 January 1998, entered into force on 1 March 2001. It has 13 states parties.
442 Opened for signature on 24 January 2002, not yet in force. One state party only.
443 Nowak 183.
444 Nowak 182.
445 Referred to as the 'OAS' from now on.
446 Heyns *et al* (n 354 above) 309.
447 Nowak (n 23 above) 190; Buergenthal (n 223 above) 175.
448 Buergenthal 175.
449 Buergenthal 175.
450 Buergenthal 175.

Human rights protection in the Inter-American system is based on two documents – the Charter of the OAS and the American Convention on Human Rights.[451] The Charter applies to all member states of the OAS, while the American Convention on Human Rights binds only state parties that have signed and ratified the Convention.[452] The two systems overlap and the same case often draws on both the Charter and the Convention.[453]

The OAS Charter was opened for signature in 1948 and entered into force during 1951.[454] The Charter was amended by the Protocol of Buenos Aires of 1967, which came into force in 1970, and by the Protocol of *Cartagena de Indias*, Columbia of 1985, which came into force in 1988.[455] There are two later amendments to the Charter, the Protocols of Washington and Managua.[456]

The Charter functions as the constitution of the OAS.[457] It makes few references to human rights, most notably in articles 3(j), 3(k) and 16 which refer to civil and political rights as well as to socio-economic rights. The diplomatic conference that adopted the Charter also proclaimed the American Declaration of the Rights and Duties of Man.[458]

The Protocol of Buenos Aires brought about important changes in the protection of human rights in the Inter-American system. It established the American Commission on Human Rights as a Charter organ and described the Commission's main objective to be the protection and advancement of human rights.[459]

The American Declaration of the Rights and Duties of Man proclaimed on 2 May 1948 lists 27 human rights and ten duties.[460] It includes civil and political rights as well as socio-economic rights.[461] The classic civil and political rights, such as privacy, property, equality, health and so on are protected. The duty to society, to children, to parents and to vote, to receive instruction and to obey the law are declared as well. Initially, the Declaration was a non-binding resolution of the

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451 Nowak 191; Buergenthal 175.
452 As above.
453 As above.
454 Buergenthal 177.
455 Buergenthal 178.
456 Buergenthal 178.
457 Buergenthal 177.
458 Buergenthal 178.
459 Arts 52(e) and 111 OAS Charter; Buergenthal 179.
460 Buergenthal 179.
461 Buergenthal 179.

conference and without any legal effect. Today it is considered the main normative instrument of the 'fundamental rights of the individual' in article 3(1) of the current OAS Charter.[462] For Buergenthal, too, it 'embodies the authoritative interpretation' of the Charter.[463]

The Inter-American Commission on Human Rights was mandated in 1959 by a meeting of the Consultation of Ministers of Foreign Affairs.[464] In 1960 the OAS Council adopted the Statute of the Commission and elected the first Commissioners.[465] Article 1 of the Statute proclaims it an autonomous entity of the OAS.[466] Article 2 defines the human rights to be protected by the Commission as those listed in the American Declaration of the Rights and Duties of Man.[467]

The Commission has various powers to promote and protect human rights, including the power to make studies and to prepare reports on human rights in the member states.[468] The Commission undertakes so-called 'country studies' investigating the human rights situation in member states.[469]

In 1965 the Second Special Inter-American Conference authorised the Commission to hear individual petitions on the violation of human rights by member states.[470] This concession applies to only certain rights: the right to life, liberty and security of the person, equality before the law, freedom of religion, freedom of expression, freedom from arbitrary arrest, and the right to due process of the law.[471]

In 1970, with the entry into force of the Protocol of Buenos Aires, the 1948 Charter was amended and the Inter-American Commission was transformed into a formal organ of the OAS.[472] The main function of the Commission is to promote the observance and protection of human rights.[473]

The Inter-American Convention on Human Rights was adopted in 1978 and is binding upon states that ratify it. The Inter-American Convention on Human Rights has been ratified by 24 OAS member states.[474] The Convention guarantees a large

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462 Nowak 191.
463 Buergenthal 180.
464 Nowak 193; Buergenthal 181.
465 As above.
466 As above.
467 Buergenthal 181.
468 Nowak 193; Buergenthal 182.
469 Nowak 193.
470 Nowak 193; Buergenthal 182.
471 Buergenthal 182 – 183.
472 Buergenthal 183.
473 Arts 52 & 111(1) OAS Charter.
474 Nowak 196; Heyns *et al* (n 354 above) 309.

number of civil and political rights, including the right to life; to humane treatment; to freedom from slavery; a right to personal liberty; a right to a fair trial; to freedom of association; to freedom of movement and residence.[475] State parties also undertake, 'progressively', to realise the rights 'implicit in the economic, social, educational, scientific and cultural standards set forth in the Charter of the OAS'.[476]

The Convention has provided for the establishment of the Inter-American Commission on Human Rights and an Inter-American Court on Human Rights.[477] Each consists of seven members, elected in their personal capacities.[478] The Commission has its seat in Washington, DC; the Court in San Jose, Costa Rica.[479] Both bodies hold at least two regular sessions each year.[480] The Inter-American Commission has a dual function: first in relation to all member states of the OAS, second in relation to the parties to the Convention of 1978.[481] Most of the Commission's work relates to country studies and to the examination of individual petitions.[482] Country studies may be initiated by individual complaints or by reports from NGOs that large-scale human rights violations are taking place in a certain member state. The Commission performs on-site investigations into a specific member state to examine a human rights issue.[483]

The Commission also performs a variety of other functions as a Charter organ, including helping to draft OAS human rights instruments; sponsoring conferences; publishing human rights documents and pamphlets; and acting as a consultant to the OAS on human rights issues.[484] It has played an important role in mediating and in protecting human rights during civil wars and armed conflict.[485]

Concerning individual complaints, article 20 of the Statute of the Commission enables the Commission to hear individual complaints on any of the rights enumerated in the Declaration.[486] However, individual complaints may be directed against states that are not parties to the Convention. In that case the decisions of

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475 Nowak 196.
476 Art 26 American Convention on Human Rights.
477 Art 33 American Convention on Human Rights; art 106 OAS Charter (Nowak 193).
478 Buergenthal 198.
479 Buergenthal 198.
480 Buergenthal 198.
481 Arts 41(f), 44 – 51 Inter-American Convention on Human Rights; Buergenthal 184.
482 Buergenthal 187.
483 Buergenthal 189.
484 Buergenthal 186.
485 Buergenthal 186.
486 Art 20 Statute of the Inter-American Commission, no longer limited to the preferred freedoms; Buergenthal 193.

the Commission are sent to the General Assembly, which has shown scant interest in dealing with individual petitions, and, therefore, is not as effective a mechanism for the protection of human rights as is the system based on the Convention. [487]

The Commission's mandate to 'take action on petitions and other communications'[488] allows it to deal with individual and inter-state communications.[489] Article 44 determines that a state by becoming a party to the Convention is deemed to have consented to the individual complaints mechanism. Under the American Convention, not only the individual victim of a violation may petition the Commission, but also other persons or a group on their behalf.[490] The admissibility of a petition is conditional on the exhaustion of domestic remedies and on submission within six months of the victim being notified of the final domestic judgment.[491] The Commission may deal with inter-state complaints if both states accept its jurisdiction to receive such complaints.[492]

The Commission examines the allegation, requests information and investigates the facts.[493] The Commission calls a hearing on the matter in which all parties, including the government, participate.[494] According to article 48(b), the Commission is to 'place itself at the disposal of the parties concerned with the view to reaching a friendly settlement'.[495]

If a settlement is not reached, the Commission draws up a report containing the facts of the case and the conclusions it has reached.[496] The report is transmitted to the government of the state concerned, which has three months to comply with the recommendations or findings of the report.[497] During this period the case may be submitted to the Inter-American Court of Human Rights by the Commission.[498]

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487 Buergenthal 194.
488 Art 41 American Convention on Human Rights.
489 Art 44 – 45 American Convention on Human Rights.
490 Art 44 American Convention; Buergenthal 200.
491 Art 46(1) American Convention on Human Rights; Buergenthal 200. A petition may still be submitted if there were no domestic remedies or if there was no access to domestic remedies or if there was a delay in accessing these remedies (art 46(2).
492 Art 45 American Convention; Buergenthal 204. No such case has reached the Commission to date. The Commission also deals with the petitioning system under the OAS Charter system.
493 Buergenthal 2002.
494 Buergenthal 2002.
495 If such a friendly settlement is obtained, the Commission issues a report containing the facts of the case and the settlement obtained (Buergenthal 2002).
496 Art 50 American Convention on Human Rights; Buergenthal 2003.
497 Buergenthal 2003.
498 Buergenthal 2003.

If a case had not been settled or referred to the Court, article 51(1) determines that the Commission votes on the matter.[499] After a majority vote which agrees that the Convention has been violated, the Commission sets out its recommendations in a report and prescribes a period within which the state is to comply with its recommendations.[500] After the period has expired, the Commission must decide whether the state has complied with its recommendations.[501] The Commission may also decide to publish its report.[502] Although the report and its findings are not formally binding, as would be the decision of a court, it is still an 'authoritative legal determination'.[503] The matter may be placed on the agenda of the General Assembly, in which the report will discussed and may be acted upon.[504]

The Commission may refer cases to the Inter-American Court[505] and the Commission appears in all cases before the Court[506] as a '*Ministerio Publicd*' or protector of the legal order established under the Convention.[507] The Commission may request advisory opinions from the Court.[508]

The Inter-American Court of Human Rights has both contentious and advisory jurisdiction.[509] Article 62 of the American Convention determines that a state party merely by ratifying the Convention does not accept the contentious jurisdiction of the Court.[510]

State parties alone are permitted to bring a case to the Court;[511] individuals have to rely on the Commission or a state to bring a case on their behalf. Before the case reaches the Court, the relevant Commission proceedings applicable to it must have been completed.[512] Thus, the Commission first deals with a case before it is admitted to the Court.

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499 Buergenthal 2003.
500 Art 51(2) American Convention; Buergenthal 204.
501 Art 51(3) American Convention; Buergenthal 2004.
502 As above.
503 Buergenthal 205.
504 Buergenthal 204.
505 Art 61 American Convention; Nowak 192; Buergenthal 205.
506 Art 57 American Convention; Nowak 192; Buergenthal 205.
507 Buergenthal 206.
508 Buergenthal 206.
509 Buergenthal 207.
510 It is required further to make a special declaration to accept the jurisdiction, or enter into a special agreement to the effect (art 62).
511 Art 61(1) American Convention.
512 Art 61(2); Buergenthal 209.

Once a case is admitted, the Court may fully review the Commission's finding as to the facts of the case and the applicable law.[513] The judgment of the Court is final and cannot be appealed.[514] Article 68(1) determines that state parties undertake to comply with the decisions of the Court in any matter to which it is a party.

Article 63(1) determines that the Court may award money as compensation or render a declaratory judgment if it finds a violation of the Convention. A declaratory judgment will often include an order on how the offending state may rectify the situation.[515]

Article 65 of the Convention requires the Court to inform the OAS General Assembly of instances where the state party has not complied with its judgment. The General Assembly will then take the political measures it deems necessary to enforce the decision of the Court.[516]

Article 63(2) of the American Convention authorises the Court to issue temporary restraining orders or provisional measures.[517] The authorisation applies as well to cases before the Commission that have not yet reached the Court.

The Court's advisory jurisdiction is very broad. According to article 64 of the American Convention, it includes the interpretation of the Convention, or any other human rights treaty,[518] and advising a state party on the compatibility of its domestic laws with any of the provisions of the Convention.[519] The Court has rendered a substantial number of advisory opinions during its existence.[520]

Advisory opinions are not legally binding. They do, however, put a state 'on notice' that its actions are not complying with its obligations under the Convention.[521]

By the entry into force on 1 May 2001 of the new Rules of Procedure of the Inter-American Commission, petitioners are now entitled to request the Commission to refer cases on their behalf to the Court if it finds a violation.[522] The Commission is

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513 Buergenthal 211.
514 Art 67 American Convention; Buergenthal 212.
515 Buergenthal 213; Nowak 194.
516 Buergenthal 215.
517 Buergenthal 215; Nowak 194.
518 Art 64(1).
519 Art 64(2).
520 Buergenthal 218; Nowak 194 - 195.
521 Buergenthal 221.
522 Nowak 201. Nowak remarks that the new procedure resembles the 9th Additional Protocol to the European Convention.

obliged to comply with such a request unless a majority of its members vote against it.[523]

4.3.4 The African system

The African Charter on Human and Peoples' Rights (African Charter) was adopted on 27 June 1981 in Banjul,[524] The Gambia, and entered into force on 21 October 1986.[525] It has been ratified by all 53 member states of the Organization of African Unity (OAU), a regional intergovernmental organisation, and functions within the institutional framework of this organisation.[526]

In May 2001 the OAU was replaced by the African Union (AU).[527] The AU aims to achieve greater unity and solidarity between African countries and the peoples of Africa, but its further aim is to 'promote and protect human and peoples' rights in accordance with the African Charter on Human and Peoples' Rights and other relevant human rights instruments'.[528] Article 4 of the Constitutive Act of the African Union lists the principles by which the Union will function, and they include 'respect for democratic principles, human rights, the rule of law and good governance'.[529]

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523 Nowak 201. For more on the Inter-American system, see Buergenthal and Shelton (1995) *Protecting human rights in the Americas: Cases and materials* (4th ed) and Harris and Livingstone (eds) (1998) *The Inter-American system of human rights*.

524 Nowak 205. Its adoption in Banjul is the reason why the African Charter on Human and Peoples' Rights is often referred to as the 'Banjul Charter'.
For more on human rights in Africa, see Eze 'Human rights issues and violations: The African experience' in Shepard and Anikpo (eds) (1990) *Emerging human rights: The African political economy context* and Zeleza 'The struggle for human rights in Africa' in Zeleza and McConnaughay (eds) (2004) *Human rights, the rule of law and development in Africa*.

525 Nowak 203 – 204; Buergenthal 228.

526 The Organization of African Unity was founded on 25 May 1963 in Addis Ababa. All African states are members except for Morocco. The Organization of African Unity was changed to the African Union (see below).

527 The Constitutive Act of the African Union was accepted in Lomé, Togo, in July 2000, and entered into force in May 2001. The Assembly of the African Union had its inaugural meeting in Durban South Africa in July 2002.
For more on the coming into being of the African Union, see Baimu 'The African Union: Hope for better protection of human rights in Africa?' (2001) 1 *African Human Rights L J* 299 and Stefiszyn 'The African Union: Challenges and opportunities for women' (2005) 5 *African Human Rights L J* 358.

528 Art 3(h) Constitutive Act of the African Union.

529 Art 4(m) Constitutive Act of the African Union. The organs of the AU include the Assembly of the African Union, the Executive Council, the Commission, the Pan-African Parliament, the Court of Justice (now amalgamated with the African Court) and an Economic, Social and Cultural Council.

The African Charter differs from the systems discussed previously in this chapter in a number of important aspects. It includes not only rights, but duties, such as the duty to work and the duty to pay taxes.[530] It proclaims not only individual, but also collective or peoples' rights, such as the right to self-determination and the right to development.[531] Apart from guaranteeing a wide array of civil and political rights, the African Charter includes economic, social and political rights as justiciable rights on an equal footing.[532]

The African Charter has been criticised for its so-called 'claw-back' clauses.[533] Whereas other human rights instruments contain general derogation or limitations clauses that prescribe the circumstances under which rights may be limited or derogated, many of the provisions in the African Charter include these claw-back clauses.[534] Claw-back clauses are problematic as many argue that they have the potential to render rights meaningless and that they grant avenues for governments to restrict rights.[535] However, Ankumah argues that, in practice, the African Commission has construed claw-back clauses liberally so as to protect the human rights of victims of violations.[536]

The African Charter is rooted in an interpretation of African culture and tradition; the emphasis on culture and on traditional values is expressed in the Preamble which proclaims 'the virtues of historical tradition and the values of African civilization which should inspire and characterize their reflection on the concept of human and peoples' rights'. The emphasis on second generation rights is also highlighted.[537]

> *Convinced* that it is henceforth essential to pay particular attention to the right to development and that civil and political rights cannot be dissociated from economic, social and cultural rights in their conception as well as universality and that the satisfaction of economic, social and cultural rights is a guarantee for the enjoyment of civil and political rights.

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530 See also Ankumah (1996) 159 – 177; Mutua 'The Banjul Charter and the African cultural fingerprint: An evaluation of the language of duties' 35 *Virginia J Intl L* 339.

531 As above. See also Kiwanuka 'The meaning of "people" in the African Charter on human and peoples' rights' (1988) 82 *American J Intl L* 80.

532 In this regard, also see para 4.3.2 of ch 5 below.

533 Ankumah 176.

534 For example, art 9 guarantees freedom of expression, subject to 'reasons and conditions previously laid down by law'; art 10 guarantees freedom of association, so long as the person 'abides by the law'.

535 Ankumah 176.

536 Ankumah 177. See also Communication 129/94 and para 4.3.2 of ch 5 below.

537 See also Agbakwa 'Reclaiming humanity: Economic, Social and cultural rights as the cornerstone of African human rights' (2002) 5 *Yale Human Rights and Development L J* 177 and Howard 'The full-belly thesis: Should economic rights take priority over civil and political rights? Evidence from sub-Saharan Africa' (1983) 5 *Human Rights Q* 467

The African Charter requires of state parties to 'recognize the rights, duties and freedoms enshrined in this Charter and [...] undertake to adopt legislative and other measures to give effect to them'.[538] According to article 62, state parties are further required to report every two years on the legislative and other measures they have adopted to give effect to the rights listed in the African Charter. State parties should promote and ensure through education and publication respect for the rights in the African Charter,[539] and allow for the establishment and improvement of appropriate national institutions to promote and protect human rights.[540]

The African Charter establishes the African Commission on Human and Peoples' Rights (African Commission) within the institutional framework of the OAU and now the AU.[541] Article 30 of the African Charter outlines its function; it is to 'promote human and peoples' rights and ensure their protection in Africa'. The African Commission consists of eleven members, elected by the OAU Assembly of heads of States and Governments from a list of names presented by the state parties.[542] They serve for six-year terms in their individual capacities.[543] The African Commission meets twice yearly for two week sessions.

The functions of the African Commission as described in article 45 of the African Charter are both promotional and judicial in nature. It is empowered to undertake studies, convene conferences and to disseminate information to promote human and people's rights.[544] It is empowered to protect the rights enumerated in the Charter, to interpret the Charter and perform any other tasks entrusted to it by the Assembly of Heads of State and Government. According to article 45(1)(a) the African Commission may also give its views or make recommendations to governments. In this way, problems highlighted in the biannual reports submitted by the different governments may be addressed.

The African Commission has further powers to interpret human rights documents and to solve problems relating to human rights abuses. According to

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538 Art 1 African Charter.
539 Art 25 African Charter.
540 Art 26 African Charter.
541 Ankumah 1. Under the AU, the African Commission remains the implementing mechanisms for the African Charter and its protocols and all further reference to the OAU includes the AU.
542 Ankumah 13 – 16.
543 See Ankumah 18 – 19 on the independence and impartiality of the African Commission and its Commissioners.
544 Nowak 207; Ankumah 20 – 25; Buergenthal 240.

article 45(3), the African Commission has the power to interpret all the provisions of the African Charter at the request of a state party, the OAU or an African organisation recognised by the OUA.[545]

The African Charter establishes an inter-state complaint mechanism that provides for two different ways of solving disputes. First, during bilateral proceedings, article 47 of the African Charter allows one state party to bring a violation of the Charter by another state party to the attention of that state party in a formal communication which is copied to the Commission. The offending state has three months to submit a reply to the allegation. Either state may also submit the matter to the Commission during these three months or afterwards if the matter is not solved to the satisfaction of the states involved.[546] The African Commission does not necessarily play any active role in the proceedings under article 47.[547]

Second, article 49 of the African Charter allows for another inter-state procedure. It allows for direct communications to the African Commission on an alleged violation of the African Charter without first following the article 47 procedure.

For a complaint to be dealt with by the African Commission, it is required that all domestic remedies must be exhausted or it should be clear to the Commission that the procedure to exhaust these remedies will be unduly prolonged.[548]

Once the African Commission has found the complaint admissible, it embarks on an investigation of the matter, finding out the relevant facts. The African Commission may get its information from any source, not only that provided by the parties to the dispute.[549] It may hold hearings on the matter, during which oral and written submissions by the parties concerned are allowed. Again, the African Commission seeks to find an amicable solution to the process. Article 52 determines that should an amicable solution not be reached, the Commission must prepare a report, stating the facts of the matter and its findings, conclusions and recommendations.[550]

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545 Ankumah 26.

546 Art 47 African Charter.

547 See generally in this regard, Heyns 'The African regional human rights system: In need of reform?' (2001) 1 *African Human Rights L J* 162 – 165; Gutto 'The reform and renewal of the African regional system and peoples' rights system' (2001) 2 *African Human Rights L J* 175.

548 Art 50 African Charter.

549 Art 52 African Charter.

550 Art 52 – 53 African Charter.

The report is submitted to the states concerned and to the Assembly of Heads of State and Government. No further enforcement measures are provided for and it is supposed that the Assembly of Heads of State and Government will bring political pressure to bear on the offending parties.

The individual complaint procedure of the African Charter closely resembles that of the UN's ECOSOC Resolution 1503.[551] The procedure is described in article 55 of the African Charter. The way in which article 55 is phrased implies that not only victims, but also NGOs and other persons or groups may institute a complaint to the African Commission.[552] For the complaint to be considered by the African Commission, however, a majority vote of its members must support its consideration, so that there is no 'automatic' procedural right that a complaint will be considered.[553]

Other admissibility requirements are set out in article 56 of the African Charter, such as the requirement that there is an obligation to exhaust local remedies and the requirement that the victim's case not be based solely on news disseminated through the mass media.

The individual complaints procedure under the African Charter is not an example of a classic complaints procedure, for example, under the European system. Only complaints of a series of systematic and massive violations of human rights are considered admissible, in other words, violations must be large-scale in nature to be considered, individual or isolated violations of human rights are not admissible.[554]

Communications which the African Commission finds to reveal evidence of the existence of such large-scale violations of human rights must be referred to the Assembly of Heads of State and Government. Only if the Assembly of Heads of States and Government decides to request the Commission to undertake an investigation into the situation and to compile a report including its findings and recommendations, may the African Commission proceed.[555]

The Commission's investigation and subsequent report remain confidential and, unless the Assembly of Heads of State and Government gives permission for its findings to be published, the Commission cannot publish its findings. Article 59(3) further determines that the overall report of the African Commission on its activities

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551 Nowak 208; Buergenthal 244 – 245.
552 As above.
553 Nowak 208; Buergenthal 245.
554 Art 58(1) African Charter.
555 Art 58(2) African Charter.

during the year may be published only after it has been considered by the Assembly.[556] The publicity attached to the African Commission's activities, which has the potential to shame or expose violators of human rights, is, potentially, severely restricted.[557]

Both the individual and inter-state complaints procedures are designed to secure a friendly settlement between the parties to the dispute, as considered to be in keeping with an African tradition of consultation and dialogue.[558]

The Protocol to the African Charter on Human and Peoples' Rights on the Establishment of the African Court of Human and Peoples' Rights (Protocol on an African Court) was adopted on 9 June 1998 by the Assembly of Heads of States and Government.[559] The Protocol on an African Court entered into force in January 2004 and by 31 December 2006 has been ratified by 23 states.[560] The African Court of Human and Peoples' Rights (Africa Court) consists of eleven judges and has advisory and contentious jurisdiction.[561] These judges, including two women, were elected in January 2006.[562]

The Preamble to the Protocol establishing an African Court provides the reasons for the Court's creation. The African Court is necessary to 'complement and reinforce the functions of the Commission',[563] and to 'complement the protective mandate of the African Commission'.[564] The exact nature of the relationship between the Commission and the Court remains to be established.[565]

The African Court is to offer advisory opinions on any legal matter pertaining to the Charter or any other relevant human rights instruments. It is to advise on issues of the interpretation and the application of the African Charter and other human rights instruments, as well as its own jurisdiction.[566] According to article 30, judgments of the African Court will be binding. Article 28 determines that the

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556 Art 59(3) African Charter.

557 See further Mugwanya 'Examination of state reports by the African Commission: A critical appraisal' (2001) 2 *African Human Rights L J* 268.

558 Nowak (n 23 above) 211.

559 OAU/LEG/MIN/AFCHPR/PROT (1) Rev 2.

560 Heyns *et al* (n 345 above) 309. In July 2004 the AU Summit took a decision to merge the African Human Rights Court with the African Court of Justice.

561 Nowak 211.

562 See Viljoen (2007) Forthcoming.

563 Preamble Protocol on an African Court.

564 Art 2 Protocol on an African Court.

565 In this regard, see Viljoen (n 562 above) and Murray 'A feminist perspective on reform of the African human rights system' (2001) 1 *African Human Rights L J* 15 – 17.

566 Art 3 Protocol on an African Court.

judgments of the Court are final and not subject to the right of appeal. State parties undertake to comply with the African Court's judgments and to guarantee their execution.[567] The Executive Council is the body responsible for monitoring the execution of the Court's judgments. According to Viljoen what this entails is unclear as yet[568] but, at a minimum, would involve 'keeping a mere record of judgments' implementation in the internal legal order of recalcitrant states'.[569] In line with other regional systems, the Executive Council should inscribe the issue of implementation by a particular state on its agenda until that state complies.[570]

Cases are to be submitted to the African Court by the African Commission; a state party which has lodged a complaint with the African Commission; or a state party against which a case has been lodged at the African Commission.[571]

Article 5(3) deals with the standing of individuals (and NGOs) before the African Court. It provides that 'the court may entitle relevant non-governmental organisations with observer status before the Commission, and individuals to institute case before it, in accordance with article 46(6) of this Protocol'. Additionally, article 34(6) requires states that have ratified the Protocol to make an additional declaration to the effect that they accept the jurisdiction of the Court in these circumstances.

Many commentators are worried that the procedures of the Court will merely replicate the problems now experienced with the African Commission, and assert that, instead of establishing an African Court, attempts should have been made to improve the functioning of the African Commission.[572] These complaints include the fact that the African Commission's findings are not enforceable against the state party concerned, and the Commission's findings are only published after the Assembly of Heads of State and Government has considered them.

On the other hand, the fact that the decisions of an African Court will be binding and enforceable against the state party concerned bodes well. Article 28 of the Protocol establishing the African Court, expressly states that the African Court's decisions will be final and that there will be no right to appeal. This statement

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567 Art 30 Protocol on an African Court.
568 Viljoen (n 562 above).
569 Naldi and Magliveras quoted in Viljoen (n 562 above).
570 Viljoen (n 562 above).
571 Arts 5 – 6, Art 30 Protocol on an African Court.
572 See eg Matua 'The African Human Rights Court: A two-legged stool?' (1999) 21 *Human Rights Q* 342; Odinkalu 'Courting the Court' (1994) *African Topics Magazine* 11; O'Shea 'A critical reflection on the proposed African Court on Human and Peoples' Rights' (2001) 2 *African Human Rights L J* 285.

encourages the hope that the Court will play a positive role in the protection of human rights on the African continent.[573]

The African system for the protection of human rights has a number of additional protocols and instruments that supplement it. These are the OAU Convention Governing the Specific Aspects of Refugee Problems in Africa,[574] the Cultural Charter,[575] the African Charter on the Rights and Welfare of the Child (Children's Charter),[576] the African Convention on the Conservation of Nature[577] and the Protocol to the African Charter on Human and Peoples' Rights on the Rights of Women in Africa (Women's Protocol).[578] Of importance to the present study are the Children's Charter and the Women's Protocol, which are dealt with below.

The Children's Charter is similar to the UN Convention on the Rights of the Child. It contains an impressive number of children's rights, and is more comprehensive in the rights that it includes than the UN Convention on the Rights of the Child.[579]

The Preamble to the Children's Charter stresses the need for the Children's Charter:

> Noting with concern that the situation of most African children remains critical due to the unique factors of their socio-economic, cultural, traditional and developmental circumstances, natural disasters, armed conflicts, exploitation and hunger, and on account of the child's physical and mental immaturity he or she needs special safeguards and care...

The Preamble reiterates that the approach to children's rights is in keeping with 'traditional African virtues of their cultural heritage, historical background and the

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573 See also Udombana 'An African Human Rights Court and an African Union Court: A needful duality or a needless duplication?' (2003) 28 *Brooklyn J Intl L* 811.

574 Adopted in Addis Ababa on 10 September 1969, entered into force on 20 June 1974 and has 44 state parties (it has thus been ratified almost universally).

575 Adopted in Mauritius and entered into force in 1990. It deals with issues such as cultural diversity, national identity, education, language, the mass media and cultural co-operation.

576 Adopted in by the 26th ordinary session of the Assembly of Heads of State and Government in Addis Ababa on 11 July 1990 and entered into force on 29 November 1999 upon ratification by 15 member states (OAU Doc CAB/LEG/153/Rev 2, reprinted in Heyns (ed) (1999) 38. It has 29 state parties.

577 Adopted in 1968 and entered into force in June 1969. In 2003 in Maputu the AU adopted an amended version of the Convention, which is not yet in force.

578 Adopted in Maputu in July 2003, and entered into force on 27 November 2005.

579 See Viljoen 'Africa's contribution to the development of international human rights and humanitarian law' (2001) 1 *African Human Rights L J* 18 22 - 23.
For a more detailed discussion on the Children's Charter, see Viljoen (n 305 above) 199 and Lloyd 'A theoretical analysis of the reality of children's rights in Africa: An introduction to the African Charter on the Rights and Welfare of the Child' (2002) 2 *African Human Rights L J* 11.

values of the African civilisation', and these values and virtues should inspire and characterise the content of the rights of the child.[580]

The Children's Charter guarantees, amongst other rights, the right to non-discrimination,[581] that the best interests of the child shall always be paramount,[582] children's rights to survival and development,[583] their right to a name and identity,[584] their freedom of expression, association, thought, conscience and religion,[585] their right to protection of their privacy,[586] and their right to education, leisure, recreational and cultural activities.[587] Special mention is made in the Children's Charter of the rights of handicapped children.[588]

Also protected are children's rights to be free from child labour, child abuse and torture,[589] their right to just administration of juvenile justice,[590] the protection of the family,[591] parental care and protection and to parental responsibilities,[592] their right against sexual exploitation,[593] and the rights of refugee children.[594] As is the case in the Women's Protocol, children are protected against harmful social and cultural practices 'affecting the welfare, dignity, normal growth and development of the child'.[595] Customs and practices prejudicial to the health and the life of the child are specifically outlawed.[596]

Of note to the present study is article 14 of the Children's Charter, guaranteeing children's right to health and health services. Not only does the child have the right to enjoy the best attainable state of health, but state parties to the Children's Charter undertake to take measures to reduce infant and child mortality rates, and to 'combat disease and malnutrition within the framework of primary health care through the application of appropriate technology'.[597] Article 14 will be

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580 Para 6 Children's Charter.
581 Art 3 Children's Charter.
582 Art 4 Children's Charter.
583 Art 5 Children's Charter.
584 Art 6 Children's Charter.
585 Arts 7 – 9 Children's Charter.
586 Art 10 Children's Charter.
587 Arts 11 – 12 Children's Charter.
588 Art 13 Children's Charter.
589 Arts 15 – 16 Children's Charter.
590 Art 17 Children's Charter.
591 Art 18 Children's Charter.
592 Art 19 – 20 Children's Charter.
593 Art 27 Children's Charter.
594 Art 23 Children's Charter.
595 Art 21(1) Children's Charter.
596 Art 21(1)(a) Children's Charter.
597 Art 14(2)(d) Children's Charter.

discussed in more detail below[598] as it may be read as relating to children's participation in clinical research.

Another important feature of the Children's Charter is that it includes not only rights but responsibilities as well. Article 31 outlines children's responsibilities in relation to their family and society, to work for the cohesion of the family, to serve his national community, to strengthen social and national solidarity, and so on.

An implementation mechanism, in the form of a Committee on the Rights and Welfare of the Child, is set up by the Children's Charter to 'promote and protect the rights and welfare of the child'[599] and to fulfil functions relating to that charge.[600] The Committee was established in 2002 as a monitoring body in charge of a state reporting procedure and an individual complaints procedure.[601]

The Women's Protocol addresses human rights of concern to women in Africa.[602] The motivation behind the Protocol is the denial of women's human rights in many spheres of African society and, consequently, to the scant attention paid to their rights in the African Charter. The Preamble states:[603]

> *Concerned* that despite the ratification of the African Charter on Human and Peoples' Rights and other international human rights instruments by the majority of States Parties, and their solemn commitment to eliminate all forms of discrimination and harmful practices against women, women in Africa still continue to be victims of discrimination and harmful practices ...

The Women's Protocol guarantees civil and political rights as well as socio-economic rights. It prohibits all forms of discrimination against women.[604] Sub-section 2 of article 2 of the Women's Protocol requires state parties to:

> modify the social and cultural patterns of conduct of women and men through public education, information, education and communication strategies, with a view to achieving the elimination of harmful cultural and traditional practices and all other practices which are based on the idea of the inferiority or the superiority of either of the sexes, or on stereotyped roles for women and men.

It is clear from the quoted subsection that the drafters of the Women's Protocol realise that the protocol alone will not be able to change peoples' attitudes and that it is only through consistent programmes of education and communication strategies

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598 See para 5.2.7 below.
599 Art 32 Children's Charter.
600 See art 42 Children's Charter where its functions and mandate are outlined.
601 Nowak 211.
602 Generally on the Women's Protocol, see Murray 'A feminist perspective on reform of the African human rights system' (2001) 2 *African Human Rights L J* 205;
603 Preamble Women's Protocol.
604 Art 2 Women's Protocol.

that views may change. Of note also is the realisation in this subsection that it is not only men's attitudes, but also the attitudes of women that need changing.

The Women's Protocol guarantees women's right to dignity,[605] which includes women's right to be free from all forms of violence, especially violence of a verbal or sexual nature,[606] their right to life and integrity and security of their person.[607]

The Women's Protocol orders the elimination of harmful traditional or cultural practices, such as female genital mutilation.[608] Once again it demonstrates the realisation that legislation alone will not alter the situation, as it orders the 'creation of public awareness in all sectors of society regarding harmful practices through information, formal and informal education and outreach programmes'.[609]

The Women's Protocol further addresses topics such as equal rights in marriage, freedom to marry and the freedom of the woman to acquire and manage her own property during marriage.[610] It addresses women's access to justice and their right to equal protection before the law,[611] women's social and welfare rights,[612] as well as the right to a healthy and sustainable environment.[613]

Of importance is the section on women's health and reproductive rights.[614] Women's right to health is guaranteed, which specifically includes their right to have 'self-protection and to be protected against sexually transmitted infections, including HIV/AIDS',[615] as well as the right to be informed as to their 'health status and to the health status of one's partner, particularly if infected with sexually transmitted infections, including HIV/AIDS, in accordance with internationally recognised standards and best practices'.[616] Certain aspects relating to women's right to health of relevance to this study are discussed below.[617]

State parties to the Women's Protocol undertake to 'take all appropriate measures' to provide accessible health services, establish and expand health services

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605 Art 3 Women's Protocol.
606 Art 3(4) Women's Protocol.
607 Art 4 Women's Protocol.
608 Art 5 Women's Protocol.
609 Art 5(a) Women's Protocol.
610 Art 6 Women's Protocol.
611 Art 8 Women's Protocol.
612 Art 13 Women's Protocol.
613 Art 18 Women's Protocol.
614 Art 14 Women's Protocol.
615 Art 14(1)(d) Women's Protocol.
616 Art 14(1)(e) Women's Protocol.
617 See para 4.4.9 below.

related to pregnancy and delivery, and to provide access to abortion in specific circumstances.[618]

The Women's Protocol guarantees, among other rights, the right to food security,[619] the right to adequate housing,[620] the right to a positive cultural context,[621] the right to sustainable development,[622] widow's rights,[623] the right to inheritance,[624] and the protection of elderly women,[625] of women with disabilities,[626] and the protection of women in distress.[627]

Under articles 25 and 26 of the Women's Protocol the measures providing remedies for victims of violations and the implementation of the Women's Protocol are indicated. State parties shall undertake to provide appropriate remedies to any woman whose rights have been violated,[628] 'ensure the implementation of the Protocol at national level',[629] and indicate in their periodic reports legislative and other measures undertaken to achieve the full realisation of the rights contained in the Women's Protocol.[630]

4.3.5 OIC and League of Arab States

The regional protection of human rights is restricted to the three systems mentioned above, there exist no regional organisations in Asia, the Middle East or the Pacific for the protection of human rights. In parts of these regions the universality and thus the legitimacy of international human rights have been challenged and abuses of human rights have occurred.[631] The countries in these regions have not, on the whole, signed or ratified any of the UN instruments.[632] The values of Asian culture and Islamic Sharia law are elevated in preference to international human rights law.[633]

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618 Art 14(2) Women's Protocol.
619 Art 15 Women's Protocol.
620 Art 16 Women's Protocol.
621 Art 17 Women's Protocol.
622 Art 19 Women's Protocol.
623 Art 20 Women's Protocol.
624 Art 21 Women's Protocol.
625 Art 22 Women's Protocol.
626 Art 23 Women's Protocol.
627 Art 24 Women's Protocol.
628 Art 25 Women's Protocol.
629 Art 26(1) Women's Protocol.
630 Nowak 253.
631 Nowak 253.
632 As above. Australia and New Zeeland are the exception.
633 Nowak 253.

A declaration of human rights, the Universal Islamic Declaration of Human Rights, was adopted in 1981 by the Islamic European Council, a private organisation based in London.[634] The Organisation of the Islamic Conference (OIC) in 1990 in Cairo passed the Declaration of Human Rights in Islam,[635] which is based on the Universal Islamic Declaration, and, although non-binding, is the first inter-governmental effort at human rights protection in the region.[636] The Declaration includes all the classic first and second generation rights, as well as several collective rights of peoples, such as the right to self-determination against colonial repression, and principles of humanitarian law.[637] These rights are subject to Islamic Sharia law, which is the sole source of interpretation of these rights.[638]

In 1994 the Council of the League of Arab States (Arab League)[639] adopted the Arab Charter on Human Rights.[640] This document has not yet entered into force as it has not been ratified by any state.[641] The Arab Charter on Human Rights resembles the Universal Declaration of Human Rights and the two UN Covenants. It includes various first and second generation rights as well as rights to self-determination and the protection of minorities.[642] A seven-member Committee of Experts on Human Rights will monitor state compliance with the Arab Charter, and the Arab Charter provides for a state reporting procedure.

These documents should be seen as initial steps towards possible human rights protection in the future rather than determined efforts to provide protection now. Because this study concerns itself with HIV/AIDS and human rights in sub-Saharan Africa - the incidence of HIV is much higher than is the case of North African states - the lack of a regional mechanism for the protection of human rights is of slight relevance.

4.4 The role of customary international law

The term 'customary international law' refers to international law rules or norms that have emerged through custom or practice. Along with treaties, customary international law is the main source of international human rights law. State parties

634 Nowak 254.
635 Nowak 254.
636 As above.
637 Nowak 254.
638 Nowak 255.
639 Established in March 1945 and consists of 22 member states.
640 Nowak 255. From now on referred to as the 'Arab Charter'.
641 Nowak 255.
642 As above.

alone are bound by treaties; human rights obligations can be avoided by not becoming a party to any treaty. However, customary international law binds states which are not party to a specific treaty, if the relevant norm in that treaty has become a rule of customary international law.[643]

Article 38 of the Statute of the International Court of Justice defines custom as 'evidence of a general practice accepted as law'.[644] Courts have identified two elements that need to be proven before a norm is accepted as customary international law: consistent or settled state practice over time (*usus*) and a belief that that practice is law (*opinio iuris*).[645]

4.4.1 Settled state practice (*usus*)

There has to be evidence of consistent and uniform practice by states conforming to a certain norm. In the case of *Columbia v Peru*, the International Court of Justice observed:[646]

> the practice has been so much influenced by considerations of political expediency in the various cases, that it is not possible to discern in all this any constant and uniform usage, accepted as law, with regard to the alleged rule of unilateral and definitive qualification of the offence.

Evidence of consistent and settled state practice may be found in treaties, decisions of international courts, national legislation, diplomatic correspondence, policy statements by government officers, and resolutions of the political organs of the UN.[647]

4.4.2 *Opinio iuris*

A state practice on its own is insufficient to create a customary rule.[648] States should observe these norms because they believe that 'the practice is rendered obligatory by the existence of a rule of law requiring it ... The frequency, or even habitual character of the acts is not in itself enough'.[649] In other words, states must *consider* themselves bound by the rule.

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643 See Dugard (2001) 27 – 28.
644 Art 38(1)(b) Statute of the International Court of Justice (June 26 1995) Stat. 1055 T.S. 993; available at <http://www.icj-cij.org> (31 January 2007).
645 Dugard 28.
646 *Columbia v Peru* (1950) ICJ Reports 266 277.
647 As above; Dugard 28.
648 Dugard 31.
649 *North Sea Continental Shelf* (1969) ICJ Reports 3, para 77; see Dugard 31 - 32.

John Dugard notes that, in certain instances, it is difficult to prove the existence of *opnio iuris*.[650] It is only when actual cases come to court that a norm is confirmed as being a rule of customary international law.

Christian Tomuschat is of the opinion that custom is of little importance in establishing human rights law norms because the lack of empirical proof of the way that states deal with citizens makes it difficult to ascertain custom.[651] Nevertheless, in the field of human rights law, a number of human rights norms have evolved to obtain the status of international customary law. International customary law rules have developed primarily from those norms that are considered to be universal in character and that are proclaimed in various international instruments, for example, several of the principles contained in the Universal Declaration.[652] The following human rights norms are generally considered rules of customary international law: rules prohibiting arbitrary killing, slavery, torture, detention and systematic racial discrimination.[653] These rules of customary international law apply to all states, regardless of whether or not they subscribe to treaties prohibiting these actions. Customary international law may be more relevant than treaty law in terms of ensuring liability and accountability at the national level for non-state actors, according to Andrew Clapham.[654]

Customary international law can be influential in the implementation of human rights law in domestic legal systems. First, provisions in human rights treaties often permit the implementing body to consider customary international law.[655] For example, article 61 of the African Charter requires the African Commission to take into consideration, amongst other sources, 'African practices consistent with international norms on human and people's rights', and 'customs generally accepted as law'.[656] Second, domestic constitutions with similar provisions instruct a court to look at customary international law in the interpretation of domestic law.[657] Third, a domestic constitution may incorporate customary

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650 Dugard 32.
651 Tomuschat (2003) 34.
652 Clapham (2006) 86.
653 As above.
654 Clapham 86. In this regard, see Clapham chs 7 and 10.
655 Clapham 85.
656 Art 61 African Charter.
657 See para 6 below.

international law directly into municipal law, without the need for specific implementing legislation.[658]

Issues that relate to the significance as well as the implementation of customary international law are revisited in paragraph 6.

4.5 The role of *jus cogens* or peremptory norms and *erga omnes* obligations of international law

Jus cogens rules or 'peremptory norms' on human rights, unlike customary international law, merely need to be accepted by the international community of states to be considered binding international law, and are norms from which no derogation is permitted either by treaty of any other source of international law.[659] A *jus cogens* or peremptory norm is a norm 'accepted and recognized by the international community of States as a whole' to be of that nature.[660] In 'Serious breaches of obligations under peremptory norms of general international law', a chapter of its Articles on state responsibility, the International Law Commission states that peremptory norms that are accepted and recognised include the prohibitions of aggression, genocide, slavery, racial discrimination, crimes against humanity and torture, and the right to self-determination.[661] Other examples of prohibited acts are the 'slave trade ... apartheid ... the prohibition against torture as defined in article 1 of the Convention against Torture and Other Cruel, Inhuman and Degrading Treatment or Punishment and the basic rules of international humanitarian law applicable to armed conflict'.[662]

Erga omnes obligations are obligations owed by states to all other states – in other words, obligations owed to the international community as a whole.[663] In the *Barcelona Traction, Light and Power* case, the International Court of Justice asserted that certain basic human rights give rise to such 'obligations *erga omnes*', for example, outlawing acts of aggression, and genocide and assuring the right to

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658 Clapham 86. See para 6 below.
659 Clapham (n 652 above) 87; Dugard (n 643 above) 40 - 41.
660 Art 53 Vienna Convention on the Law of Treaties (1969).
661 Commentary to art 26, para 5. Report of the International Law Commission, GAOR, Supp. No 10 (A/56/10) 208.
662 Commentary to art 40, paras 3 – 5 Report of the International Law Commission, GAOR, Supp. No 10 (A/56/10) 283 - 284.
663 Clapham 96.

protection from slavery and racial discrimination.[664] These norms occupy an elevated status in international law.[665]

4.6 Conclusion

This section surveys the international system that contributes to the protection of human rights. First, the UN system is discussed, including the treaties which constitute human rights protection under the UN system. Next, regional human rights protection is sketched, and the European, Inter-American and African systems are described.

The interaction between the national and international systems of human rights law is debated; and questions are asked about the validity of drawing a distinction between 'soft' and 'hard' human rights law. It is suggested, in some circumstances, so-called 'soft' law creates binding obligations upon states and it sometimes has strong persuasive force.

The role customary international law plays in the protection of human rights was raised and its value was found to lie in that provisions in human rights treaties permit the implementing body to consider international law or that domestic constitutions have similar provisions, as well as other valuable contributions.

Finally, the concepts of *jus cogens* or peremptory norms and *erga omnes* obligations are introduced to highlight their function in the international implementation of human rights norms.

Within the framework of the international human rights law system that has been outlined, the next section of the thesis analyses specific provisions in international human rights instruments which are relevant in protecting the interests of clinical HIV-related research participants in Africa.

5 INTERNATIONAL HUMAN RIGHTS NORMS RELEVANT TO CLINICAL RESEARCH IN SUB-SAHARAN AFRICA

5.1 Introduction

Over the past decades, various international bodies have used a rights-based approach as a basis for programmes fighting HIV/AIDS. For example, the World Health Organization (WHO) has committed itself to strengthening its 'capacity to

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664 *Barcelona Traction, Light and Power Co (Belgium v Spain)* (1970) ICJ Reports 4 para 33.

665 Dugard 41.

integrate a human rights-based approach in its work'; to supporting 'governments in integrating a human rights-based approach in health development'; and to advancing 'the right to health in international law and international development processes'.[666]

In September 1996 UNAIDS[667] and the Office of the High Commissioner for Human Rights (OHCHR) convened an international consultation on HIV/AIDS in response to a request by the United Nations Commission on Human Rights to elaborate guidelines on promoting and protecting respect for human rights in the context of HIV/AIDS.[668] At this consultation the International Guidelines on HIV/AIDS and Human Rights (UNAIDS Human Rights Guidelines) were adopted. The intention is for states to use the UNAIDS Human Rights Guidelines in 'promoting and protecting a respect for human rights in the context of HIV/AIDS'.[669] There are twelve guidelines, aimed at implementing 'an effective rights-based approach'. The guidelines translate international human rights principles into practical steps for action in the context of HIV/AIDS.

Following another international consultation on HIV/AIDS in 2002, Guideline 6, dealing with 'access to prevention, treatment, care and support' was revised to reflect recent developments in the medical treatment of HIV/AIDS and international law on HIV/AIDS. A central tenet of the revised Guideline 6 is that '[u]niversal access to HIV/AIDS prevention, treatment, care and support is necessary to respect, protect and fulfil human rights related to health; including the right to enjoy the highest attainable standard of health.[670] HIV/AIDS prevention, treatment and care are therefore considered a prerequisite for the full realisation of an individual's human rights.

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666 See WHO *Health and human rights* <http://www.who.int/hhr/en/> (1 April 2006).

667 UNAIDS was established by six international organisations as a joint programme on HIV/AIDS. They are the UN Children's Fund (UNICEF), the UN Development Programme (UNDP), the UN Population Fund (UNFPA), the UN Educational Scientific and Cultural Organisation (UNESCO), the World Health Organisation (WHO) and the World Bank. As the organ assigned with the role of co-ordinating the global strategy for combating HIV/AIDS and its consequences, its mission is to lead, strengthen and support an expanded response. This response is aimed at preventing the transmission of HIV, providing care and support for people living with HIV/AIDS, reducing the vulnerability of individuals and communities to HIV/AIDS, and also of alleviating the effects of the epidemic.

668 E/CN.4/1995/45, para 135.

669 E/CN.4/1997/37, available at <http://daccessdds.un.org/doc/UNDOC/GEN/G97/102/19/PDF/G9710219.pdf?OpenElement> (1 April 2006).

670 UN *HIV/AIDS and Human Rights: International Guidelines – Revised Guideline 6,* HR/PUB/2002/1.

In June 2001, the member states of the United Nations General Assembly adopted the Declaration of Commitment on HIV/AIDS (Declaration of Commitment).[671] The Declaration of Commitment endorses an international commitment to human rights as a central element of the global response to HIV/AIDS. It recognises that the full realisation of human rights and fundamental freedoms for all is an essential element in a global response to the HIV/AIDS pandemic. It also recognises that it reduces vulnerability to HIV/AIDS and prevents stigma and related discrimination against people living with or at risk of HIV/AIDS.[672]

In relation to Africa, the Declaration of Commitment notes as follows:[673]

> Noting with grave concern that Africa, in particular sub-Saharan Africa, is currently the worst-affected region, where HIV/AIDS is considered a state of emergency which threatens development, social cohesion, political stability, food security and life expectancy and imposes a devastating economic burden, and that the dramatic situation on the continent needs urgent and exceptional national, regional and international action.

UNAIDS delivered its first report on the progress that has been made toward the targets set in the Declaration of Commitment in 2003. In Gillian MacNaughton's view, progress has been slow and disappointing.[674] She declares that, although there is international consensus on the necessity of respecting and protecting human rights in efforts to combat HIV/AIDS, translated into resolutions, declarations and guidelines at the international level, this consensus has not been put into law or action at the national level.[675] This failure may be ascribed to the fact that the documents and declarations outlined above are not legally binding on the member states of international organisations.[676]

The section above outlines the declarations and indications of commitment of international political bodies such as the United Nations. Because these are mere declarations, they have not the power to legally bind state members of international organisations, although as instances of soft law, they have considerable persuasive and political power.[677]

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671 UN General Assembly *Declaration of Commitment on HIV/AIDS*, A/RES/S-26/2, <http://www.unhchr.ch/huridocda/huridoca.nsf/e06a5300f90fa0238025668700518ca4/7e8440165be48ce0c1256aaa0052d754/$FILE/N0143484.pdf> (1 April 2006).

672 Para 16 Declaration of Commitment.

673 Para 8 Declaration of Commitment.

674 See MacNaughton (2004) 14.

675 As above.

676 See para 3.5 above.

677 See para 4.1 above.

In contrast to soft law and non-binding ethical guidelines, international human rights treaties are able to provide a legal framework for defining state obligations in protecting human rights and they may serve as a resource for implementing human rights protection for research participants.[678]
International human rights law in the form of binding treaties and conventions provides participants in HIV-related clinical research in Africa with recourse to national and international courts and tribunals.

The section below focuses on specific provisions in international and regional human rights instruments that can be of use in this regard. International human rights instruments such as ICCPR, ICESR, CRC and CEDAW, as well as regional instruments such as the African Charter on Human and Peoples' Rights, the African Charter on Rights and Welfare of the Child and the Protocol to the African Charter on Human and Peoples' Rights on the Rights of Women in Africa are singled out for attention.[679]

Provisions which, primarily, have implications for the position of clinical research participants are examined, rather than only those that deal with health care, or access to health. The same provisions tend to be included in each of the seven international and regional documents discussed below, for example, the right to dignity which is included in various forms in each of the documents, so, to avoid repetition, the discussion will focus on different rights in each document.

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678 It is important to note that, although these instruments generally place the duty to fulfil their obligations upon state parties, the duty to protect and promote human implies that state parties must also ensure that others (such as members of the clinical research team or research sponsors) do not violate these rights. States do this by enacting legislation. In that way, not only state actors, but also private entities and groups are bound by the obligation to respect human rights. See Clapham (n 652 above).

679 The Universal Declaration of Human Rights is not included in this discussion as, by definition, it is not a legally binding instrument, although it has become the 'common standard' against which to evaluate attempts by the world to promote a respect for human rights.
Although not a binding treaty, certain provisions in the Universal Declaration of Human Rights have established themselves as a part of the body of customary international law, and, as such, may be regarded as binding upon many states. See the discussion in para 6 which deals with sec 232 of the South African Constitution, which stipulates that customary international law is the law of the Republic. If the Universal Declaration could successfully be argued to be part of international customary law it will be binding upon South Africa. See also Humphrey 'The Universal Declaration of Human Rights: Its history, impact and judicial character' in Ramcharam (ed) (1979) *Human rights: Thirty years after the Universal Declaration* 21 - 28.

5.2 Specific human rights provisions in universal and regional instruments relevant to HIV-related clinical research in Africa

5.2.1 ICCPR

At the outset it is acknowledged that both the ICCPR and the ICESCR were drafted before the first cases of HIV infection were reported, and before the world became aware of a HIV epidemic. It is only in later human rights instruments, such as the Protocol to the African Charter on Human and Peoples' Rights on the Rights of Women in Africa, that specific reference is made to HIV/AIDS.[680]

The ICCPR recognises a number of rights that are relevant in the context of responding to the needs of participants in HIV-related clinical research in Africa. For example, the ICCPR recognises the right to life,[681] the right to physical integrity, the right to dignity and the right to be free from 'arbitrary or unlawful interference' with one's 'privacy, family, home or correspondence'.[682]

All clinical research touches upon the participants' right to life and their right to physical integrity. Clinical research tests unproven methods and experimental medicines, so, at worst, participants' lives are threatened, and, at best, their physical integrity is put at risk. There are numerous examples in the literature of clinical research participants who have lost their lives, and also of participants who were seriously injured.[683] All the effects of new medications and treatments are not known at the time they are tested upon humans and they thus pose a potential threat.

Participants' right to dignity may be infringed during the clinical research process. Again, there are many examples in the literature of how participants in research were degraded and dehumanised; the experimentation undertaken by doctors under National Socialism is an obvious example.[684] Any research design which treats participants as mere objects instead of as autonomous human beings, by definition, violates their right to dignity.

With respect to the autonomy of research subjects, article 7 of the ICCPR provides for free consent to research participation:

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680 CRC, adopted in 1989, years after the first HIV-cases were reported, makes no mention of HIV/AIDS.

681 Art 6(1) ICCPR.

682 Art 17 ICCPR.

683 See para 4.2 of ch 3 above.

684 See ch 3 above. Also, no person is treated with dignity if that person is not respected as an individual capable of making his or her own decisions. The right to dignity therefore implies autonomy, and the right not to be subjected to clinical research without having given informed consent.

> No one shall be subjected to cruel, inhuman or degrading treatment or punishment. In particular, no one shall be subjected without his free consent to medical or scientific experimentation.

Article 7 of the ICCPR is discussed in detail in chapter 5.[685] Nevertheless, it is important to recognise that, although the term *informed*[686] is not used, the use of 'free' prescribes that the research participant should be viewed as an autonomous agent and not as a means to achieving an end (a certain outcome in the research). Research which permits undue influence on research participants so that their consent is no longer 'free', is not in line with the ICCPR, for example, in a situation in which consent is compromised by offers of excessive monetary compensation, free medical care in a setting of dire poverty and other rewards for participation.[687] General Comment 20, which deals with article 7, is presented in detail elsewhere in the thesis.[688]

Research participants' right to privacy may be violated by their participation in research. It is conceivable that their status is made known to others without their consent; or that other people perceive them, as participants in HIV-related clinical research, to be HIV positive. The violation of privacy may result in discrimination and stigma.[689] Article 17 of the ICCPR prohibits the unlawful and arbitrary interference in a person's 'privacy, family, home or correspondence'. Knowledge about the health status of a clinical trial participant, especially the participant's *HIV* status, according to article 17, should be kept strictly private by researchers. In settings in which HIV positive status leads to stigmatisation and discrimination, a guarantee of privacy should be issued by research sponsors to HIV-related clinical trial participants.

Further, the ICCPR prohibits discrimination,[690] and guarantees equal protection and equality before the law.[691] Article 26 states that 'the law shall prohibit any discrimination and guarantee to all persons equal and effective protection against discrimination on any ground such as race, colour, sex, language, religion,

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685 See para 4.3.1 of ch 5 below.

686 Probably because it is a relatively new term. It was only during the eighties with the shift in thought away from the traditional paternalistic attitude of doctors towards their patients, that emphasis was placed on the nature of the information given, and that the term 'informed' consent was first used. See ch 5 below.

687 See ch 5 below.

688 See para 4.3.1 of ch 5 below.

689 See paras 2.3.2 and 2.3.3 of ch 5 below.

690 Art 2(1) ICCPR.

691 Art 26 ICCPR.

political or other opinion, national or social origin, property, birth or other status'.[692] Research initiatives contrary to these guarantees are prohibited. An example would be instances where research brings a significant benefit, but which excludes a certain class or group of people. Research testing a promising new antiretroviral, but which excludes people who do not belong to the dominant ethnic group in a specific country is therefore prohibited.

The UN Human Rights Committee (HRC) is charged with monitoring compliance with the ICCPR. Aside from its other functions, it receives and reviews state reports and individual complaints[693] submitted under the ICCPR. In General Comment 6, the UN Human Rights Committee commented that the right to life too often has been interpreted to narrowly:[694]

> The expression 'inherent right to life' cannot properly be understood in a restrictive manner, and the protection of this right requires that states adopt positive measures. In this connection, the Committee considers that it would be desirable for states parties to take all possible measures to reduce infant mortality and to increase life expectancy, especially in adopting measures to eliminate malnutrition and epidemics.

The Human Rights Committee expressly includes health issues, specifically epidemics, in its understanding of the realisation of the right to life. This General Comment has implications for HIV-related research as aimed at lessening or eliminating the HIV epidemic. From General Comment 6 one may deduce that there is a positive duty on states to undertake HIV-related research, not only in terms of the right to health in the ICESCR, but also in terms of the right to life in the ICCPR.[695] Domestic constitutions containing a guarantee of the right to life may be interpreted in a similar vein.

5.2.2 ICESCR

Article 2(1) of the ICESCR provides that each state party must take steps, individually and through international assistance and co-operation, especially economic and technical, 'to the maximum of its available resources, with a view to achieving progressively the full realisation of the rights recognised in the present

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692 Art 26 ICCPR.

693 Individual complaints may only be filed in cases where states have signed and ratified the Optional Protocol to the ICCPR.

694 Para 5 General Comment 6 Right to Life.

695 Ratifying only the ICCPR and not the ICESCR in order to escape the obligations imposed by the right to health in this regard will thus not enable states to escape the wider obligations they incur under the right to life in ICCPR. (South Africa, for example, has signed but not ratified ICESR.)

Covenant by all appropriate means, including the adoption of legislative measures'. Article 2(1) therefore places a positive obligation on member states to realise the rights enumerated in the ICESCR. The 'full realisation' of the rights should be aimed for, and the only limitation expressed is the resources that a country has at its disposal. States must further guarantee the rights enunciated in the ICESCR 'without discrimination of any kind as to race, colour, sex, language, religion, political or other opinion, national or social origin, property, birth or other status'.[696]

The ICESCR contains several provisions relevant to the protection of participants in HIV-related clinical trials. Among these is the right 'to enjoy the benefits of scientific progress and its applications'.[697] These 'benefits' include advances in medical treatment and methods against HIV/AIDS. This subsection should be useful in compelling states to ensure that research is undertaken to fight disease, and that the results of such research are available to the benefit of their people, with the result that, as science develops new technologies to combat HIV/AIDS, these technologies should become accessible.

This subsection has further important implications for the design aspect of clinical trials. In a previous chapter the Ugandan vertical HIV-transmission trials, in which a placebo was used in the control arm of a study, while AZT is the standard of care in the developed world, has been mentioned.[698] The 'right to enjoy the benefits of scientific progress' could be interpreted to render illegal a research design such as that, as it denies the women in the placebo arm of the trial the benefit of an existing treatment, or 'scientific progress'.

Moreover, this subsection could also be read to prohibit other exploitative research, such as if research is undertaken to develop new drugs and treatments, but which does not give individuals and the community who participated in the research post-trial access to the drugs and technologies developed. In these circumstances it cannot be said that research participants or the wider community realises 'the benefits of scientific progress and its applications'.

In the context of the right to enjoy the benefits of scientific progress, the UN's General Assembly has requested member states to 'promote access of all peoples to appropriate preventive, diagnostic, and therapeutic technologies and

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696 Art 2(2) ICESR.
697 Art 15(1)(b) ICESCR.
698 See para 4.2.2 of ch 3 above.

pharmaceuticals and to help make these technologies and pharmaceuticals available at an affordable cost'.[699]

The ICESCR guarantees the right of everyone to the 'enjoyment of the highest attainable standard of physical and mental health'.[700] States should take steps to achieve, among other things, 'the prevention, treatment and control of epidemic, endemic, ... and other diseases',[701] and to create 'conditions which would assure to all medical service and medical attention in the event of sickness'.[702] The right to health in the ICESCR is, probably, the most comprehensive of all the documents.

The right to health isolates aspects of health which need special attention. They are the still-birth rate and infant morality,[703] as well as environmental and industrial hygiene.[704] The *travaux préparatoires* clearly indicate that the right to health in ICESCR was formulated along the lines of the World Health Organization's Constitution.[705] Article 12 of ICESCR 'delineates concrete steps and establishes a measure of accountability through the use of specific indicators, such as the reduction in stillbirths and infant mortality'.[706]

Article 12 has successfully been used in the past to implement the right to the highest attainable standard of health at the domestic level, forcing a state to respond adequately to an epidemic. In the case of *Mariela Viceconte v Ministry of Health and Social Welfare,*[707] a number of community groups brought an application to ensure that the state of Argentina would manufacture a vaccine against Argentine hemorrhagic fever. This disease is endemic to Argentina, threatening the lives of 3.5 million people, most of whom do not have access to adequate health care.

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699 UN General Assembly Resolution 44/236, 22 December 1989 Prevention and control of Acquired Immunodeficiency Syndrome (AIDS).

700 Art 12 ICESCR.

701 Art !2 (2)(c) ICESR.

702 Art 12(2)(d) ICESR.

703 Art 12(2)(a) ICESR.

704 Art 12(2)(b) ICESR.

705 Gostin and Lazzarini (n 227 above) 5. The Preamble of the World Health Organization's Constitution reads:
'The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social conditions'.

706 As above, 6. However, the right to health does not give a standard that these indicators have to comply with. We do not know when there are few enough still births, or exactly when the 'highest attainable standard of physical and mental health' will be reached.

707 Case no 31.777/96 (1998). Also see Byrne 'Making the right to health a reality: Legal strategies for effective implementation' paper delivered at the Commonwealth Law Conference, London, UK, September 2005.

The Argentine government succeeded in vaccinating 140 000 people between 1991 and 1995, far short of the number of people threatened by the disease. The application was aimed at compelling the Argentine Ministry of Health to manufacture and distribute further doses of the vaccine to people who live in the areas most affected by the disease.

The Argentine Court of Appeals decided that there exists a duty upon the Argentine state to manufacture and provide the vaccine. In reaching its judgment, the court drew on regional and international human rights instruments guaranteeing the right to health, including the right to health as guaranteed in article 12 of ICESR.[708] In this case, ICESR was used both as an interpretive tool and as a substantive right.[709]

By analogy, because of the magnitude of the threat posed by HIV/AIDS, in terms of article 12 of ICESR, there is a duty on all governments to undertake HIV-related clinical research. This is especially true in the case of sub-Saharan Africa, where the threat of HIV/AIDS is the greatest.

The Committee on Economic, Social and Cultural Rights, which monitors compliance with the ICESCR, has issued General Comment 14 on the right to health in article 12, in order to provide guidance to state parties on the content and implementation of the right.[710] General Comment 14 details various state obligations related to HIV/AIDS:[711]

> The right to health contains both freedoms and entitlements. The freedoms include the right to control one's health and body, including sexual and reproductive freedom, and the right to be free from interference, such as the right to be free from torture, non-consensual medical treatment and experimentation. By contrast, the entitlements include the right to a system of health protection which provides equality of opportunity for people to enjoy the highest attainable level of health.

General Comment 14 observes that article 12 prohibits 'any discrimination in access to health care and underlying determinants of health, as well as to the means and entitlements for their procurement, on the grounds of . . . health status (including HIV/AIDS)',[712] and outlines the content of the right to health:[713]

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708 All these instruments have been incorporated into domestic law by the Argentinean legislature.

709 See n 707.

710 Committee on Economic, Social and Cultural Rights General Comment 14 (2000), The right to the highest attainable standard of health, UN Doc E/C/12/2000/4.

711 Para 8 General Comment 14.

712 Paras 8 and 18 General Comment 14.

713 Para 9 General Comment 14.

> The right to health must be understood as the right to the enjoyment of a variety of facilities, goods, services and conditions necessary for the realisation of the highest attainable standard of health.

The fact that General Comment 14 indicates that the right to health includes the right not to be subjected to 'non-consensual medical treatment'[714] is of especial relevance to the issue of informed consent to HIV-related clinical research.

The right to 'essential drugs, as defined by the WHO',[715] is guaranteed, as well as the right to 'seek, receive and impart information and ideas concerning health issues'.[716] Research participants' privacy is guaranteed in the right to health facilities, goods and services 'designed to respect confidentiality'.[717]

General Comment 14 stipulates that article 12 requires state parties to respect, protect and fulfil the right. With regard to their mandate 'to respect' they are required to refrain from interfering directly or indirectly in the enjoyment of the right, for example, through discrimination against individuals or groups within a health system; their protective mandate requires them to take measures (legislative and other measures) to prevent third parties from interfering with the right to health, for example, putting legislation in place governing the conduct of clinical trials by multinationals in a specific country; and, 'to fulfil the right', state parties are required to adopt budgetary, administrative, legislative, promotional and judicial measures, amongst others, towards the full realisation of the right to health. These measures would include establishing prevention and education programmes for behaviour-related health concerns such as HIV/AIDS,[718] ensuring the provision of a 'health insurance system which is affordable for all', establishing a comprehensive national health policy aimed at realising the right to health,[719] and promoting medical research, education and information campaigns with respect to HIV/AIDS.[720]

General Comment 14 stresses that any limitations on rights imposed by state parties with respect to health or on the grounds of protecting public health, such as restricting the movement of or incarcerating people with transmissible diseases such as HIV/AIDS, should be in accordance with the limitations clause in article 4 of the

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714 Para 8 General Comment 4.
715 Para 12(a).
716 Para 13(b).
717 Para 13(c).
718 Para 16.
719 Para 36.
720 Para 36.

ICESCR.[721] Therefore, such limitations must be 'in accordance with the law, including international human rights standards, compatible with the nature of the rights protected by the Covenant, in the interest of legitimate aims pursued, and strictly necessary for the promotion of the general welfare in a democratic society'.[722]

Further, the General Comment asserts the requirement that any limitations must be 'proportional'; that the 'least restrictive alternative' must be adopted, and that such a limitation must be of 'limited duration and subject to review'.[723]

Finally, it is important to remember that the right to health is interlinked with various other rights. The General Comment remarks that the right to health is closely related to, and dependant upon, the realisation of other human rights, as contained in 'the international Bill of Rights'.[724] The rights that are mentioned include the rights to food, housing, work, education, human dignity, life, non-discrimination, equality, the prohibition against torture, privacy, access to information, and the freedoms of association, assembly and movement. The General Comment stresses that these and other rights and freedoms 'address integral components of the right to health'.[725]

5.2.3 CEDAW

The CEDAW also enumerates rights which are relevant in protecting the interests of participants in HIV-related clinical research. The Committee on the Elimination of Discrimination against Women (CEDAW Committee) receives and reviews state reports and individual or group complaints,[726] and has the task of implementing the rights listed in CEDAW.

Article 11(1) guarantees women's right to 'protection of health and to safety in working conditions, including the safeguarding of the function of reproduction'.[727] On that basis, women may not be exposed to risks in HIV-related clinical research which can not be justified in relation to the potential benefits of the research.

Article 12 compels state parties to the Convention to 'take all appropriate measures to eliminate discrimination against women in the field of health care

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721 Para 28.
722 Para 28.
723 Para 29.
724 Para 3.
725 Para 3.
726 Individual complaints may only be filed in cases where states have signed and ratified the Optional Protocol to CEDAW.
727 Art 11(1)(f) CEDAW.

services, including those related to family planning'[728] and to 'ensure to women appropriate services in connection with pregnancy, confinement and the post-natal period, granting free services where necessary'.[729]

Unless research into issues relating to the HIV-related health-care needs of women is promoted, there will be no scientific advance and women will suffer harm as a result. For example, research into antiretrovirals or microbicides that limit specifically vaginal transmission of HIV should be undertaken; otherwise women are discriminated against, contrary to article 12. Excluding women as a group from the clinical research design and process could also cause women to lose access to medical care during the research process and access to the knowledge and advances that resulted from such research.

The CEDAW Committee has issued several general comments that address women's health issues and HIV/AIDS, including General Recommendation 24 which deals specifically with women and health.[730] General Recommendation 24 declares that the issues of 'HIV/AIDS and other sexually transmitted diseases are central to the rights of women and adolescent girls to sexual health'.[731] The General Recommendation notes that women and girls suffer from a lack of adequate information and of services, that they do not have sufficient power to refuse sex or insist on safe sexual practices, and that they are often subjected to marital rape and polygamy, exposing them to HIV infection.[732] HIV-related clinical research which takes cognisance of the General Recommendation in its research design, or which does not encourage or indirectly support unequal power relations in the research process alone is in line with the Recommendation.

General Recommendation 24 compels states to ensure the right to sexual health information for all women and girls, especially sex workers and trafficked women and girls, in programmes designed to respect their rights to privacy and confidentiality.[733] It is mandatory under the Recommendation to provide such information in a HIV-related clinical research setting. The privacy and confidentiality of participants during the research is guaranteed.

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728 Art 12(1) CEDAW.
729 Art 12(2) CEDAW.
730 Committee on the Elimination of Discrimination against Women *General Recommendation 24 Women and Health* <http://www.unhchr.ch/tbs/doc.nsf/(Symbol)/77bae3190a903f8d80256785005599f> (1 April 2006).
731 Para 18.
732 As above.
733 As above.

5.2.4 CRC

The CRC contains a number of rights relevant to the protection of participants in HIV-related clinical research. The Committee on the Rights of the Child (CRC Committee), amongst other tasks, is responsible for the implementation of the Convention.[734]

While article 2 prohibits 'discrimination of any kind, irrespective of the child's or his or her parent's or legal guardian's race, colour, sex, language, religion, political or other opinion, national, ethnic or social origin, property, disability, birth or other status',[735] article 3 determines that 'in all actions concerning children ... the best interests of the child shall be of primary consideration'.[736]

This sub-section establishes a strict requirement with which HIV-related clinical research must comply: children's participation in HIV-related research should be in the 'best interests of the *child*' - in the singular. It would seem as if HIV-related clinical research which is not in the best interests of the *specific child* who is taking part in the research is not in accordance with this sub-section. Most HIV-related clinical research which aims to develop effective drugs for illnesses, other than that from which the specific children taking part in the research suffer, is thus prohibited. Even if the research aims to find a drug to treat that specific child's condition, the research and participation of children must still be shown to be in the best interests of the child. Research which exposes the child to too high a risk in relation to the potential benefits of the research, therefore, will not be acceptable in terms of CRC.[737]

Article 16 establishes the child's right to privacy. This right has obvious implications for children's participation in HIV-related clinical research. The privacy of a child participating in such research should always be guaranteed, especially in matters such as HIV-status.

Article 24 is of especial importance with reference to HIV-related clinical research in Africa. It guarantees 'the right of the child to the enjoyment of the highest attainable standard of health and to facilities for the treatment of illness and

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734 Such as monitoring state compliance with CRC.
735 Art 2(1) CRC.
736 Art 3(1) CRC.
737 See also the discussion of art 4(1) of the African Children's Charter in para 4.3.8 below.

rehabilitation of health'.[738] State parties to the Convention further undertake to pursue the 'full implementation of this right'[739] and shall take appropriate measures to diminish child mortality,[740] to combat disease and malnutrition,[741] to ensure the provisioning of medical assistance and health care to all children,[742] to develop preventive health care[743] and so on.[744] Research which supports state parties' duties only as outlined above will be in line with the CRC.

Article 36 of the CRC demands state parties protect 'the child against all other forms of exploitation prejudicial to any aspect of the child's welfare'. As a kind of catch-all prohibition on exploitation, this sub-section is of particular relevance to children's participation in HIV-related clinical research in Africa. No research that is exploitative in nature is allowed, for example, in terms of the use of placebo groups in settings where there is no standard of care available, or where research is done in Africa because it is cheaper or because it would never have been allowed to take place in the 'developed world'.

In 2003 the CRC Committee issued General Comment 3 on HIV/AIDS and the rights of the child.[745] In General Comment 3 the Committee notes that 'the majority of new HIV infections are among young people' and that 'women and girls are increasingly becoming infected'.[746] The General Comment emphasises that 'effective HIV/AIDS prevention requires states to refrain from censoring, withholding or intentionally misrepresenting health-related information' and that states must ensure that children 'acquire the knowledge and skills to protect themselves'.[747] Furthermore, it stipulates that state parties should ensure children 'access to voluntary, confidential HIV counselling and testing'.[748]

General Comment 3 addresses issues concerning children who are especially vulnerable to HIV infection and to discrimination on the basis of their HIV status.

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738 Art 24(1) CRC.
739 Art 24(2) CRC.
740 Art 24(2)(a) CRC.
741 Art 24(2)(c) CRC.
742 Art 24(2)(b) CRC.
743 Art 24(2)(f) CRC. This sub0section is of particular relevance to HIV-related and other vaccine efficacy research.
744 See art 24(2)(a) – (f) CRC.
745 Committee on the Rights of the Child General Comment 3 (2003) CRC/GC/2003/3 (17 March 2003) <http://www.unhchr.ch/tbs/doc.nsf/(Symbol)/309e8c3807aa8cb7c1256d2d0038caaa ?opendocument> (1 April 2006).
746 Para 2.
747 Para 16.
748 Para 22.

This group includes children who are orphaned by HIV/AIDS, child victims of sexual and economic exploitation and child victims of violence and sexual abuse.[749] It is difficult to think of any example of HIV-related clinical research undertaken in such a setting, which would not violate the CRC. Before clinical research in these settings complies with the CRC, extra safeguards against violating the welfare of the children would have to be implemented.

5.2.5 African Charter on Human and Peoples' Rights

The African Charter on Human and Peoples' Rights (African Charter) states in article 4 that 'human beings are inviolable', and that 'every human being shall be entitled to respect for his life and integrity of his person'. Article 5 ensures that every 'person shall have the right to liberty and to the security of his person'. Even though informed consent to research participation is not mentioned, these two provisions of the African Charter can be used in support of the notion that HIV-related clinical research participants give free and informed consent to research participation. Research without such consent violates the integrity and security of the person.

However, it is not only informed consent that is at issue. Research which harms the person or which is exploitative can also be regarded as violating the integrity and security of the person. It is submitted that research such as that described in chapter 3, where Pfizer treated children for spinal meningitis in Kano, Nigeria with the experimental drug Trovan, violates article 5 of the African Charter. At the time the drug was being tested in Nigeria, Trovan had never been tested on children, and earlier that year it had been withdrawn from US markets due to its serious side-effects.[750] No matter the urgency, only existing, proven medication should have been used.

Article 16 provides that 'every individual shall have the right to enjoy the best attainable state of physical and mental health'.[751] Also, state parties are to 'take the necessary measures to protect the health of their people and to ensure that they receive medical attention when they are sick'.[752] HIV-related clinical research, whether state-sponsored or not, is a measure to protect the health of Africa's people, and, thus, fulfils the duty assigned by this article. However, research specifically aimed at protecting the health of that particular group of people, and not research

749 Arts 30 –39.
750 See para 4.2.2 of ch 3 above.
751 Art 16(1) African Charter.
752 Art 16(2) African Charter.

which is aimed at meeting the health needs of another country or continent, alone meets the requirement of this article.

The African Commission is responsible for the implementation of the African Charter.[753] It must promote human (and peoples') rights in Africa,[754] it must protect these rights,[755] and it must interpret the provisions of the African Charter.[756] As far as its interpretive and protective mandates are concerned, the African Commission has given substance to the right to health in the African Charter by stipulating that the enjoyment of the human right to health 'is vital to all aspects of a person's life and well-being, and is crucial to the realisation of all other fundamental human rights and freedoms'.[757] The Commission considers the right to health to 'include the right to health facilities, access to goods and services to be guaranteed to all without discrimination of any kind'. [758]

On the impact of the prevailing conditions in Africa on the realisation of the right to health, the Commission states that it is aware that 'millions of people in Africa are not enjoying the right to health maximally because African countries are generally faced with the problem of poverty which renders them incapable to provide the necessary amenities, infrastructure and resources that facilitate the full enjoyment of this right'.[759] The African Commission proceeds to 'read into' article 16 the 'obligation on part of states party to the African Charter to *take concrete and targeted steps, while taking full advantage of its available resources*, to ensure that the right to health is fully realised in all its aspects without discrimination of any kind'. [760]

HIV-related clinical trials can be viewed as an example of 'concrete and targeted steps' that take 'full advantage of [...] available resources'. The results of such trials, if used to improve the condition of the health of Africa's people and if

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753 According to art 45(4) of the African Charter it must also perform any other tasks 'which may be entrusted to it by the Assembly of Heads of State and Government. See also Gumedze 'HIV/AIDS and human rights: The role of the African Commission on Human and Peoples' Rights' (2004) 4 *African Human Rights L J* 181.

754 Arts 30 and 45(1) African Charter.

755 Arts 30 and Art 45(2) African Charter.

756 Art 45(3) African Charter.

757 Communication 241/2001 *Purohit and Moore v The Gambia* Sixteenth Annual Activity Report of the African Commission on Human and Peoples' Rights, para 80. The case was brought in regard to the legal and material conditions of detention in a Gambian mental health institution.

758 As above.

759 Para 84.

760 Para 84. My emphasis.

they get access to the products of such research, would advance the right to health in Africa.

The African Commission has adopted a number of resolutions and principles of relevance to clinical research in Africa.[761] The 2003 Principles and Guidelines in the Right to a fair Trial and Legal Assistance in Africa[762] (Principles and Guidelines) in paragraph M.7(f) stipulate that 'no detained person shall, even with his or her consent, be subjected to any medical or scientific experimentation which could be detrimental to his or her health'.

Detainees and prisoners constitute easy prey for unscrupulous researchers. Usually an easily accessible population, in an environment where outside factors influencing research results can be controlled, detainees and prisoners have been approached to take part in 'harmless' research, without cognisance of the fact that, in such a setting their consent is probably not 'free' and 'informed'.

The qualifying words in the paragraph are significant: 'even with his or her consent'. The consent of a detained person is not valid: the guidelines protect against instances where consent is obtained by means of coercion and other measures; insisting, in these circumstances, that research is illegal.

The phrase 'which could be detrimental to his or her health' implies that not *all* research is prohibited, only that which could be detrimental to the health of the detainee or prisoner. The drafters of the Principles and Guidelines might have had in mind a measure akin to the 'minimal harm' or 'negligible harm' principle that is often seen in ethical guidelines.[763]

It is submitted that there are a number of problems associated with the phrase 'which could be detrimental to his or her health'. Who is to judge what is detrimental to the prisoner or detainee's health - the prison authorities; the detainee herself; the researcher or research sponsor? The damage a person's health sustains may manifest only after several years. All side-effects of a specific drug are not known at the beginning of the research. Research which appears harmless may have unexpected consequences later. All research endeavours, carry this risk, however, where there is doubt about the research participant's informed consent as

761 This is an example of 'soft' law. See para 2.1 above.

762 Adopted by the African Commission following the appointment of the Working Group on the Right to a Fair Trial per its 1999 Resolution on the Right to a Fair Trial and Legal Assistance. Reprinted in *Compendium of key human rights documents of the African Union* (2005) 210.

763 See para 3.4.1 of ch 5 below.

a result of his or her incarceration or detention, no research that has the potential to harm the participant should be allowed.

It is submitted that the drafters of the Principles and Guidelines should not have inserted the qualification, and the guideline should read, 'no detained person shall, even with his or her consent, be subjected to any medical or scientific experimentation'.

Apart from the provisions of the African Charter and the resolutions by the African Commission, the political organs of the OAU, later the AU, have adopted resolutions relevant to clinical research in Africa. For example, the Grand Bay (Mauritius) Declaration[764] reflects upon the vulnerability and human rights of people living with HIV/AIDS:[765]

> The Conference notes that the rights of people with disability and people living with HIV/AIDS, in particular women and children, are not always observed and urges all African states to work towards ensuring the full respect of these rights.

These reflections require that HIV-related clinical research sponsors have mechanisms in place which ensure the protection of vulnerable research participants, such as those living with HIV/AIDS.

In April 2001, the Heads of State and Government held a special summit to deal with issues specifically related to the challenges of HIV/AIDS, TB, malaria and other diseases. The meeting adopted the Abuja Declaration on HIV/AIDS, Tuberculosis and other related infectious diseases (Abuja Declaration),[766] and the Abuja Framework for Action for the fight against HIV/AIDS, tuberculosis and other related infectious diseases (Abuja Framework). The latter has as its aim the implementation of the Abuja Declaration.

The Abuja Declaration acknowledges that 'stigma, silence, denial and discrimination against people living with HIV/AIDS increase the impact of the epidemic' and that they constitute 'a major barrier to an effective response to it'.[767] Consequently, the Abuja Framework expresses strategies and activities by means of which states may implement the contents of the Abuja Declaration. Amongst these are relevant legislation to protect the rights of people infected and affected by

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764 Issued by the First OAU Ministerial Conference on Human Rights, which held a meeting from 12 – 16 April 1999 in Grand Bay, Mauritius.

765 Para 7 Grand Bay (Mauritius) Declaration.

766 <http:/www.onusida-acoc.org/Eng/Abuja%20declaration.htm> (30 April 2006).

767 Para 12 Abuja Declaration.

HIV/AIDS and TB, strategies to strengthen existing legislation aimed at addressing human rights violations and gender inequalities and to promote a respect for the rights of infected and affected people and assistance to women in taking appropriate decisions to protect themselves against HIV infection.

The Assembly of Heads of State and Government of the OAU at its 32nd ordinary session in Yaounde, Cameroon, from 8 to 10 July 1996, adopted the Resolution on Bioethics (African Bioethics Resolution).[768] The African Bioethics Resolution acknowledges that:

> scientific progress benefits the individual human being and is achieved under condition of respect for fundamental human rights, and *stressing* the need for international co-operation in order to enable humanity as a whole to benefit from the achievements of the science of life and obviate any use thereof for purposes other than the promotion of humanity's well-being ...

The African Bioethics Resolution endorses the priority placed upon informed consent by the ICCPR,[769] and stresses the 'obligation to obtain the free and enlightened consent' to research, and 'the definition of rules to protect vulnerable populations, the incapacitated, persons deprived of freedom as well as the sick under emergency conditions'.[770] The African Bioethics Resolution further reaffirms the right to benefit from scientific progress and the application of such progress without discrimination,[771] and the right of everyone, especially children, to protection 'from all forms of trade and exploitation'.[772]

The African Bioethics Resolution pledges to take legislative and other measures to give effect to the Resolution, as well as setting up consultative bodies at all levels to promote the exchange of experience.

5.2.6 African Charter on Rights and Welfare of the Child

Article 43(1) of the Children's Charter compels state parties to submit to the African Committee of Experts of the Right and Welfare of the Child, through the Chairperson of the Commission of the African Union, 'reports on the measures they have adopted to give effect to the provisions of the Children's Charter, as well as the progress made in the enjoyment of the rights guaranteed in the African Children's Charter'. According to the Guidelines for Initial Reports of State Parties under the African

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768 AHG/Res 254 (XXXII) 1996.
769 Para 2 African Bioethics Resolution.
770 Para 3 African Bioethics Resolution. See also para 4.3.2 of ch 5 below.
771 As above.
772 As above.

Children's Charter, states should indicate the measures that are in place to ensure the safety of children in need of special protection, such as in the case of AIDS orphans.[773]

Article 14 of the African Children's Charter guarantees to every child the 'right to enjoy the best attainable state of physical, mental and spiritual health'.[774] State parties to the African Children's Charter 'shall undertake to pursue the full implementation of this right'.[775] In particular, they shall take measures which include[776] the reduction of the infant and child mortality rate; the provisioning of necessary medical assistance and health care to all children with emphasis on the development of primary health care; and measures ensuring the provision of adequate nutrition and safe drinking water, to combat disease and malnutrition within the framework of primary health care through the application of appropriate technology and to ensure appropriate health care for expectant and nursing mothers.[777]

Article 15 of the African Children's Charter deals with child labour. Although participation in HIV-related clinical research cannot be seen as 'labour', the phrasing of article 15 compels state parties to protect children from 'all forms of economic exploitation'.[778] The participation of children in clinical research which is exploitative is thus strictly prohibited by the African Children's Charter. Examples of exploitative treatment of children in clinical research are easily found in the literature. These examples include experiments such as those performed at the Willowbrook State School,[779] the Trovan experiments on children in Nigeria,[780] the testing of medications which will not eventually be available to those children on whom it was

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773 Para 21(g) Guidelines for Initial Reports of State Parties under the African Charter on Rights and Welfare of the Child.

774 Art 14(1) African Children's Charter.

775 As above.

776 Art 14(2)(a) – (j) African Children's Charter.

777 They have the further task of ensuring the development of preventive health care and family life education and provision of service, the integration of basic health service programmes in national development plans; that all sectors of the society, in particular parents, children, community leaders and community workers are informed and supported in the use of basic knowledge of child health and nutrition, the advantages of breastfeeding, hygiene and environmental sanitation and the prevention of domestic and other accidents; the meaningful participation of non-governmental organisations, local communities and the beneficiary population in the planning and management of basic service programmes for children; and to support, through technical and financial means, the mobilisation of local community resources in the development of primary health care for children.

778 Art 14(1) African Children's Charter.

779 See para 4.2.1 Ch 3.

780 See para 4.2.2 of ch 3 above and para 5.2.6 above.

tested, the testing of HIV-medication which, due to its toxicity, is not suitable for use in children, and the exploitation of children through payment for participation in clinical research in poverty-stricken communities where participation in such research is the only means of income for those children and their families. According to article 15 of the African Children's Charter, state parties are to 'take all appropriate legislative and administrative measures to ensure the full implementation of this article'.[781]

Article 16 deals with the protection of children against child abuse and torture. Sub-section 1 reads as follows:

> State parties to the present Charter shall take specific legislative, administrative, social and educational measures to protect the child from all forms of torture, inhuman or degrading treatment and especially physical or mental injury or abuse, neglect or maltreatment including sexual abuse, while in the care of a parent, legal guardian or school authority or any other person who has the care of the child.

HIV-related clinical research which exploits children in the ways described above may be considered within the ambit of the prohibition in this sub-section.

Harmful social and cultural practices are prohibited in article 21.[782] The relevance of this sub-section to HIV-related research becomes clear when one considers that much research in Africa necessarily takes place within a context in which these practices are present. For example, practices such as female genital mutilation have implications for the transmission of HIV, as do traditional practices which support girl-children's and women's subordinate role in African society. Research which supports or turns a blind eye to the existence of these practices is necessarily in violation of the African Children's Charter. HIV-related clinical research cannot be complicit in the perpetration of practices that are harmful.

The African Children's Charter prescribes a measure or standard against which children's participation in HIV-related clinical research can be measured. Article 4(1) reads as follows, '[i]n all actions concerning the child undertaken by any person or

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781 Art 15(2).

782 The article reads:

1. State parties to the present Charter shall take all appropriate measures to eliminate harmful social and cultural practices affecting the welfare, dignity, normal growth and development of the child and in particular:

(a) those customs and practices prejudicial to the health or life of the child; and
(b) those customs and practices discriminatory to the child on the grounds of sex or other status.

2. Child marriage and the betrothal of girls and boys shall be prohibited and effective action, including legislation, shall be taken to specify the minimum age of marriage to be eighteen years and make registration of all marriages in an official registry compulsory.

authority, the best interests of the child shall be the primary consideration'. HIV-related clinical research which does not have the best interests of the child as its aim is thus prohibited. As in the case of CRC, the singular noun, 'child', indicates that the best interests of the specific child taking part in the research is to be considered, and not the interests of children generally. [783]

The African Children's Charter also ascribes responsibilities that children have in relation to their family and society. The child is to 'serve his national community by placing his physical and intellectual abilities at its service'.[784] Children's participation in HIV-related research, if it is not exploitative and is in the best interests of the child, can be viewed as sanctioned by this sub-section of the African Children's Charter. In this view, children are part of a community which may benefit from their participation.

The Tunis Declaration on AIDS and the Child was adopted by the OAU at the Assembly of Heads of State and Government in Tunisia in 1994 (Tunis Declaration).[785] The Declaration embodies Africa's commitment to elaborate 'a national policy framework to guide and support appropriate responses to the needs of [HIV/AIDS] affected children covering social, legal, ethical, medical and human rights issues'.[786] Thus far little has been done to give effect to the Tunis Declaration.[787]

5.2.7 Protocol to the African Charter on Human and Peoples' Rights on Rights of Women in Africa

Article 2 of the Women's Protocol deals with the elimination of discrimination against women. It prohibits 'all forms of discrimination against women'.[788] State parties must take measures which modify 'social and cultural patterns of conduct of women and men', 'achieving the elimination of harmful cultural and traditional practices and

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783 Viljoen points out that the use of '*the* primary consideration' (instead of '*a* primary consideration' as used in CRC) sets a higher level of protection for children under the African Children's Charter than under the CRC. See Viljoen 'Africa's contribution to the development of international human rights and humanitarian law' (2001) 1 *African Human Rights L J* 18.

784 Art 31(b).

785 AHG/Decl 1 (XXX) 1994.

786 Para 2(1) Tunis Declaration.

787 As evidenced by the fact that at the 32nd ordinary session of the Assembly of Heads of State and Government in 1996, the Resolution on Regular Reporting of the Implementation Status of OU Declarations on HIV/AIDS in Africa was adopted. Governments were urged to implement resolutions and declarations of the OAU, especially the Tunis Declaration.

788 Art 2(1) Women's Protocol.

all other practices which are based on the idea of the inferiority or the superiority of either of the sexes, or on stereotyped roles for women and men'.[789]

HIV-related clinical research that collaborates with harmful cultural practices or stereotyped roles for women is consequently prohibited. For example, in many African cultures, because of the inferior position society assigns to women, it is expected that the researcher first asks 'permission' for a woman's participation in research from the woman's father or husband, sometimes even before the woman herself is approached. Researchers react in two ways to this practice. Firstly, they may follow the cultural norm and approach the woman's father or husband, but make sure that the woman herself also consents. In doing this, they reinforce harmful practices and stereotypical roles of women: they 'buy into' the idea that women's consent of itself is not sufficient, and that someone in a role of authority over her should consent on her behalf as well. Secondly, they may exclude women altogether from their research design because they do not want to enforce such negative cultural practices. Consequently women are excluded from the benefits attaching to research participation, and are discriminated against indirectly as any knowledge gained from the research will not be applicable to women. Even worse still, the results and knowledge gained from the research will be applied to women despite the fact that they did not take part in the research, without taking into account the specific peculiarities of the female body.

The dilemma sketched above presents a very difficult choice for researchers, and there is no easy answer. The first alternative presented is marginally better than the second, in the sense that, at least, women are not excluded from the possible benefits of the research. However, research which reinforces society's stereotypical views of women should never be condoned.

Of special importance to the present study are sections in the Women's Protocol which deal with women's health and reproductive rights.

Under section 14 of the Women's Protocol, state parties undertake to ensure that the right to sexual and reproductive health of women is respected and promoted, specifically their right to have 'self-protection and to be protected against sexually transmitted infections, including HIV/AIDS'.[790]

The implications of this provision of the Women's Protocol for HIV-related clinical research in Africa are clear. The assurances that women are protected

789 Art 2(2) Women's Protocol.
790 Art 14(1)(d) Women's Protocol.

against sexually transmitted diseases, such as HIV, during the duration of the research, and, by the nature of the research design, are not exposed to these diseases, are requirements in terms of the Women's Protocol. Women need to be educated, not only by government but also by researchers, about the possibility of contracting sexually transmitted diseases, including HIV/AIDS, and also the ways in which they may protect themselves against such diseases. It may also be necessary for research sponsors to provide medication and other treatment for such diseases during the research endeavour.

Women have the right to be informed on their 'health status and the health status of [their] partner, particularly if infected with sexually transmitted infections, including HIV/AIDS, in accordance with internationally recognised standards and best practices'.[791] If a researcher, or a member of the research team, becomes aware of the health status, especially the HIV status, of a woman's sexual partner, the Women's Protocol places an obligation upon the researcher, 'in accordance with internationally recognised standards and best practices' to inform her of the health status of the partner, failing which they are in violation of the Women's Protocol. With this provision the drafters of the Women's Protocol make a laudable effort to protect women's health.

However, the matter is not as straightforward as it appears. The situation may arise that the researcher becomes aware of the woman's HIV-positive status. The Women's Protocol does not place a similar obligation upon the research team to inform her sexual partner (nor can it really be said that such a duty is implied by the Women's Protocol). One could argue that, in some societies, women may be stigmatised, ostracised or even killed if their status becomes known, and therefore, there should be no such obligation to inform her partner. But that begs the question: not only women's, but also men's health surely should be protected, especially in the case of an epidemic as devastating as HIV/AIDS. It is submitted that the impact of this provision of the Women's Protocol, if adhered to by researchers, could have a disproportionately negative impact on men. It is further submitted that, unless there are clear prohibitive indications, such as that it endangers the woman's life or exposes her to harm, researchers should inform a woman's sexual partner of her status. Women should also be informed at the beginning of the research endeavour that the possibility exists that their partners will be told if it becomes clear that they are HIV-positive.

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791 Art 14(1)(e) Women's Protocol.

Further, state parties must take appropriate measures to 'provide adequate, affordable and accessible health services ...'[792] and 'establish and strengthen existing pre-natal, delivery and post-natal health and nutritional services for women during pregnancy and while they are breastfeeding'.[793] This obligation relates to the duty of state parties to human rights treaties to *fulfil* the human rights of the inhabitants of the country, HIV-related research which assists in this task is in support of the fulfilment of that duty.[794]

5.3 Conclusion

The section focuses on specific provisions in international and regional human rights instruments that are valuable in protecting participants in HIV-related research in Africa from abuse. International human rights instruments, such as ICCPR, ICESR, CRC and CEDAW, as well as regional instruments such as the African Charter on Human and Peoples' Rights, the African Charter on Rights and Welfare of the Child and the Protocol to the African Charter on Human and Peoples' Rights on the Rights of Women in Africa are singled out for attention. Examples of 'soft' law are highlighted.

The analysis demonstrates that international human rights instruments do provide an effective legal framework for the protection of participants in HIV-related clinical research in Africa. Many of the provisions contained in these instruments enunciate rights that are relevant in the context of HIV/AIDS-related clinical research participation in Africa, either through specific reference to clinical research or experimentation, or through more general prohibitions against 'degrading treatment' and violations of physical integrity, privacy and equality.

Significant progress has been made in the implementation of international human rights, despite the challenges which remain, such as holding non-state actors responsible for the violation of human rights under international law. In the context of the present study, human rights violations in clinical research in Africa most likely will be the result of actions by multi-national or transnational pharmaceutical corporations, international research bodies and other individuals.[795] However, as

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792 Art 14(2)(a).

793 Art 14(2)(b).

794 For more about the obligations of governments to respect, protect and fulfil human rights, see para 6.4 below.

795 Nowak points out (on 343) that many of these multinational corporations are more powerful and financially stronger than many states. On that ground it seems to him

human rights treaties confer a duty upon state parties to *protect* the human rights enunciated in the treaties, a violation by third parties (both state and non-state actors) in terms of those treaties holds the states accountable for failing to protect the rights of research participants.[796] Political pressure could be brought to bear on the government of countries in which the multinational corporations, international research bodies or individuals have their headquarters or on the government of the countries in which they operate and carry out their research[797] in the hope that they will force these organisations to comply with human rights standards, and will act as the 'watch-dogs' of the international community.

Consumer boycotts and the 'mobilisation of shame', usually by NGOs and the press are alternative strategies.[798] The public outcry created by these strategies changes the behaviour of corporations and individuals so that they adopt voluntary codes of conduct and of corporate responsibility.[799]

A more far-reaching proposal to make non-state perpetrators of human rights violations bear responsibility for their actions is to transfer responsibility to the individual.[800] Under international criminal law, not only governments but also the individual perpetrators of gross and systematic human rights violations are held responsible for their actions, for example, members of the Bosnian Serb armed forces, as well as 'individual' perpetrators of genocide in Rwanda have been found guilty and sentenced for war crimes.[801] It is to be doubted, however, whether violations during clinical research are ever going to be of the magnitude that they can be considered 'gross and systematic' human rights violations. International criminal law, therefore, has little to offer the victims of violations of human rights during clinical research.

Ultimately it is up to governments to adopt measures which make international human rights binding and justiciable within their own territories under domestic

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'somewhat anachronistic that states should remain the only subjects of international law capable of signing and ratifying treaties under international law'.

796 See also Clapham (n 652 above).

797 Nowak 343.

798 As above.

799 Nowak 343. Examples are the UN Global Compact and the OECD Guidelines for Multinational Enterprises.

800 Nowak 343.

801 Nowak (n 23 above) 244.

law.[802] Cognisant of this fact, the next section of the chapter scrutinises the domestication of international human rights in sub-Saharan Africa, with special reference to South Africa.

6 DOMESTICATION OF INTERNATIONAL HUMAN RIGHTS IN SUB-SAHARAN AFRICA, WITH SPECIAL REFERENCE TO SOUTH AFRICA

6.1 Introduction

As indicated in the preceding sections, international human rights law depend on a functioning national system of human rights law: not only is the national system the first line of defence against human rights abuses, but international human rights treaties have value only if states give effect to the provisions by implementing them at a national level.

In instances in which effective national human rights systems coexist with international systems for the protection of human rights the primary responsibility for the protection rests with the national authority and the protection offered under the international system is subsidiary.[803] An effective remedy is available at national level and, therefore, the requirement is that domestic remedies be exhausted before a complainant turns to a regional or UN forum.

By becoming a state party to an international human rights treaty, states undertake to fulfil a variety of obligations.[804] Governments of states must 'respect',[805] 'protect',[806] 'fulfil'[807] and 'promote'[808] the human rights contained in the

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802 See para 6 below. See also generally Adjami 'African courts, international law and comparative case law: Chimera or emerging human rights jurisprudence?' (2002) 24 *Michigan J Intl L* 103.

803 Nowak 37.

804 Dugard defines a 'treaty' or 'convention' as a 'written agreement between states or between states and international organisations, operating within the field of international law'. There are three different types of treaties, namely, contractual, which deals with matters such as trade and air and landing rights; legislative, which codify existing rules of customary international law or which create new rules of law; and constitutional treaties which create international organisations such as the UN. The Charter of the UN is thus a constitutional treaty (see Dugard (n 643 above) 26 - 27).

805 Individual states must *respect* rights by refraining from interfering with the enjoyment of these rights, such as not enacting legislation which limits freedom of the press.

806 Individual states must *protect* rights by protecting the people within a state from violations of those rights by third parties. This is usually done by means of legislating, for example, in the case of South Africa which adopted legislation (Act 4 of 2000) which protects against discrimination.

treaty. However, these obligations do not require states to transform the treaty or convention word for word into national constitutional law, but rather that the obligations deriving from international law are implemented under national or domestic law.[809]

The following section investigates the ways in which international human rights obligations are implemented under domestic or national law in sub-Saharan Africa. Later specific reference is made to the South African system, in preparation for the next chapter which deals with informed consent in preventive HIV vaccine efficacy trials in South Africa.

6.2 General overview of different views on the place of international law with regard to national law

Differing views exist on the relationship or place of international law with regard to national law. These views have consequences not only for the mechanisms used for incorporating international human rights law into national law, they affect the interpretation of the place of international human rights law in national law as well.

The first view of international law falls into the monist or monistic system. The monist view, as the name indicates, considers international law and national law as one system of law.[810] In other words, international law and national law are a single integrated system. International human rights treaties in 'monist' states are thus considered equal to, or superior to, the national constitution by virtue of an express constitutional order.[811] In cases such as these,[812] international law is incorporated into national or municipal[813] law without any act of adoption or transformation, and courts have to apply the rules of international law directly.[814]

In the second view, a strict distinction is made between international and national law, as they are seen as two different systems of law.[815] It is referred to as

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807 State parties to a treaty must *fulfil* human rights by taking positive measures aimed at ensuring the fulfilment of those rights, for example by building schools and training teachers to give effect to the right of access to education.

808 Individual states *promote* human rights by making sure that people are aware of the nature and extent of their human rights. This is usually done through awareness-raising campaigns.

809 Nowak (n 23 above) 37.

810 Dugard 43.

811 Nowak 36.

812 The Netherlands is an example; additional examples are given below.

813 The term 'municipal' is used in international law to refer to the national law of a state.

814 Dugard 43.

815 As above.

the dualist or dualistic view or theory. 'Dualist' states may not incorporate or transform international human rights treaties into national law except through an express order from the national legislator.[816] Tijanyana Maluwa remarks that, as a general rule, dualists accord international law primacy over municipal law in the international sphere, and municipal law enjoys primacy over international law in the national sphere.[817]

States do not necessarily adhere to the same system consistently; some states follow a dualist view in respect of some aspects of international law, and a monist view in respect of others.[818] The degree of implementation can also differ. For example, in some states which follow a monist view, international human rights law may be considered even superior to domestic law. In others, which adhere to the dualist view, international law has no force and effect unless and until it has been given substance by domestic courts.[819]

Moreover, a rigid distinction between 'monist' and 'dualist' systems is less credible in practice and the 'antithesis between monist and dualist approaches to the relationship between international and municipal law must be viewed with some caution'.[820] First, the application of international human rights law depends upon *municipal law* in the specific country; usually the constitution assigns the status of international law in the legal system.[821] Second, a wide range of approaches spans the two systems, incorporating to some extent elements of both.[822] Finally, countries in the monist tradition, in some circumstances, refuse in practice to give effect to treaties which under international law are binding.[823] Viljoen characterises it as an 'unhelpful and deceptive' categorisation and is in favour of discarding the distinction for an approach which identifies whether treaty provisions serve as grounds *for independent legal action* in the absence of domestic enactments 'grounding' these treaties.[824]

With regard to the situation of international human rights law in Africa, Maluwa indicates that the practice in African states in incorporating the substantive norms of international human rights law into national law, or in using them as an aid

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816 The United Kingdom is an example; Nowak 36.
817 Maluwa (1998) 23 *SA Ybk Intl L* 49.
818 Dugard 43.
819 Nowak 36.
820 Maluwa (n 817 above) 49 – 50.
821 As above, 50.
822 As above.
823 As above.
824 Viljoen (n 562 above). See the section on self-executing treaties below.

to interpretation, depends in part upon the colonial experiences and their inherited colonial legal cultures and systems.[825] It is possible to distinguish African countries with an English common law tradition (former British colonies) from countries with a civil law tradition (former colonies of France, Germany, Italy, Portugal and Spain).[826]

African countries in an English common law tradition follow a dualist approach. Their constitutions stipulate that international human rights law does not become part of national or domestic law without explicit incorporation by an act of parliament.[827] For example, the Malawi Constitution in article 211(1) stipulates that an agreement ratified by Parliament 'shall form part of the law of the Republic *if so provided for in the Act of Parliament ratifying the agreement*'.[828]

African countries in a civil law tradition follow a monist approach. The rules of international law are part of domestic or municipal law in terms of the constitution of the state and, in certain instances, enjoy preference over domestic legislation.[829] For example, article 9 of the Constitution of the Federal Republic of Ethiopia provides that '[a]ll international agreements ratified by Ethiopia are an integral part of the law of the land'. Article 147 of the Constitution of Benin provides that '[t]reaties or agreements lawfully ratified shall have, upon their publication, an authority superior to that of laws, without prejudice for each agreement or treaty in its application by the other party'. The Preamble to the Constitution of Benin declares that principles of international law as contained in UN Charter, the Universal Declaration and the African Charter 'make up an integral part of this present Constitution and of Benin law and have a value superior to the internal law'.

An alternative approach to role of international human rights law in the domestic legal system is presented below.

6.3 Self-executing provisions

'Self-executing' provisions are rules of international law which are considered to apply *directly* in domestic legal systems or, stated differently, they are treaty provisions or a treaty which of their own force constitute rules of municipal law which municipal courts must apply in deciding cases involving the rights of

825 Maluwa 50.
826 As above, 50 – 51.
827 Maluwa (n 817 above) 51.
828 My emphasis.
829 Maluwa 52.

individuals.[830] Self-executing treaties do not require legislation to make them private rights of action, while non-self-executing treaty provisions do require such legislation.

The South African Constitution makes provision for the self-execution of treaty provisions in section 231(4), which reads (my emphasis):

> Any international agreement becomes law in the Republic when it has been enacted into law by national legislation; but a *self-executing provision* of an agreement that *has been approved by Parliament* is law in the Republic *unless it is inconsistent with the Constitution or an Act of Parliament.*

There are three important aspects to self-executing provisions in this provision: First, Parliament has to have approved the agreement containing the self-executing provision. Michéle Olivier argues correctly that this proviso does not imply that parliament must recognise the self-executing status of a treaty provision, but rather that the agreement, itself, had been approved.[831] In other words, in the case of self-executing provisions there is no necessity for legislative incorporation of the treaty.[832] Second, the self-executing provision must not be inconsistent with an act of Parliament or the Constitution. Third, it is for the national courts to decide whether a particular treaty provision is self-executing or not.

Self-executing treaties are recognisable in the following ways: the intention of the drafters of the treaty;[833] the intention of the contracting parties to the treaty;[834] the precision of detail in the language employed in the treaty (the broad and general nature of a provision may prevent it from being regarded as self-executing);[835] the subject matter of a treaty (for example, treaty provisions establishing negative obligations or prohibitions are regarded generally as self-executing as no measure to implement them is required);[836] and if the provision benefits individuals (a provision which creates private rights is assumed *prima facie* to be directly applicable).[837]

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830 Olivier (2002) 27 *SA Ybk Intl L* 99.
831 In terms of sec 231(2); Olivier 115.
832 As above.
833 See Craven (1993) 40 *Netherlands Intl L Rev* 372 384; Olivier 104.
834 See Olivier 105.
835 Olivier (n 830 above) 106.
836 Olivier 107.
837 Treaties such as the ICESR, generally, are usually worded in such a way that they lay down obligations on states and their legislators rather than addressing the position of individuals. The ICCPR, instead, refers directly to the rights of individuals (see Olivier 107). This approach is criticised by Craven (n 830 above) 394.

Olivier is of the opinion states adopt policies favouring direct application for a number of theoretical and practical reasons.[838] Since all law belongs to one system in a monist system, direct application enhances the effectiveness of international law as it decreases the possibility that states will refuse or neglect to transform treaties into domestic law. It increases the effectiveness of a treaty in that individuals may rely on such a treaty in domestic legal institutions and it gives an assurance that all parties will honour their obligations in terms of the treaty.[839]

Dualists, however, have arguments against self-execution. In their view national and international law are separate systems, so there is no *a priori* reason why an international instrument should automatically form part of a national system. Parliamentary transformation of a treaty into domestic law serves as a democratic check and compensates for the lack of direct participation by parliament in the treaty-making process.[840] Further, it may be necessary to change or 'tailor' the treaty to match domestic circumstances. For example, legislators may wish to limit direct application to specific provisions in the treaty. Olivier holds the view that in domestic law the interpretation of a treaty by an international body is definitive and, therefore, is binding on domestic courts.[841]

Self-execution appears to offer an effective method of incorporating treaty obligations into national law. However, it is not guaranteed that the interpretation adopted by the domestic court coincides with either that of the treaty supervisory body or with those of courts in other states. Usually, national courts are in the best position to apply provisions of a treaty in a domestic context, and provide realistic and suitable interpretations of the norms in the treaties.[842]

Self-executing treaties are discussed in the South African context in paragraph 6.5 below.[843]

6.4 Implementation measures

In a period of 50 years, international human rights law has progressed through three stages, namely, promotion, protection and prevention.[844]

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838 Olivier 108.
839 As above.
840 As above, 109.
841 Olivier 109.
842 Olivier 112. Not all scholars agree with Olivier. Dugard, for example, holds that the term 'self-executing' is 'essentially meaningless'. See Dugard (n 643 above) 56 – 58.
843 Also see para 4.3.1 of ch 5 below.

From the discussion on the UN system above, it is clear that the UN Charter requires state parties only to 'promote' human rights.[845] The subjects of international law were independent states rather than individuals, groups or peoples, and interference in state sovereignty was not even hinted at, and the international protection of human rights was a rarity.[846]

In the decades which followed the international community took steps to go beyond promotion, drafting human rights treaties which would constitute legally binding obligations under international law.[847] The universal system and the regional systems for the protection of human rights are the products of this endeavour.

The prevention of human rights violations relies on strategies such as objective fact-finding missions, early warning systems that are effectively implemented, preventive visits, educational activities, publicity and campaigns like Amnesty International's 'mobilisation of shame'.[848] Nowak adds effective enforcement and implementation measures to the list.[849]

Nowak rightly observes, the terms 'human rights protection or implementation' apply only in instances where international bodies (such as political bodies of international organisations or international courts) are granted the right to monitor compliance with international human rights agreements.[850] Without the monitoring or 'policing' function of these bodies, state compliance depends on the goodwill of individual governments.

Latterly, a system of mechanisms for the implementation of international human rights has developed. Some are more successful than others.

Measures exist for the implementation or protection of international human rights; namely, the state reporting procedure, the inter-state reporting procedure, the individual complaints procedure, the inquiry procedure and on-site visits. Each is discussed below.

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844 Nowak (n 23 above) 27. Nowak refers to the three stages as the 'three P's'.
845 Art 1(3) of the UN Charter, for example, merely speaks of the 'promotion' of human rights.
846 Nowak 27.
847 As above.
848 Nowak 29 – 30.
849 Nowak 29.
850 Nowak 28.

State reporting is relied upon by organisations such as the UN, the AU and the Council of Europe and is usually mandatory for states parties.[851] State reporting is considered less effective than other measures of treaty monitoring.[852] It aims to attain a 'comprehensive overview' of the state party's measures, at a domestic level, to implement its obligations under international human rights law.[853] State reports are usually prepared on a biannual basis by the individual state, and reflect the human rights situation in that state, reporting on difficulties that have been observed, as well as legislative or other measures taken to improve the situation.

Nowak argues that the effectiveness of state reporting requires governments to take their obligations under international law seriously, and draft honest, objective and serious state reports, engaging in constructive dialogue during the examination stage.[854]

The inter-state complaints procedure requires states parties to make a complaint against other states parties about human rights violations. This procedure is used at both the universal and the regional level. The procedure is optional or mandatory.[855]

Generally, very few inter-state complaints have been lodged. States are hesitant to criticise their neighbours, fearing that it will be seen as an act of hostility or that the state accused will retaliate. In any case, states are reluctant to criticise other states if they have no interest in the outcome of the complaint.[856]

The individual complaints procedure is designed to provide relief to victims of specific human rights violations.[857] The procedure is either mandatory or optional.[858] Sometimes it is relegated to an optional protocol, which allows states parties to opt out.[859]

The individual complaints procedure investigates a 'concrete individual human rights violation' or a situation in which there are 'gross and systematic human rights violations'.[860] Further hurdles are admissibility criteria, such as the exhaustion of

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851 Nowak 265.
852 As above.
853 Nowak 266.
854 Nowak 266.
855 Eg mandatory for, amongst others, the European Charter, the African Charter and CERD, but optional for ICCPR and CAT.
856 As above.
857 Nowak 266 – 267.
858 Eg mandatory for, amongst others, the European Charter and the UN 1503 procedure but optional for CERD and CAT.
859 Eg Optional Protocol to ICCPR.
860 Nowak 267.

domestic remedies, requirements relating to standing, and others.[861] The outcome of the procedure may be legally binding or have non-legally binding effects. Examples of outcomes are: a report from a Special Rapporteur or a commission of experts, a decision of a quasi-judicial treaty monitoring body, a resolution of a political body or a binding judgment of a human rights court. Mediation is frequently called upon during the process of investigation in order to reach a friendly resolution.[862] Procedures for collective complaints, the *actio polularis*, as well as inquiry procedures and fact-finding missions, are all part of the individual complaints procedure.[863]

Presently, the individual complaints procedure under Protocol 11 of the European Charter is the most effective and accessible in dealing with individual complaints.[864] The individual complaints procedure may, amongst other remedies, result in relief to the victim, interpretation of the normative content of the provision, changes in national law and practice and may have a preventive effect on the national level.[865]

The inquiry procedure, like the individual complaints procedure, is the result of evidence of concrete instances of human rights violations, but is not dependent on actual complaints of human rights violations.[866] It functions as *ex officio proceedings*, usually held *in camera*.[867] The fact that the proceedings for this mechanism usually are confidential is its greatest weakness.[868] The proceedings, also, are often long and complicated.[869] The procedure is optional or mandatory. Visits to the sites where the violations are reported to have occurred depend on permission being granted by the state party.[870]

Other forms of human rights implementation exist, such as Commissions of experts, *ad hoc* human rights tribunals that hear cases of violations, other methods of fact-finding by missions of experts and Rapporteurs, and human rights monitoring by NGOs who report cases of violations to the various international bodies.[871]

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861 See Nowak 267.
862 Nowak 267.
863 As above.
864 See para 3.2.2 above.
865 As above.
866 Nowak 268.
867 As above.
868 As above.
869 As above.
870 Nowak 268.
871 Nowak 269.

Unlike the individual complaints procedure that deals with violations of human rights that have already taken place, the system of preventive visits attempts to forestall human rights violations.[872] International bodies carry out unexpected visits to sites, especially to sites where prisoners are held, where there is evidence of possible gross human rights violations such as torture and the like.[873] It is hoped that the anticipation of these visits will have a restraining effect on the perpetrators of human rights violations.[874]

The implementation measures outlined above can be considered effective only if the international body's or court's recommendation or decision on the human rights violation is enforced against the state concerned.[875] Non-compliance with a recommendation or decision is censored in a variety of ways; by exerting political or other pressure, by expelling countries from international organisations, suspending development or financial co-operation, and imposing economic or other sanctions against that country.[876] If these measures fail, not much remains to be done at the international level. David Thomasma comments: '[s]tigmatizing violators of human rights with international sanctions and public outcries, although necessary, does not seem to be enough to ensure the protection of human rights'.[877]

International implementation of human rights cannot be as effective as the domestic implementation of human rights. If a bill of rights is incorporated in a domestic constitution within a system of constitutional supremacy, it is immediately justiciable.[878]

The implementation of human rights law, which for long had been seen as a matter that fell within the domestic jurisdiction of sovereign states, is now part of international law. Human rights apply universally across state borders, and can be protected and implemented through the various mechanisms that were established under the international and regional systems.

Increasingly, human rights have become the shared responsibility of individual states and the international community. Not only do non-justiciable human rights declarations exist but binding human rights treaties as well. States

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872 Nowak 268.
873 Nowak 268 – 269.
874 Nowak 267 – 268.
875 Nowak 28.
876 Nowak 29.
877 Thomasma (1997) 25 *J L, Med & Ethics* 296.
878 See para 5.2 ch 5 below.

are monitored and forced to account for the measures undertaken to enforce human rights within their borders. Under certain treaties individuals may compel state parties to answer to the violations of human rights. This development constitutes a break with previous concepts of state sovereignty and non-interference of the international community in the domestic affairs of a state.

6.5 International human rights in the South African system

6.5.1 A constitutional approach

The development of a notion of justiciable human rights or human rights as legal rights is closely linked to the development of the concept of constitutionalism.[879] Constitutionalism 'is a movement born out of the spirit of enlightenment to ensure that the state's main tasks and structures were written down in a constitution, which as the highest legal standard within the state, was considered binding and lasting'.[880] Constitutionalism, in other words, is the notion that government should 'derive its powers from a written constitution and that its powers should be limited to those set out in the constitution'.[881]

Constitutions usually consist of two distinct parts. The first is formal; describing aspects such as the functioning of the organs of the state, the separation of powers, procedures for the appointment of office bearers, and so on.[882] The second is the material part which lays down the values, aims and objectives professed by the state, as well as fundamental human rights if these are included in the constitution.[883] Bills of rights, therefore, are a representation of the values and aims a particular state wants to pursue.[884]

As government derives its power from a constitution; a constitution serves to limit the power of government. This is done in two ways. First, a constitution imposes limitations on power that are structural or procedural.[885] Government

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879 Up until after World War II, human rights were rights contained in national constitutions rather than international human rights instruments.

880 Nowak 15.

881 de Waal *et al* (2000) 7. See generally, Udombana 'Interpreting rights globally: Courts and constitutional rights in emerging democracies' (2005) 5 *African Human Rights LJ* 47.

882 Nowak (n 23 above) 15.

883 Nowak 15. Initially it was thought that the state merely had to respect human rights through non-interference. Presently, with the acceptance of theories related to the interdependence and indivisibility of human rights, it is accepted that these are positive obligations upon the state.

884 Nowak 17.

885 de Waal *et al* (n 881 above) 7.

institutions may exercise constitutionally prescribed powers, in a prescribed way.[886] Second, through the operation of a bill of rights, substantive limitations are imposed as government cannot exercise its power in such a way that it will violate the human rights of the inhabitants of the country.[887]

Under international human rights law, states have the obligation to respect, fulfil and protect human rights.[888] States respect human rights through refraining from intervention, provided their intervention is not permissible under any reservation clauses. Unjustified interventions are considered violations of human rights.[889] South Africa is a party to the Charter of the United Nations and, therefore, is bound to respect human rights.[890]

Nowak explains the effect of the out-sourcing of state assets upon the protection of human rights. As current trends encourage the state to privatise or outsource assets, such as health care, the state's duty with respect to health care consequently is diminished,[891] but its obligation to protect the right to health care has increased proportionately as the extensive transfer of state responsibility may have the violation of rights as a consequence.[892]

The obligation to fulfil human rights is the state's obligation to take legislative, administrative, judicial and other measures (such as resource allocation) that are necessary to ensure that the rights are implemented to the greatest extent possible.[893] Here attention should also be given to prevention of human rights violations – legislation and other measures should be in place to prohibit actions which could interfere with the fulfilment of human rights. In South Africa, equality legislation is an example of such an action by the state to fulfil and protect human rights.[894]

The obligation to protect human rights requires state action in that it requires the state to avoid human rights violations by private persons.[895] The extent to which the state has to protect private persons, however, is still unclear.[896]

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886 As above.
887 As above. Other principles which support constitutionalism are constitutional supremacy, justiciability and entrenchment
888 Nowak 49. Dugard argues that the observation of human rights is an international legal norm (see Dugard in Chaskalson *et al* (1996) 13 – 17.
889 Nowak 49.
890 See Dugard in Chaskalson *et al* 13 – 18.
891 Nowak 49.
892 Nowak 49.
893 Nowak 49.
894 Act 4 of 2000.
895 As above.

Because, under international law, individuals are the bearers of rights and states are the bearers of duties, private persons are generally not obliged by international agreements to act or refrain from acting.[897] The exception is in terms of international criminal law – persons who commit gross and systematic human rights violations, as state or as private persons, are responsible for these actions.[898] Nevertheless, the classical procedures used by international human rights law to protect human rights are directed at states (such as, state reporting, individual complaints procedure).[899] Private individuals do not have the same accountability as states that have to show what has been done to offer protection against human rights violations.[900]

Furthermore, human rights that are codified in international treaties are to be protected first and foremost by the relevant national legal protection institutions. International courts and monitoring bodies are appealed to only as a last resort in the event that the national legal process is unsuccessful or the treaties are interpreted in conflicting ways.[901] Many treaties require that domestic remedies be exhausted before an appeal may be made to an international body.

As mentioned above,[902] human rights were first incorporated into national constitutions, and national legal systems were responsible for their implementation and enforcement. The constitutions of countries such as the United States of America contained justiciable bills of rights long before human rights became part of international law,[903] and before their implementation became a matter for international law.

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896 As above. Nowak argues that states usually take measures to protect the rights of its citizens. In the case of domestic violence legislation, the state is taking legislative measures to protect the rights of its citizens, and to ensure that a violation does not happen. Also, historically, the aim of human rights protection was protection against private abuses – such as freedom of religion is against the monopoly of a universal church. Therefore, at national level, such human rights violations are always enforceable against private persons and state bodies.
An example in international law where the same situation exists is in international criminal law. Art 3 of four Geneva Conventions of 1949 and the 2nd additional protocol of 1977 are binding also on non-state combatants (Nowak 53).

897 Nowak 50.

898 As above.

899 As above.

900 Nowak 53. Such as a state must have sufficient penal provisions etc to ensure the citizen's right to personal security – else states fail to fulfil the treaty obligation to respect or protect.

901 Nowak 38.

902 Para 2.3.

903 Nowak 38.

The international human rights system not only coexists with the national system, but the national system is usually the first level of defence against human rights abuses. In states in which a national system for the protection of human rights is in place, it is often contained in a national constitution; the victim of abuse first turns to the national system, and then to the international system for human rights protection.

In South Africa, a national system of human rights protection exists within the Constitution.[904] In the following paragraphs, the relationship between international and national human rights law is explored with specific reference to sections 39(1)(b), 231, 232 and 233 of the South African Constitution.

It is important to remember that until 1994 international human rights instruments played a minor role in South African jurisprudence. Dugard indicates that South Africa was party to the Charter of the United Nations alone, and that was not incorporated into national or municipal law.[905] South Africa was not a party to other human rights conventions, which, therefore, could not be used as a guide to statutory interpretation.[906]

The promulgation of the 1993 Constitution introduced a dramatic change. Dugard comments on this development.[907]

> As a result of the new Constitution it has now become common place for the Constitutional Court and other courts to invoke human rights norms and decisions by international human rights tribunals and supervisory bodies to interpret the Bill of Rights and to set aside laws and administrative practices that violate human rights.

The following paragraphs explore the interaction between the international human rights system and the South African national system for the protection of human rights, including the implementation of international human rights obligations within the South African system.

a) Section 39(1)(b)

Section 39(1) requires an interpretation of the Bill of Rights which promotes the values which underlie an open and democratic society based on human dignity, equality and freedom. Of particular relevance to the present thesis is subsection 39(1)(b) which demands that, when interpreting the Bill of Rights, a court, and

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904 Constitution of the Republic of South Africa 1996.

905 Dugard 263. For a list of international human rights instruments to which South Africa is a party, see para 5.3 below.

906 As above.

907 Dugard 265.

tribunal or forum 'must consider international law'. This section of the Constitution compels the use of international law as an interpretive tool when interpreting the Bill of Rights. Guidance should thus be sought from international human rights declarations, treaties, conventions and covenants.

Whether these treaties have been signed or ratified by South Africa is not significant as no qualification to that effect is included in section 39(1). In this regard, the Constitutional Court stated the following in *S v Makwanyane*[908] about section 35(1) of the Interim Constitution,[909] the section equivalent to section 39(1):[910]

> In the context of section 35(1), public international law would include non-binding as well as binding law. They may both be used under the section as tools of interpretation. International agreements and customary international law accordingly provide a framework within which chapter 3 can be evaluated and understood, and for that purpose, decisions of tribunals dealing with comparable instruments, such as the United Nations Committee on Human Rights, the Inter-American Commission on Human Rights, the Inter-American Court on Human Rights, the European Commission on Human Rights, the European Court of Human Rights and, in appropriate cases, reports of specialised agencies such as the International Labour Organisation, may provide guidance as to the correct interpretation of particular provisions of chapter 3.

Apparently a wide interpretation is to be given to the term *public international law* as it was used in the Interim Constitution,[911] and includes international human rights treaties, declarations, agreements and decisions of international bodies such as commissions and courts under the universal and the different regional systems, as well as the decisions of so-called 'specialised agencies' such as the International Labour Organisation.[912] In *Makwanyane* the Constitutional Court referred to a wide

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908 *S v Makwanyane and Another* 1995 (3) SA 391 (CC).

909 Act 200 of 1993.

910 Paras 36 - 37.

911 The Final Constitution uses the term 'international law', which is a wider term than public international law as it would encompass private international law as well. There is uncertainty about what exactly qualifies as international law. Does international law encompass all forms of international law such as *ius cogens* and customary international law, or only public international law?

912 In this regard, the Court refers to Dugard in fn 36 of its judgment. According to Dugard, a court must in terms of s 39(1) consider not only those treaties and conventions to which South Africa is a party to, but also:
(a) international conventions, whether general or particular, establishing rules expressly recognised by the contesting states;
(b) international custom, as evidence of a general practice accepted as law;
(c) the general principles of law recognised by civilised nations;
(d) judicial decisions and the teaching of the most highly qualified publicists of the various nations, as subsidiary means for the determination of rules of law.
This definition is taken from the definition of international law given in art 38(1) of the Statute of the International Court of Justice.

range of sources of international law, such as the International Covenant on Civil and Political Rights, the European Convention on Human Rights, the American Convention on Human Rights and the African Charter on Human and Peoples' Rights, as well as the writings of well-known and qualified authors in the field.[913]

It is important to note that section 39(1) should be used as an interpretive tool and in determining the scope of the rights in the Bill of Rights, and not for proving that they exist.[914]

In *Government of the Republic of South Africa and Others v Grootboom and Others*[915] the Court held that the relevant international law may act as a 'guide to interpretation but the weight to be attached to any particular principle or rule of international law will vary'.[916] The Court stated that, where the relevant principle of law binds South Africa, it may be directly applicable.[917]

The statement by the Court appears to distinguish between two different aspects or roles of international law in relation to the South African Constitution and the Bill of Rights: first, as an interpretive tool in accordance with section 39(1), and second, as a binding international agreement in terms of section 231 and 232 of the Constitution, in which case 'it will be directly applicable'.

Another aspect of section 39(1)(b) needs to be mentioned. The section requires a court, tribunal or forum to *consider* international law; it does not provide that a court, tribunal or forum will be *bound by* international law, but merely that it should consider such law when interpreting the rights in the Bill of Rights. In this regard, the Court remarks as follows in *Dawood and Another v Minister of Home Affairs and Others; Shalabi and Another v Minister of Home Affairs and Others; Thomas and Another v Minister of Home Affairs and Others*:[918]

> [section 39(1) of the Constitution] provides that a court, when interpreting the Bill of Rights, '(b) must consider international law; and (c) may consider foreign law'. As pointed out by Chaskalson P in *S v Makwanyane and Another* at para [39] 'in dealing

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See generally Dugard in Chaskalson *et al* 1 (n 888 above) 13 – 17 and Dugard (1994) 101 *SA J Human Rights* 208.

913 Dugard (n 643 above) 206 observes that recourse to international law under s 39(1)(b) may be detrimental to the rights of the individual. He points out that in *Prince v President of the Law Society, Cape of Good Hope* 1998 (8) BCLR 976 984 – 5 and 988 – 989, the court found that international norms on religious freedom were outweighed by South Africa's international obligations to suppress drug abuse.

914 de Waal *et al* (n 881 above) 130.

915 2001 (1) SA 46 (CC).

916 Para 57.

917 Para 57.

918 2000 (1) SA 997 (C) 1035D.

> with comparative law we must bear in mind that we are required to construe the South African Constitution, and not an international instrument or the constitution of some foreign country, and that this has to be done with due regard to our legal system, our history and our circumstances, and the structure and language of our own Constitution'.

Significantly, the Court acknowledges it can derive *assistance* from public international law and foreign case law, but is not bound to follow them: [919]

> It must, however, also be borne in mind that the lawmakers of the Constitution should not lightly be presumed to authorise any law which might constitute a breach of the obligations of the state in terms of international law.

A court has to take into account 'the history and our circumstances, and the structure and language of our own Constitution' when applying international law to the interpretation of the Bill of Rights. In the words of Kriegler J in *Sanderson v Attorney-General, Eastern Cape*:[920]

> In this context I wish to repeat a word of warning I have expressed in the past. Comparative research is generally valuable ... Nevertheless the use of foreign precedent requires circumspection and acknowledgement that transplants require careful management. Thus for example, one should not resort to the *Barker* test or *Morin* approach without recognising that our society and our criminal justice system differ from those of North America.

b) Section 231

Unlike section 39(1), which gives guidance on the interpretation of the rights in the Bill of Rights, section 231 deals with the negotiation and signing of international agreements,[921] the steps to be taken before such an agreement is binding upon the Republic,[922] and the binding nature of international agreements that were entered into before the Constitution came into effect.[923]

According to section 231(1), all international agreements should be negotiated and signed by the national executive. The conclusion of international agreements is thus an executive prerogative.[924] The legislature has no part in the process of concluding international agreements; their powers are limited to transforming international agreements into national or municipal law.[925]

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919 Para 1035E – 1036F.
920 1996 3 SACLR I (SE) para 26.
921 Art 231(1).
922 Arts 231(2) – 231(4).
923 Art 231(5).
924 Dugard (n 643 above) 49.
925 See below.

The term used in section 231(1) is 'international agreement' instead of 'treaty'. Dugard observes that the term 'international agreement' is not a wider term than treaty, but, more or less, is synonymous with the term 'treaty'.[926]

Section 231(2) states that international agreements bind the Republic only after they have been approved by resolution[927] in both the National Assembly and the National Council of Provinces, unless they are of the type of agreement referred to in subsection (3). International agreements that require ratification, thus require an act in the form of a resolution by the legislature to transform them into national or municipal law.[928]

According to section 231(3), an international agreement of a technical, administrative or executive nature, or an agreement which does not require either ratification or accession, entered into by the national executive, binds the Republic without approval by the National Assembly and the National Council of Provinces, but must be tabled in the Assembly and the Council within a reasonable time.

It is unclear exactly what is an agreement of a 'technical, administrative or executive nature'.[929] It could be argued that many agreements fall within this category, especially subsidiary agreements that give effect to, and provide for the implementation of principal agreements (such as the technical details and implementation, for example, of environmental agreements). Until this provision is given substance through interpretation by the South African courts, it will remain unclear exactly what is meant by its wording.[930] Olivier suggests that the approach

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926 Dugard 59.

927 'Resolution' refers to a number of actions used to make an international agreement part of national law. They are: an Act of Parliament; subordinate legislation made in terms of an Act of Parliament; and legislation that was in force when the Constitution took effect and that is administered by the national government (sec 239 Constitution of the Republic of South Africa 1996.

928 Dugard 56 - 57. This was the position even before the 1993 and 1996 Constitutions. The need for legislation to transform an international agreement into municipal law was explained by Steyn CJ in *Pan American World Airways Inc v South African Fire and Accident Insurance Co Ltd* 1965 (3) SA 150 (A):
'... that in this country the conclusion of a treaty, convention or agreement by the South African government with any other government is an executive and not a legislative act. As a general rule, the provisions of an international agreement so concluded, are not embodied in our law except by legislative process ... In the absence of any enactment giving ... relevant provisions the force of law, [it] cannot effect the rights of the subject' (para 161C-D).

929 See eg Botha (1997) 22 *SA Ybk Intl L* 95, where he comments on the confusing nature of these terms.

930 Dugard is of the opinion that the intention of the parties concluding the agreement will determine the nature of the agreement. He remarks that art 14 of the Vienna Convention on the Law of Treaties emphasises the intention of parties in deciding

to section 231(3) adopted by the state international law advisors, who interpret the terms used in the section to 'refer to agreements of a routine nature, flowing from the daily activities of government departments', may help the courts in determining the meaning of these terms.[931]

Another aspect of section 231(3) requires comment. An agreement entered into by the national executive which does not require either ratification or accession binds the Republic without approval by the National Assembly and the National Council of Provinces. Such a treaty would thus become binding upon signature.

Section 231(4) provides that any international agreement becomes law in the Republic when it is enacted into law by national legislation; on the other hand, a self-executing[932] provision of an agreement that has been approved by Parliament is law in the Republic unless it is inconsistent with the Constitution or an Act of Parliament.[933]

Section 231(5) makes it clear that international agreements that were in effect when the Constitution came into effect, will continue to bind the country. This subsection is significant for our discussion below;[934] a number of international human rights agreements were concluded before the Final Constitution came into effect, which will continue to be binding.

Section 231 of the Constitution was the subject of litigation in the case of *S v Harksen; Harksen v President of the Republic of South Africa and Others; Harksen v Wagner NO and Another.*[935] In this case, Harksen, in terms of the Extradition Act[936]

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whether a treaty requires ratification or not. This principle was also supported in *S v Eliasov* 1967 (4) SA 583 (A). See Dugard 56.

931 See Olivier (1997) 22 *SA Ybk Intl L* 63 64.

932 Dugard 58 remarks that the concept of a self-executing treaty is problematic, as it is never exactly clear when the provisions of a treaty are self-executing or not. (In the case of a self-executing treaty, existing legislation is considered enough for the Republic to comply with its obligations under that treaty without any further act by the legislature incorporating that treaty into South African law.) He is of the opinion that to decide which treaties are self-executing, the courts will have to decide each case on its own merits, and that courts will have to have due regard to the nature of the treaty, the precision of its language and the existing South African law on the subject.

933 Dugard distinguishes three main methods by which the legislature may transform treaties into municipal or national law. They are the embodiment of the provisions of a treaty in the text of an Act of Parliament; the treaty may be included as a schedule to a statute; and an enabling Act of Parliament may give the executive the power to bring a treaty into effect in municipal law by publishing a notice or proclamation in the *Government Gazette* (see Dugard 57 – 58).

934 See para 6.5.2 below.

935 2000 (1) SA 1185 (C).

936 Act 67 of 1962.

appealed against his extradition to Germany where he was wanted for fraud. The Court had to consider whether the President's consent to Harksen's extradition was constitutional, in the light of the fact that no extradition agreement existed between South Africa and Germany. It was argued that the President's consent to Harksen's extradition brought into existence an international agreement in contravention of section 321 of the Constitution. The court had to determine the meaning of the term 'international agreement' in terms of section 231, and whether the President's correspondence with the German government constituted an international agreement in terms of the Constitution.

The Court held that, in order to establish whether an international agreement had been established, it had to consider the relevant documentation and correspondence to find out whether the parties had intended to conclude an internationally binding agreement with reciprocal rights and duties.[937]

The Court examined the definition of a treaty in the Vienna Convention,[938] and held that there could be no agreement without the requisite intention or consensus between the parties.[939] The Court further held that it is this intention and consensus which separates formal international agreements from mere informal arrangements between parties. The Court thus held that no international agreement had been concluded between the parties.

In the light of this case, the phrase 'international agreements' as used in section 231 must be given a very narrow interpretation, to mean formal and legally binding international agreements only. Section 231 would not include informal international arrangements and agreements and international law as contemplated in section 233.[940]

The distinction between informal international arrangements and formal agreements is potentially of great importance when considering that most

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937 1200 paras D – E.

938 The Vienna Convention on the Law of Treaties 1969 defines a treaty as:
'An international agreement concluded between states in written form and governed by international law, whether embodied in a single instrument or in two or more related instruments and whatever its particular designation'.

939 1201 paras A – B.

940 See Olivier (n 931 above) 63 who argues: 'the term 'international agreement' as it appears in section 231 is used in the narrow sense of the word to refer only to legally binding documents. Informal or legally non-binding international agreements fall outside the ambit of section 231, although they can, strictly speaking, also be regarded as agreements of an international nature' (on 75).

arrangements for international collaborative clinical research could be classed as merely informal arrangements.

To sum up: international law, other than customary international law,[941] is not law in the Republic unless it meets the requirements of section 231, that is, that it has been approved by resolution in the National Assembly and the National Council of Provinces; or, if it is an international agreement of a technical, administrative or executive nature, it meets the requirements in section 231(3).

c) Section 232

Section 232 of the Constitution deals with customary international law.[942] It provides that customary international law 'is law in the Republic unless it is inconsistent with the Constitution or an Act of Parliament'. Even if South Africa has not ratified an international human rights treaty (in which case that treaty would be binding as international law in terms of section 231), its provisions could be considered part of customary international law and binding in terms of section 232.

As stated, customary international law is national law of South Africa, unless it is inconsistent with the Constitution or an Act of Parliament. Unlike other international law, customary international law is national law, is not subject to subordinate legislation,[943] and is not simply a tool for interpreting the Bill of Rights in terms of section 39(1)(b). It implies that, when interpreting a right in the Bill of Rights, according to section 39(1)(b), a court, tribunal or forum must apply customary international law as it is the law of the country.

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941 See para 4.4 above.

942 'Customary international law' is a narrower term than 'international law' and can be considered a component of international law. Customary international law, however, is not easily defined. It is formed by a general state practice that is accepted as law (as per the definition given in section 38 of the Statute of the International Court of Justice). For a custom or rule of law to qualify as international customary law, there must be a wide and uniform practice of states in the belief that the practice is binding upon them and legally required. The International Court of Justice, for example, requires sufficient state practice and *opinio juris* before it accepts that a certain rule is a rule of customary international law (in this regard, see O'Shea *International law and organization: A practical analysis* 20 – 23). Many of the rights contained in the Universal Declaration of Human Rights, for example, may be considered part of international customary law, as well as humanitarian conventions, such as the Geneva Conventions. A rule of international law may become customary international law if enough time has elapsed in which the legal rule is considered as binding by states, and if states generally consider the rule as binding upon them. The distinction between international law generally, and customary international law, specifically, does not seem very clear-cut. See Dugard 24 – 32.

943 Dugard 52.

It is important to note the proviso contained in section 232. Customary international law is national law only if it does not conflict with the Constitution or an Act of Parliament.

Section 232, however, does not provide any guidance as to exactly which rules of customary international law apply in South Africa. Keightley argues that, because the 1996 Constitution no longer includes the words 'customary international law *binding on the Republic*', as contained in the Interim Constitution, all rules of customary international law are now part of South African national law, whether they are binding upon the Republic or not, and regardless of whether South Africa supports them.[944] Keightley uses the *dictim* in the *Makwanyane* case[945] to support his argument, forgetting, it seems, that *Makwanyane* referred only to the use of customary international law in the interpretation of the Constitution.

In contrast to Keightley, Botha argues that the words 'binding on the Republic' were not included in the 1996 Constitution merely because they were unnecessary and tautologous.[946] Botha's interpretation is more acceptable, as the proviso in section 232 that customary law should not conflict with an Act of Parliament or the Constitution suggests that rules of customary international law which are not supported by South Africa are not applicable to the country.

In order to decide exactly which rules of international customary law are binding on South Africa, and how they should be proved, is a matter for judicial precedent as no guidance is given in this regard in section 232.[947] Dugard argues that the omission of the word 'binding' in the 1996 Constitution lends support to the idea that customary law rules that are generally accepted - instead of those which are universally accepted - is sufficient for proof of the existence of customary international law.[948] He observes that this is the standard set by the International

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944 Keightley (1996) 12 *SA J Human Rights* 408. See also Kinney (2001) 34 *Indiana L Rev* 1457, where she argues that widespread ratification of UN and regional treaties recognising international human rights norms establishes an international customary law of human rights. Treaties, declarations and the like become evidence of a general state practice in which states take part because of their sense of legal obligation. She further argues that the International Convention on Economic, Social and Cultural Rights is customary international law due to its widespread acceptance in many countries around the world.

945 See n 782 above, '[i]n the context of section 35(1), public international law would include *non-binding* as well as *binding* law' (my emphasis).

946 Botha (1994) 9 *SA Public L* 255.

947 As above.

948 Dugard 54.

Court of Justice, and that there is no reason why South Africa should require proof of rules which are *universally* accepted.[949]

It is also important to note that, according to section 232, customary international law is law in South Africa, and that the courts have no discretion whether to apply it or not – they must apply customary international law as it is the law of the Republic.

d) Section 233

Section 233 deals with the application of international law when interpreting legislation. It provides that, 'when interpreting any legislation, every court must prefer any reasonable interpretation of the legislation that is consistent with international law over any alternative interpretation that is inconsistent with international law'. The common law presumption requiring a court to interpret legislation in compliance with international law is now made a constitutional provision.[950]

As the Constitution and the Bill of Rights were promulgated as legislation, their interpretation should be included in section 233.[951] If section 233 is read together with section 39(1)(b), when interpreting the Bill of Rights, a court must not only consider international law but it should also prefer an interpretation of the rights in the Bill of Rights that is consistent with international law over one which is not.

Again, the term 'international law' presents problems. Unlike section 39(1) where the courts have interpreted the term to include both binding and non-binding international law,[952] section 233 has not yet been given substance by the courts. However, in terms of the rules of statutory interpretation, the term 'international law' in section 233 should be interpreted in the same way as it was interpreted in section 39, unless clear indications to the contrary exist; in this case they do not. Given that the Constitutional Court in *Makwanyane* gave a wide interpretation to the term as used in the 1993 Constitution,[953] it follows that the same interpretation will be given

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949 As above.

950 Dugard 60. See also Devenish (1992) 212.

951 This is not the only view on the issue. Some writers hold that the Constitution and the Bill of Rights are not just 'any legislation' as used in s 233, and that, therefore, there is express provision for their interpretation in terms of s 39. According to this view, sec 233 refers only to legislation other than the Bill of Rights and the Constitution (see in this regard eg Dugard in Chaskalson *et al* 13 – 17).

952 See para 4.1 above.

953 n 908 above.

to the term as used in section 233, which means that 'international law' as used in section 233 includes both binding and non-binding international law.

Further, it should be noted that section 233, in its requirement to prefer any reasonable interpretation of the legislation that is consistent with international law, does not contain the same condition as the one contained in section 232 – that it should not be inconsistent with the Constitution or an Act of Parliament.

What will happen when a court interprets legislation in compliance with international law, but that interpretation is in conflict with an Act of Parliament or the Constitution? The second possibility, if the interpretation is in conflict with the Constitution, does not present a substantial problem: the Constitution, as the 'supreme law of the Republic',[954] will always be the preferred interpretation, making an interpretation in conflict with its provisions invalid.

In the case of the first possibility, an interpretation which is in keeping with international law but in conflict with an Act of Parliament, it should be noted that section 233 uses the phrase 'reasonable interpretation'. Although the courts have not yet interpreted section 233, it is expected that in the future an interpretation that is in conflict with an Act of Parliament will not be considered 'reasonable'. [955]

6.5.2 The status of international human rights instruments in South Africa

The mechanisms used by states to transform or translate international (human rights) law obligations into national law consist of a variety of possible actions. International treaties may be 'adopted', 'signed', 'accepted', 'approved', 'acceded to' and/or 'ratified' by states. Each of these terms has a different meaning.

The adoption of a treaty or agreement under international law refers to the formal or legal act by which the content or text of a treaty is accepted or established. For example, treaties or agreements are often established by a meeting or international conference of a (political) body which is held for the express purpose of setting up or agreeing on the content of such a treaty. Voting on the treaty or agreement usually completes this process.

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954 Art 2 Constitution of the Republic of South Africa 1996.

955 Also see *Azapo v President of the Republic of South Africa* 1996 (4) SA 671 (CC) para 26, which reads '[i]nternational law and the contents of international treaties to which South Africa might or might not be a party at any particular time are, in my view, relevant only to the interpretation of the Constitution itself, on the grounds that the lawmakers of the Constitution should not lightly be presumed to authorise any law which might constitute a breach of its obligations of the state in terms of international law'. See also Botha (n 946 above) 102.

The signing of a treaty or international agreement reflects a state's willingness to be bound by the provisions of the treaty. It does not mean that the state is automatically bound to the provisions of the treaty upon signature. Signature is often subject to ratification and merely indicates the state's agreement to proceed to the next step. Usually, the signing of the treaty, indicates a state's acknowledgment that it will refrain from actions which may defeat the objects of the treaty.

The acceptance or approval of a treaty or international agreement refers to the action by which a state expressly consents to be bound by the treaty and its obligations. It has the same legal effect as ratification, and is used in instances where the national constitution of a state does not require international agreements to be ratified before they have the force of law.

To accede to a treaty or international agreement refers to the act by which the state accepts an offer or opportunity to become a party to a treaty. The treaty by this act is binding upon the state in question. This act has the same effect as ratification.

Ratification refers to the act by which a state indicates that it wishes to be bound by the treaty or international agreement, and is carried out by enacting national law or by another act. In some systems,[956] a treaty is ratified when domestic law is enacted to give effect to the treaty.

Dependent on the character of the domestic or national constitutional system, and the specific provisions of the constitution or enacting legislation, the status international human rights law may have in relation to the constitution and other domestic law differs in the various domestic legal systems. In some systems international law is elevated above domestic law and even the domestic constitution; in others international law is superior in status to ordinary domestic law, but not to the constitution. In this case international law may have an equal status with the domestic or national constitution. Yet others view international law as inferior to all domestic law – whether ordinary law or constitutional law. The latter situation seldom occurs because a state party to a treaty undertakes to hold itself bound to the provisions of that treaty; if international law is deemed inferior to national law, such an undertaking would be defeated.

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956 See below.

The present status of international human rights instruments in South Africa is set out below in schematic format.[957] Only human rights instruments of relevance to the present study are included.[958] Abbreviations are used, and in cases where human rights instruments have not been ratified by South Africa, the date of signature is indicated in the right-hand-side column.

Declaration / Treaty /Convention	**Ratification / accession by South Africa**	**Signature by South Africa[959]**
UN		
Universal Declaration of Human Rights		SA abstained.[960]
ICCPR	10 March 1999	
Optional Protocol I to ICCPR	28 November 2002	
Optional Protocol II to ICCPR	28 August 2002	
ICESCR		3 October 1994
CEDAW	14 January 1996	
CEDAW Optional Protocol	X	X
CRC	16 July 1995	
OTHER		
European Convention on Human Rights and Biomedicine	N/A[961]	N/A
AU		
African Charter on Human and Peoples' rights	9 July 1996	
African Charter on Rights and Welfare of the Child	7 January 2000	
African Women's Charter	17 December 2004	
African Court Protocol	3 July 2002	

6.6 Conclusion

South Africa's new democratic constitutional order, which requires courts to interpret all legislation,[962] and particularly the Bill of Rights,[963] to accord with international law, shows the importance international human rights holds in the South African legal order. From the analysis of the different roles of international law in the Constitution

957 Information on South Africa's ratification of these instruments obtained from the websites of the different treaty organisations.

958 These are the instruments referred to in para 4 above.

959 In cases where South Africa signed the treaty, but has not yet ratified it. In general, once having signed a treaty, that country should in good faith not do anything that would violate the provisions of that treaty.

960 South Africa abstained together with seven other countries. 48 votes were in favour of the Universal Declaration. However, should the Universal Declaration be accepted as part of customary international law, as is argued by many, its content is law in South Africa.

961 This Convention is not limited to members of the EU, but makes specific provision for states outside of the EU to sign and ratify it. South Africa has done neither and it appears that this instrument is relatively unknown in South Africa.

962 Sec 233 Constitution of the Republic of South Africa 1996; see above.

963 Sec 39(1)(b) Constitution of the Republic of South Africa 1996.

in the first part of this section, it is clear that international law can be used as an interpretive tool (in terms of section 39(1)(b) and section 233) and as a source of law (when it satisfies the requirements of sections 231 and 232 of the Constitution). In cases where a rule of customary international law is not in conflict with the Constitution or an Act of Parliament, the rule may be used as an interpretive tool in terms of section 39. In terms of section 232, international customary law is also to be applied as law in South Africa. In cases where the rule of international law is in conflict with the Constitution and an Act of Parliament, it may still be used as an interpretive tool.

From the table outlining the status of different international and regional human rights instruments in South Africa it is clear that South Africa has ratified the major international human rights treaties, and that, as international law, these treaties are the law of South Africa.

7 CONCLUSION

A major problem in relation to clinical research ethics is that it tends not to take account of the wide range of inequalities in a research setting.[964] Not only is there a gap in knowledge between the researcher and the research participant, but in Africa, where there is poverty, little attention is paid to the unequal distribution of power created by poverty and other social circumstances.[965] In their criticism of bioethics, Paul Farmer and Nicole Gastineu Campos comment:[966]

> The majority of such international biomedical research has inequality as its foundation, and ethical codes developed in affluent countries are quickly ditched as soon as affluent universities undertake research in poor countries. Then come a series of efforts to develop alternatives (read, less stringent) codes 'appropriate' to settings of destitution.

Their sentiments are echoed by dos Anjos:[967]

> First, to what level of quality can medical ethics aspire, if it ignores callous discrimination in medical practice against large populations of the innocent poor? Second, how effective can such theories be in addressing the critical issues of medical and clinical ethics if they are unable to contribute to the closing of the gap of socio-medical disparity?

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964 Farmer and Gastineau Campos (2004) 4 *Developing World Bioethics* 23.

965 Farmer and Gastineau Campos comment: 'It [the research enterprise] is also a fundamentally inegalitarian exercise in the sense that medicine and science are expanding rapidly, but in a social context of growing global inequality, which ensures that the fruits of medicine and science are not available to many who need them most' (on 25).

966 As above, 22.

967 Dos Anjos (1996) 21 *J Med and Philosophy* 629.

These statements are generalisations; there are countless instances of research initiatives in the developing world which take account of inequalities, as there are of researchers who rigorously follow clinical research ethical guidelines. There are, on the other hand, instances in which research undertaken in the developing world would never be performed in the developed world.[968] Marcia Angell comments:[969]

> The fact remains that many studies are done in the Third World that simply could not be done in the countries sponsoring the work. Clinical trials have become big business, with many of that same imperatives. To survive, it is necessary to get the work done as quickly as possible, with a minimum of obstacles.

Farmer and Gastineau Campos quote a Haitian woman who is dying of AIDS: 'We are good enough to study but not good enough to care for'.[970] If true, this statement would be a terrible indictment of the clinical research undertaken in the developing world. It represents the view of the research participant who feels that she has been let down by the research initiative, and has been exploited and discarded.

With regard to exploitation or the perception of exploitation, the chapter has explored justiciable human rights as an alternative means to protect participants in clinical research in Africa. The international system for human rights protection has been contrasted with the ethical guidelines that were examined in chapter 3.

The origin and nature of human rights were explored and a brief philosophical background to the development of the notion of human rights has been given. It was mentioned that the application of human rights to a field traditionally considered the ambit of clinical research ethics or bioethics is criticised by bioethicists. Some bioethicists consider human rights discourse incapable of accommodating the philosophical moral reasoning that is a necessary part of bioethics or clinical research ethics.[971]

Critics of bioethics, on the other hand, consider bioethics and clinical research ethics 'too philosophical'. Churchill asserts:[972]

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968 See para 4.2.2 of cha 3 above.

969 Angel (1997) 337 *New Eng J Med* 847.

970 Farmer and Gastineau Campos (n 964 above) 22. They comment that such critiques of research ethics are often dismissed as 'confused and ill-informed commentary' or as 'conspiracy theories' (Farmer and Gastineau Campos 20).

971 See para 2.6 above.

972 Churchill (1999) 128 *Daedalus* 255.

> Bioethical disputes – as measured by the debates in journals and conferences in the United States – often seem to be remote from the values of ordinary people and largely irrelevant to the decisions they encounter in health care.

Arguments which relate to the universality or relativity of human rights have been presented, and the position is argued that human rights, by definition, are universally applicable. If human beings have rights by virtue of their common humanity, it can only be because there are general moral standards that are universal in application.

In this chapter the protection international and regional human rights documents and instruments offer participants in clinical research has been critically examined and the development and impact of the United Nations' Charter-based and treaty-based systems and the three regional systems have been surveyed.

The investigation of human rights provisions which are relevant to the protection of clinical research participants in domestic constitutions of selected sub-Saharan African countries, shows that an adequate human rights framework exists for the protection of participants in HIV-related clinical research in Africa.

Specific human rights provisions, as contained in international human rights documents, are applied to a clinical research setting in order to determine the measure of protection they offer participants in clinical research in Africa. In this regard, the discussion demonstrates that these provisions are able adequately to accommodate many of the issues relevant to clinical research in Africa that were traditionally considered the exclusive jurisdiction of clinical research ethics, such as distributive justice, access to treatment and autonomy.

Finally, in this chapter international human rights are situated in a South African context. Sections 39(1), 231, 232 and 233 of the Constitution were sketched, and the status of specific international human rights instruments in South Africa charted. The chapter shows that the most important human rights treaties have been ratified by South Africa, and that human rights norms thus offer a justiciable framework for the protection of clinical trial participants in South Africa.

Chapter 4 aims to establish the foundation of the discussion in chapter 5 below, which deals specifically with informed consent in HIV vaccine efficacy trials in South Africa. Chapter 5 investigates the effectiveness of ethical guidelines and human rights standards for the protection of participants in these trials.

CHAPTER 5

INFORMED CONSENT IN PREVENTIVE HIV VACCINE EFFICACY TRIALS IN SOUTH AFRICA

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6 Conclusion

1 INTRODUCTION

Informed consent is a relatively modern concept. It is only after World War II that the notion of informed consent received formal recognition in the standards set for research in humans in the Nuremberg Code.[1] The primacy which the drafters of the Nuremberg Code accorded informed consent is shown in the fact that it is the first principle in the Code: an acknowledgement that the consent of human subjects is absolutely essential to ethical practice.[2]

Informed consent is a primary precondition of legal and ethical clinical research[3] and is regarded as the 'cardinal principle for judging the propriety of

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1 The Nuremberg Code was written in 1946 as the final part of the judgment in the Nuremberg trials. It is the first comprehensive set of guidelines on how to conduct ethical research on humans. See para 3.3.1 of ch 3 above. Also see Pross 'Nazi doctors, German medicine, and historical truth' in Annas and Grodin (eds)(1992) 32; Taylor 'Opening statement of the prosecution December 9, 1946' in Annas and Grodin 67 – 93; Grodin 'Historical origins of the Nuremberg Code' in Annas and Grodin 94 – 107.

2 Nuremberg Code, reprinted in Levine (1986) 425 – 426; Annas and Grodin 2.

3 For a discussion on how the Nuremberg trials led to the birth of both medical ethics and human rights, see ch 4 above.

research with human beings'.[4] The following paragraphs provide an introduction to the origins, application and components of the concept.

Informed consent is based on the ethical principle of respect for persons, or autonomy. This principle is central to Kantian philosophy (among others), and is expressed in the assertion that respect for persons flows from a recognition that all persons have unconditional worth.[5] Ronald Dworkin maintains that the 'value of autonomy' originates from:[6]

> the capacity it protects: the capacity to express one's own character - values, commitments, convictions and critical as well as experiential interests - in the life one leads. Recognizing an individual right of autonomy makes self-creation possible. It allows each of us to be responsible for shaping our lives according to our own coherent or incoherent - but in any case, distinctive - personality. It allows us to lead our own lives rather than be led along them, so that each of us can be, to the extent a scheme of rights can make this possible, what we have made of ourselves. We allow someone to choose death over radical amputation or a blood transfusion, if that is his informed wish, because we acknowledge his right to a life structured by his own values.

Beauchamp and Childress stress that respect for autonomy not only is an acknowledgement of another person's right to hold views and to make choices, but that their actions are based on *personal* values and beliefs, which, in themselves, are valuable.[7]

In a research environment such recognition means that a subject enters a study only after she has been provided with adequate information and has freely given her informed consent.[8] Respect for persons further implies that those unable to make autonomous decisions, such as the very young, the mentally ill and others, are protected.[9] The requirement of *freely* given informed consent is very important: explicitly, that no coercion is present. Barry defines informed consent in research as:[10]

> freedom of individual choice, with no element of coercion or constraint. It dictates further that a person should understand the subject matter of the research sufficiently to make an enlightened decision.

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4 Katz (1972) 532.
5 Beauchamp and Childress (2001) 63. See also Gillon (1994) 63 – 64 where he presents Kant's argument in favour of respecting autonomy.
6 Dworkin (1993) 225.
7 Beauchamp and Childress 63.
8 Smith (1999) 6.
9 Smith 6.
10 Barry (1988) 319 *N Engl J Med* 1083.

Originally, the context in which informed consent was viewed was paternalist. The researcher 'explained' to the research participant that which was regarded as necessary (by the researcher) for the participant to know.[11] For example, the 1964 revision of the Declaration of Helsinki reads:[12]

> *If at all possible*, consistent with patient *psychology*, the doctor should obtain the patient's freely given consent after the patient has been given a *full explanation*. [Note the use of 'consent', instead of 'informed consent'.]

The emphasis was thus on the consent - or agreement - of the participant, and not on the information given. The researcher (who often also is the treating physician) was regarded as being in a better position than the participant to take decisions regarding the health of the participant.

Gradually, the paternalistic model gave way in the face of the notion of the participant as a fully autonomous individual who makes decisions independently. In the South African case of *Castell v De Greef*,[13] the High Court held that the 'paramount consideration is that a person is entitled to make his own decisions about his life',[14] sustaining Van Oosten's view that:

> [w]hen it comes to a straight choice between patient autonomy and medical paternalism, there can be little doubt that the former is decidedly more in conformity with contemporary notions of and emphasis on human rights and individual freedoms and a modern professionalized and consumer-orientated society than the latter, which stems largely from a bygone era predominantly marked by presently-outmoded patriarchal attitudes. The fundamental principle of self-determination puts the decision to undergo or refuse a medical intervention squarely where it belongs, namely with the patient.

The focus has shifted from mere 'consent' to an emphasis on the quality of the information that is given to the participant and the participant's understanding of that information. The elements of informed consent are outlined by Beauchamp and Childress as competence, disclosure, understanding, voluntariness, and consent.[15]

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11 Also see Van Oosten (1989) 'The doctrine of informed consent in medical law' (unpublished LLD thesis, University of South Africa) 23.

12 Art II.1 Declaration of Helsinki (1964 rev). My emphasis.
The Declaration of Helsinki was later amended to provide for the review of research by a research ethics committee, introducing a review of the consent process (2000 rev).

13 1994 (4) SA 408 (C). This case may be regarded as the *locus classicus* on informed consent in South African law, as it 'imported and introduced the doctrine into South African law' (Carstens and Pearmain (2007) 891 – 892).

14 *Castell v De Greef* 425, quoted by the court from Van Oosten (n 11 above) 414.

15 Beauchamp and Childress (n 5 above) 79. It is not within the scope of this thesis to discuss each of these elements or requirements fully – emphasis will be placed on those elements which are likely to be problematic in the context of preventive HIV

Generally, informed consent is situated within an unequal power-relation.[16] The research participant, as a lay person, is unlikely to understand fully the scientific basis and the implications or the risks of a specific research endeavour.[17] In contrast, the researcher, a scientific and medical expert, is familiar with all the known risks and implications of the research. Therefore, there is a duty laid on the researcher to communicate these implications and risks to the research participant, in order to place her in a position where she can make an *informed* decision to take part in the research.[18]

Meier remarks that informed consent compensates for the inherent conflict of interest between the researcher and research participant.[19] Although the researcher may claim that she has the best interests of the subject in mind, especially in cases where she is also the treating physician, she may have professional and personal interests which conflict with the participant's interests, such as getting research underway, advancing science, and obtaining research grants and advancing her own professional career.[20]

Informed consent has become the pivotal point of balance between the interests of the individual and the interests of society: medical research is promoted (in the interest of the community) without violating the autonomy of the research participant (the interest of the individual).[21] It is not always easy to achieve this balance - there are instances where society's interest in research is very great. Cook *et al* claim that the HIV/AIDS epidemic is an example of such a situation: as the epidemic worsens, the community's interest in finding a cure or vaccine increases.[22] There are arguments which even propose that there may come a time when 'sacrifices' will have to be made in the interest of saving the community; the individual's autonomy will have to be sacrificed to the greater good of the community.[23]

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vaccine efficacy trials in South Africa. For a more general discussion of informed consent, see Beauchamp and Childress 79 – 104 and Van Oosten (2000) 63 *J Contemporary Roman Dutch L* 24.

16 Van Oosten (n 11 above) 23.

17 As above.

18 Van Oosten (n 15 above) 24.

19 Meier (2002) 20 *Berkeley J Intl L* 515 – 516.

20 Meier 516.

21 Cook *et al* (2003) 343; see Meier (n 19 above) 530, where he argues that this balance is not always achieved, especially not by certain of the revisions of the Declaration of Helsinki.

22 Meier (n 19 above) 575.

23 As above.

The search for an effective preventive vaccine for HIV is underway in South Africa. The occurrence of clinical trials that test the efficacy of HIV vaccines is likely to be most frequent in communities in which economic, medical, educational and other resources are limited, yet where there is a high risk of HIV infection.[24] Because of the stigma that attaches to HIV infection and the victimisation of people who are (or are perceived to be) HIV positive, the rights of the participants in the various HIV vaccine efficacy trials should be inviolable, as should be the rights of the communities in which the trials are conducted.

The focus of this chapter is specific: it is on informed consent in preventive HIV vaccine efficacy trials in South Africa. Therefore, the aim is threefold:

- It investigates the protection *ethical guidelines* on informed consent afford HIV vaccine trial participants, in order to attain a comprehensive understanding of the extent of that protection.
- It further investigates the protection *human rights instruments* on informed consent afford HIV vaccine trial participants, in order to attain a comprehensive understanding of the extent of that protection.
- Finally, it arrives at an understanding of the relationship between the different systems of protection afforded vaccine efficacy trial participants in South Africa, such as ethical guidelines, human rights, common law and legislation.

This chapter is central to the research question of the thesis. Its purpose is to explore whether, as a vehicle for the protection of HIV vaccine efficacy trial participants in South Africa, human rights afford more effective protection than is afforded by ethical guidelines, and it explores the nature of the relationship between the two systems.

The chapter is structured as follows: A background to clinical research establishing vaccine efficacy in South Africa is sketched. The scientific and epidemiological risks inherent in HIV vaccine trial participation are raised within the South African socio-economic and political contexts. The aim here is to establish whether potential preventive HIV vaccine trial participants are vulnerable to exploitation. Throughout, the focus is on the problem in obtaining informed consent to HIV vaccine trial participation in South Africa. Processes and actors in human

subject research in South Africa are presented, including the context of internationally collaborative research. The international and national ethical frameworks on informed consent, relevant to HIV vaccine efficacy trials in South Africa, are discussed, and then the attention turns to the international and national human rights frameworks dealing with informed consent. Finally, the focus falls specifically on issues of relevance to informed consent in HIV vaccine efficacy trials underway in South Africa, such as whether preventive HIV vaccine research in South Africa may be considered 'therapeutic' or 'non-therapeutic' research.

A number of articles published recently deal with adolescent preventive HIV vaccine trial participation in the light of new statistics[25] showing the increasing incidence of HIV infection in that age group.[26] The articles investigate the implications of the new National Health Act,[27] the Constitution and local and international ethical guidelines upon adolescents' vaccine trial participation and the notion of informed consent. By contrast, this chapter (and thesis) focuses on informed consent with respect to adults; the problems presented by adolescent participation are referred to only in passing.

Next the discussion turns to an analysis of the clinical research context in South Africa.

2 BACKGROUND TO CLINICAL RESEARCH INTO ESTABLISHING PREVENTIVE HIV VACCINE EFFICACY IN SOUTH AFRICA

2.1 Introduction

In many ways, South Africa provides an ideal setting for clinical trials into establishing HIV vaccine efficacy.[28] South Africa has a high rate of HIV infection, but, at the same time, it has a reasonably well-developed health infrastructure.

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24 See para 5.4.4 of ch 2, as well as paras 2.3.1 - 2.3.3 below.

25 See HSRC (2005) *South African national HIV prevalence, HIV incidence, behaviour and communication survey 2005* 37.

26 See eg Van Wyk (2005) 68 *J Contemporary Roman Dutch L* 35; Strode *et al* (2005) 101 *SA J Science* 225; Slack and Kruger (2005) 96 *SA Med J* 269; Jaspan *et al* (2005) 95 *SA Med J* 685; Slack *et al* (2005) 95 *SA Med J* 682. On the scientific justification for adolescent participation, see Jaspan *et al* (2005) 95 *SA Med J* 785.

27 Act 61 of 2003.

28 In this regard, Abdool Karim comments: 'South Africa is well-placed to play a valuable role in the global effort to find an HIV vaccine because the country has a well-established clinical trial infrastructure and capability in the midst of one of the world's worst HIV epidemics' (Abdool Karim (2002) 20 *CME* 588 588). See also Van Wyk

Eminent South African social and natural scientists work in the field of HIV and AIDS. Thus, South Africa offers HIV vaccine researchers a developing country's HIV epidemic, combined with a developed country's clinical and scientific expertise.[29]

In order to be a statistically valid demonstration of vaccine efficacy, Phase III preventive HIV vaccine efficacy trials logically can be undertaken only in communities where trial participants are at high risk[30] for HIV infection: participants in a HIV vaccine efficacy trial must be in a situation where they are exposed to HIV so that the candidate vaccine is able to demonstrate that it protects them against infection. Therefore, unless a high risk[31] of HIV infection exists in a community, vaccine efficacy cannot be demonstrated – either at all, or conclusively.

In sub-Saharan Africa, unlike countries in Eastern and Western Europe and Central Asia, HIV is transmitted in adults mainly through heterosexual intercourse.[32] In South Africa, the communities at greatest risk for HIV infection are those living in KwaZulu-Natal, Mpumalanga and the Free State.[33] In addition, people living in informal settlements in urban and rural areas are at higher risk for HIV infection.[34] One may deduce that, generally, people in informal settlements, in the three provinces mentioned above, are at greatest risk for HIV infection. Therefore, HIV vaccine efficacy trials are likely to be undertaken in these communities.

(2004) 67 *J Contemporary Roman Dutch L* 1 – 2: she holds the view that, generally, South Africa offers an ideal setting for medical research.

29 There are a number of likely sponsors of HIV vaccine trials in South Africa, such as the HIV Vaccine Trials Network, funded by the US National Institutes of Health; the South African AIDS Vaccine Initiative, which is sponsoring the development in South Africa of subtype C vaccine constructs (this is funded by the South African government and parastatal organisations such as the MRC); private pharmaceutical companies; and the International AIDS Vaccine Initiative, mostly funded by donor funds (see Abdool Karim (n 28 above) 588 and para 5.1 below).

30 'Risk' is used here as a statistical term and refers to 'the degree of increased risk associated with a specific behaviour or other factor and is measured as the relative risk or relative odds of infection comparing those with the factor and those without the factor' (Brookmeyer and Gail 1994) quoted in Barnett and Whiteside (2002) 80).

31 The term 'risk' should be used advisedly, because in public opinion the exact statistical nature of the term becomes blurred, 'and the term "risk" is no longer the observed characteristic which raises the odds of being infected, but rather the "risk" which "they" (those who possess an observed characteristic – sex worker, African, gay man – but may not be identified) pose to "us" the uninfected ... Specialised and precise epidemiological language has been translated into everyday and less precise language, becoming connected to ideas and emotions such as those of blame and stigma' (Barnett and Whiteside 80 – 81).

32 See para 3.3.3 of ch 2 above. In Western Europe the predominant mode of HIV transmission is MSM; in Eastern Europe and Central Asia it is IDU.

33 HSRC (n 25 above) 39.

34 As above, 40.

Communities at high risk for HIV infection, and therefore likely to participate in HIV vaccine efficacy trials are, for the most part, poor, unemployed, uneducated and powerless. Keymanthri Moodley remarks that:[35]

> [d]eveloping communities around the world are seen as excellent candidates for medical research, largely because of the unfortunate but typical characteristics of these communities – they tend to be over-populated, poor, malnourished, illiterate and desperate. Under these conditions, together with a fragile health-care infrastructure, diseases thrive, especially infectious diseases. In this scenario empirical scientific research also thrives – statistically significant data can be obtained form large-scale clinical trials on thousands of 'volunteers'.

2.2 Procedures, roles and responsibilities with regard to human subject research in South Africa

2.2.1 Introduction

In South Africa, clinical trials[36] on human subjects into establishing the efficacy or safety (or both) of new drugs[37] (such as vaccines), are governed by legislation,[38] and by international and local principles and guidelines for medical and research ethics.[39] The relevant local guidelines are: the Guidelines for Good Clinical Practice in the Conduct of Clinical Trials in Human Participants in South Africa: Clinical Trial Guidelines[40] (Good Practice guidelines), issued by the Department of Health; and the MRC Guidelines on Ethics for Medical Research (MRC guidelines),[41] issued in terms of section 17(1) and 17(2) of the Medical Research Council Act.[42]

The discussion below draws on the above in order to outline procedures, roles and responsibilities with regard to human subject research in South Africa. Although the discussion is more general than is presented in paragraph 2.3 below, in

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35 Moodley 'HIIV vaccine trial participation in South Africa: An ethical assessment' in Van Niekerk and Kopelman (eds) (2005) 161.

36 See ch 2 for a discussion of the definition and nature of clinical research and trials (paras 2.2 and 5.3.3), as well as the different types of clinical research (paras 5.2.1 – 5.2.2) and research methodology (para 5.2).

37 Or new indications of existing drugs.

38 eg Act 101 of 1965, Act 61 of 2003 and Act 2 of 2000.

39 As discussed in ch 3.

40 Issued in 2000 by the Department of Health; see para 3.3.3 of ch 3 above for a general discussion of the content of these guidelines.

41 4th (revised) edition published in 2004, previous editions are those of 1977, 1987, and 1993. See para 3.2.2 of ch 3 above for a general discussion of the content of these guidelines.

42 Act 58 of 1991. Section 17(1) of the Act determines that the MRC Board must regulate and control research on or experimentation upon humans. Section 17(2) empowers the Board to determine ethical directives to be followed in research and experimentation, and to take the necessary steps to enforce the ethical directives. The MRC guidelines govern all research carried out by or on behalf of the MRC, and research funded by the MRC, and approved by its ethics committee.

many instances clinical trials to establish HIV vaccine efficacy are referred to specifically.

Firstly, the South African ethical review procedure is detailed. Secondly, the various actors in clinical trial processes are introduced, and aspects of their responsibilities during a clinical trial outlined. (Note that stages and procedures during clinical trials are not described in this chapter; they are considered in detail in chapter 2.[43]) Finally, internationally collaborative research efforts (likely in HIV-vaccine efficacy research) are discussed.

2.2.2 Ethical review[44]

Clinical (and other) human subject research in South Africa is subject to review by an ethical review committee.[45] If a research protocol involves the development of a new drug or a new application for a licensed drug, it additionally needs to be reviewed by the ethical review committee of the Medicines Control Council (MCC).[46] Before any recruitment may begin in relation to a clinical trial, the principal investigator (PI) has to obtain a statement from the relevant ethics review committee or committees stating that the research or clinical trial has received ethical approval.[47]

Most research institutions[48] and universities in the country have research ethics review committees (REC). Usually, at the different universities, the faculties within which the research is to be undertaken have their own ethical review committees.[49] For example, at the University of Pretoria, the Faculty of Health Sciences has a main ethics committee and a sub-committee, overseeing health-related research by staff and students in the different teaching hospitals and

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43 See paras 5.3 and 5.4 in ch 2.

44 This section revises some aspects of para 3.3.4 of ch 3.

45 See para 3.3.4 of ch 3; guideline 9 of the MRC guidelines requires that all research involving healthy volunteers and patients must be subject to independent ethical review and that this should be conducted by a research ethics committee.

46 In terms of the South African Medicines and Related Substances Control Act 101 of 1965, as amended. Such research, therefore, will be reviewed by two ethics committees – that of the Medicines Control Council, and that of the institution under the auspices of which the research takes place. This will be the case when a potential HIV preventive vaccine is tested.

47 For research findings of human subject research to be accepted for publication in a scholarly journal, proof of such ethical approval needs to be shown. This is especially true in the case of foreign journals.

48 For example, the South African Medical Research Council. An exception is the CSIR, which has its research protocols reviewed by RECs at the University of Pretoria.

49 This is mainly due to the need to have protocols reviewed by experts in the field, and the large numbers of research protocols that are received by certain faculties.

institutions affiliated to the Faculty, as well as independent research (that is, research by persons not affiliated to the university) that is conducted in one of the teaching hospitals under the control of the Faculty.

The ethical review process is summarised below. [50]

i) The PI[51] submits a research protocol for review to the relevant REC.[52]

ii) Depending on the nature of the proposed research, the research protocol contains, amongst others:[53] the aims of the research; the research methodology; a literature study which sets out the rationale for and background to the study;[54] the method of and rationale for the selection of participants and statistical considerations; an estimate of the financial implications of the research and the details of the persons responsible for financing the research project; the details of any insurance taken out if there are risks attached to participation; a copy of the application in terms of Act 2 of 2000[55] (if required); and finally, the proposed participant or patient information leaflet (PIL)[56] and applicable informed consent forms[57] to be signed by the research participants.[58]

iii) The MCC requires a fee to be paid when a research protocol is reviewed; not all ethics committees charge fees for review.[59]

iv) The research protocol is checked by the secretariat of the ethics committee for its compliance with the formal requirements of the specific committee,[60]

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50 Also see Van Wyk (n 28 above) 5 for a summary of the process of initiating or conducting a clinical trial.

51 The chief researcher or the person carrying responsibility for the project. See para 2.2.3(e) below.

52 Usually, another committee (housed within the academic faculty or department from which the protocol originates) has already determined the scientific merit of the study by the time ethical approval is sought. This is not a fool-proof system, often research ethics committees reject protocols already approved by the internal faculty committee because of the protocol's lack of scientific merit.

53 This is not all the details contained - see guideline 9.11.1 of the MRC's guidelines.

54 In the case of drug studies a literature study would include pharmacological and toxicological data and information on previous clinical trials on the substance.

55 In terms of Act 2 of 2000: in cases where access to patients' records or other data or records is sought, and where it is not feasible to seek informed consent from them, the PI must lodge an application to the 'information officer' of the particular institution to access these records.

56 On the content of the PIL, see paras 3 and 4 below.

57 See below.

58 Different ethics committees have different requirements that the research protocol has to comply with, but most include these details.

59 Most ethics committees charge a fee in the case of the ethical review of research on behalf of a pharmaceutical company.

after which it is circulated among the members of the committee who review the protocol and discuss it at the committee's next meeting.[61]

v) Queries are directed to the PI, and matters for clarification are raised.

vi) The time take taken from initial submission to the eventual approval of the protocol varies from committee to committee. In the case of the MCC, the process of review takes approximately ten weeks.[62] It is also possible to apply for expedited review from the MCC and other ethics committees in certain circumstances.[63]

vii) When all problematic ethical issues regarding the protocol have been resolved, the study is approved or conditionally approved,[64] and a certificate or statement stating approval is issued. A copy of the statement or certificate is then be submitted to the National Research Ethics Council.[65] A unique study number is issued upon registration of the study in the health information system database.

viii) The PI may begin with the trial, usually by recruiting trial participants.

In reaching its decision to approve a clinical trial protocol, the REC should focus on the following:[66]

i) the nature and merit of the proposed research activity: badly planned, poorly designed research that appears unlikely to produce useful or valid results is unethical.

ii) the possibility of harm to the participant, judged on the protocol which should describe possible risks or side-effects;

iii) the possible benefits of the proposed research;

iv) consent - how the participant is to be informed about the proposed research and the precise way in which consent is to be sought;

v) risk (or cost) benefit evaluation of the proposed research.

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60 eg, the format of the PIL, whether all the relevant signatures are on the application forms, etc.

61 See below for the criteria for consideration and approval by the ethics committee.

62 See para 4.1 of the Good Practice guidelines. At the time of writing, the MCC took much longer than ten weeks to review a protocol.

63 See para 4.1 of the Good Practice guidelines regarding the circumstances when applications for expedited review are allowed by the MCC. An additional fee is often charged for expedited review.

64 When ethical compliance depends on a few minor changes made to the protocol, such as changing the exact title of the proposed project.

65 See para 4.3 of the Good Practice guidelines.

66 Guideline 9.8.1 MRC guidelines.

vi) in internationally collaborative research (which is likely to be the case in HIV-vaccine preventive trials), the research proposals should conform to both South African and international guidelines, and indigenous communities should not be exploited.

It is argued by some that the institution of RECs in South Africa and in other countries is paternalistic; that responsibility for taking part in research rests with the research subject alone and the REC has no role.[67] The argument rests on the perception that the competent individual research participant, and not the ethics committee, is best placed to determine what is in their best interest.[68]

Garrard and Dawson reject claims that competent participants are able at all times to reach an independent decision in their own interest.[69] They argue that RECs have an important role to play in the protection of research participants:[70]

- research participants should be protected from participation in research that is outright harmful – 'paternalism', thus, is aimed at preventing such harm;
- in particular situations otherwise well-informed research subjects may have their reason or judgment clouded, and thus be unable to see what action is in their best interest;
- individuals outside of the research endeavour are sometimes better placed objectively to decide on what is in the best interests of research participants; and
- the expertise of the REC (which contains laypersons, but also lawyers, scientists and physicians) may make them better judges of what risks are inherent in the particular trial.

Criticism of RECs as paternalistic institutions tends to 'overvalue' the ethical principle of autonomy, according to Garrrard and Dawson. The REC's authority to make decisions about whether to subject research participants to the risks of research does not stem form a misplaced sense of paternalism, but rather from:[71]

> the process of deliberation by the REC, as a lawfully established committee with representatives from the research and wider community, which has been given as its primary task, protecting potential research participants from unnecessary harm. Its authority comes from the fact that the REC consists of

67 See eg Edwards *et al* (2004) 30 *J Med Ethics* 88 - 91. They argue that competent research subjects do not need the protection of a REC.
68 As above.
69 Garrard and Dawson (2005) 31 *J Med Ethics* 419 - 423.
70 As above, 420 - 423.
71 Garrard and Dawson (n 69 above) 423.

a diverse group of experts (including lay experts), reaching agreement though discussion and consensus.

As part of their assessment of a research protocol, REC members need to be able to assess the potential for harm to research participants of a particular research protocol. To assess the potential for harm, members of the committee need some knowledge of the scientific field from which the specific protocol originates. In the case of HIV vaccine efficacy trials it may very well be that the RECs that have to make an assessment about the risks of the research lack knowledge in particular areas of vaccine research and that they therefore do not have the capacity to deal adequately with such research protocols.

In this regard an empirical study has been done of the resources and needs of RECs in Africa in relation to their ability to deal with the ethical assessment of HIV vaccine efficacy trial proposals.[72] This research is presented in a later section of the chapter.[73]

In the next section, the different actors and their responsibilities in clinical research in South Africa are presented.

2.2.3 Clinical trial actors

a) The MCC (as regulatory authority)[74]

All clinical trials of non-registered medicinal substances, as well as new indications of registered medicinal substances, must be reviewed by the MCC. The MCC has a statutory obligation to ensure that the drugs available in the country fulfil the requirements for safety, quality and efficacy.

b) National Health Research Ethics Council

The National Health Act makes provision for the establishment of a National Health Research Ethics Council,[75] to consist of fifteen members selected from nominations by interested parties after an advertisement in the Government Gazette.[76]

The National Health Research Ethics Council is intended as an umbrella body, overseeing and auditing the functioning of RECs in the country, rather than a replacement for these committees or interfering with their day-to-day activities.

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72 See Milford *et al* (2006) 28 *IRB: Ethics & Human Research* 1 - 9.
73 See para 2.3.4 below.
74 See 1.5.1 Good Practice guidelines.
75 Sec 72 Act 61 of 2003; also see guideline 1.5.3 Good Practice guidelines.
76 Sec 72(2)(a).

According to the Act, the National Health Research Ethics Council must determine guidelines for the functioning of health RECs; register and audit health RECs; set norms and standards for conducting clinical trials; adjudicate complaints about the functioning of health RECs and hear any complaint by a researcher who believes that he or she has been discriminated against by a health REC; refer to the relevant statutory health professional council matters involving the violation or potential violation of an ethical or professional rule by a health care provider; institute disciplinary action against any person found to be in violation of these norms and standards; and advise the national department and provincial departments on any ethical issues concerning research.[77]

The National Health Research Ethics Council reports directly to the Minister of Health and is provided with secretarial support from the Directorate Health Systems Research, Research Co-ordination and Epidemiology (HSRRCE).[78]

c) The health information system

In section 74, the National Health Act makes provision for the establishment and co-ordination of a health information system. The health information system or database reflects specific information on all medical research with humans undertaken in South Africa. The database, known as the South African National Clinical Trial Register, is up and running and researchers submitting protocols for research enter the details of their research on the database; such as who is to undertake the research, the sponsors of the research, the type of research undertaken, its methodology, the selection of subjects, and so on.[79] Some RECs require that a copy of the database entry form be submitted with the research protocol when ethical approval is sought.[80]

d) Health research ethics committees[81]

Overall, health RECs ensure the protection of and respect for the rights, safety and well-being of clinical trial participants.[82] RECs consist of scientific experts,[83] legal

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77 Sec 72(6)(a)–(g).

78 Guideline 1.5.3 Good Practice guidelines.

79 The database entry form is available at <http://www.ethicsapp.co.za/> or <www.sactr.gov.za> (30 November 2006).

80 For example, this is standard practice at the ethics committee of Faculty of Health Sciences at the University of Pretoria, the MCC and the ethics committee of the School of Health at the University of the Witwatersrand.

81 Also see para 3.3.4 of ch 3, for a discussion of the role of research ethics committees in South Africa and the ethical guidelines governing their functioning. This section focuses on legal aspects of research ethics committees in order to present the processes and actors involved in HIV vaccine research.

82 Guideline 1.5.4 Good Practice guidelines.

advisors and, in the case of health-related human subject research, lay persons. Committee members, as a rule, do not get paid for their services, although most institutions charge to review protocols, especially those originating from pharmaceutical companies.

The duties and functions of health RECs are described by the National Health Act[84] in section 73(2). The Act stipulates that a health REC must:

> (a) review research proposals and protocols in order to ensure that research conducted by the relevant institution, agency or establishment will promote health, contribute to the prevention of communicable or non-communicable diseases or disability or result in cures for communicable or non-communicable diseases; and
> (b) grant approval for research by the relevant institution, agency or establishment in instances where research proposals and protocols meet the ethical standards of that health research ethics committee.

Note that the Act does not prescribe the ethical standards to which the REC must conform to, but merely states that research proposals or protocols must meet the ethical standards of the committee.

The duties of the REC do not end with the granting of ethics approval; the progress of the clinical trial is monitored by the relevant REC as well.[85] The PI is required to submit reports on the trial's progress at regular intervals and to report any serious adverse events during the trial to the REC.[86] These reports should contain information on the progress of the trial; the number of participants included in relation to the number expected; the number of drop-outs and withdrawals; and if the planned time schedule is still appropriate.[87]

The PI should also submit a final report on completion of the study to the relevant ethics committee or committees. Finally, together with the PI, ethics

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83 Usually, not only experts in the different fields, such as medicine or engineering, but also experts in research methodology.

84 n 27 above.

85 See guideline 10.9.7 MRC guidelines.

86 See guideline 3.14 Good Practice guidelines. A trial may be terminated by the MCC or another ethics committee if it is shown that the drug that is being tested poses a risk to participants of serious adverse events. A 'serious adverse event' is an adverse event during the trial, whether proven to be because of the study drug or not, such as the death of a clinical trial participant. See, eg, clause 34(7) of the Draft General Regulations in terms of the Medicines and Related Substances control Act which authorises the MCC to terminate the clinical trial if it is of the opinion that the safety of the trial subjects is compromised.

87 See guideline 3.14 Good Practice guidelines.

committees are responsible for storing data on adverse events. They must review their ethical approval from time to time subject to this information.[88]

e) The principal investigator or PI

The main responsibility for conducting a clinical trial lies with the PI. Usually, the PI is either a member of an academic department or a student.

According to the Good Practice guidelines, the PI is a 'scientist who has a sole or joint responsibility for the design, conduct, delegation of trial responsibilities, analysis and reporting of the trial'.[89] The PI is accountable to the sponsor and regulatory authorities.

The REC will examine the curriculum vitae of the PI to determine whether he or she has the necessary academic qualifications and experience to conduct the research. The PI must be resident in South Africa (also in the case of multi-centre trials); qualified by education, training, and experience to assume responsibility for the proper conduct of the trial; and meet all the qualifications specified by the applicable regulatory requirement(s), and should provide evidence of such qualifications.

Usually, the PI enters into an agreement with a sponsor[90] to test a study drug or intervention (such as a vaccine) in return for payment.[91] The PI is often assisted by sub-investigators.

The PI's responsibilities include, amongst others, the following.[92]

i) Prior to beginning recruitment for a clinical trial, the PI must:

- submit the research protocol to the relevant REC (and the MCC if applicable);
- obtain a study number;
- be familiar with the requirements of, and information provided by, the trial sponsor and other matters related to the trial;
- develop proper mechanisms to obtain ethically the informed consent of participants[93] and compile an information package for the trial participants;[94]

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88 See guidelines 3.12 and 4.8 Good Practice guidelines. Not all the responsibilities of the PI are given.

89 Guideline 1.5.5.

90 See below.

91 Payment may take the form of a cash amount for undertaking the study, a PI fee, cash for every participant recruited to be deposited in the PI's research fund, and so on.

92 Good Practice guidelines 3.1 – 3.15. Only some of the responsibilities of the PI are mentioned. For a complete list, refer to the Good Practice guidelines.

93 In the case of research sponsored by an international pharmaceutical company, the protocol will usually include informed consent documents. In such a case it is the responsibility of the PI to adapt such documents to South African circumstances.

- ensure that proper safety reporting procedures are in place;
- demonstrate a potential for recruiting the required number of suitable trial participants; and
- ensure that all persons assisting with the trial are adequately informed about all aspects of the trial.

ii) During the trial, the PI must, amongst others:

- not impede the work of monitors who review and verify quality-control procedures and data;
- allow a possible audit and/or inspection by an independent auditor;
- inform participants about any illness(es) of which he / she becomes aware;
- obtain the informed consent of the participant in accordance with the ethical and legal principles;
- if the trial is a multi-site, and/or multi-country study, ensure that informed consent procedures take cognisance of the characteristics of the site participants and tailor the informed consent content and procedures accordingly;
- bear the responsibility for investigational product(s) and be accountable for the product at the trial site or sites;
- explain the correct use of the investigational product(s) to each subject and ensure that this is done correctly;
- take responsibility for decisions and actions relevant to the clinical management and safety of participants in acute situations;
- ensure that adequate provisions are made for dealing with adverse events that may occur unexpectedly in the study participants;
- report adverse events to the sponsor and REC; and
- submit progress reports as required by the sponsor, the regulatory authority and/or the relevant REC(s).

iii) After completion of the trial, the PI should:

- analyse the trial outcome; and
- submit the results to the Department of Health via the National Health Research Ethics Council, irrespective of the outcome of the trial.

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94 See below.

f) The trial sponsor

Because of the costs involved in conducting clinical research, most clinical trials have trial sponsors, who are responsible for the design, initiation, management and, most importantly, the financing of a clinical trial.[95]

A pharmaceutical corporation, a funding body, an individual (sometimes the PI) or an organisation may sponsor a clinical trial. For example, clinical trials are sometimes sponsored by academic departments at universities, private research institutions or the MRC. Pharmaceutical corporations and funding bodies may also nominate other individuals or organisations to sponsor a trial.[96]

g) The trial monitor

The trial monitor is appointed by and reports to the trial sponsor.[97] The trial monitor is responsible for overseeing the progress of a clinical trial and ensuring that it is conducted, recorded and reported in accordance with protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), Good Laboratory Practice (GLP), Good Pharmacy Practice (GPP), the Good practice guidelines and other applicable legislation and regulations.[98]

h) The trial auditor

The trial auditor is an independent individual appointed by the trial sponsors to conduct a systematic and in-depth examination of trial conduct and compliance with the protocol, SOPs, GCP, GLP, GPP and the applicable regulatory requirements.[99] An audit is to be distinguished from routine monitoring or quality-control functions. The MCC may also appoint an auditor to a trial.[100]

i) Trial inspectors

The trial inspector is an employee of the MCC who is responsible for announced or unannounced inspection visits at clinical trial sites as required/instructed by the MCC.[101]

j) Trial participants

Trial participants are those individuals who take part in a clinical trial as recipients of the investigational drug or device. They may be healthy volunteers in 'non-

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95 See guideline 1.5.6 Good Practice guidelines.
96 See guidelines 1 – 23 Good Practice guidelines for the responsibilities of a trial sponsor.
97 Guideline 1.5.7 Good Practice guidelines.
98 As above.
99 Guideline 1.5.8 Good Practice guidelines.
100 As above.
101 Guideline 1.5.9 Good Practice guidelines.

therapeutic' research (as is the case in HIV preventive vaccine trials) or suffering from the disease for which a cure or treatment is being tested in 'therapeutic' research (for example, participants in a 'therapeutic' HIV ART trial).[102]

Different ethical guidelines and legal rules apply to the two types of trial participants. For example, trail participants suffering from the disease for which a cure is being investigated ethically are allowed to carry a heavier burden or risk than healthy volunteers.[103]

Special classes of participants receive special consideration and safeguards as a potential for exploitation exists in such cases. Investigators must ensure that research protocols exclude groups (or make special provision for groups) that might markedly be more at risk than others, unless their inclusion is absolutely necessary. Examples of such groups or individuals are prisoners, children, pregnant women, the elderly, the dying, unconscious patients, the indigent, and the mentally ill.[104]

Guideline 12.2 of the MRC guidelines require that the inclusion of an individual or class of individuals who may be especially vulnerable, such as children, be approved only if the research ethics committee considers such inclusion to be essential, and that the participation of less-vulnerable subjects would not answer to the purpose of the research.

The next section examines special issues in international collaborative research.

2.2.4 Internationally collaborative research

Clinical research demonstrates the presence of globalisation[105] and has resulted in an increase in internationally collaborative research, that is, researchers and institutions collaborate in research that is conducted across national borders.[106]

Internationally collaborative research (such as multi-centre studies), in which clinical trials are conducted in more than one country, or instances where the

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102 See guideline 9.12.4.4 MRC guidelines. There is much dispute over whether preventive HIV vaccine research qualifies as therapeutic or non-therapeutic research. See para 3.2 below.

103 See eg secs 71(2) and 71(3) Act 61 of 2003 and guideline 9.12.4.4 MRC guidelines.

104 See guidelines 5.3.1.1.1 – 5.3.1.1.2 MRC guidelines.

105 See para 2.5 of ch 4 for a more general discussion on globalisation and its implications for in clinical research.

106 See generally, Geller *et al* 'Conducting international collaborative research in developing nations' (2004) 87 *Intl J Gynecology and Obstetrics* 267-271; Kilama (2003) 'Equipping Africa's researchers for global collaboration' <http://www.scidev.net/dossiers/index.cfm?fuse-action=dossierreaditem&dossier=5&type=3> (31 August 2006).

sponsor is from one country (usually developed) and the PI and trail participants are from another (usually less developed) country, relates to HIV vaccine efficacy trials, as it is likely that at least some vaccine efficacy trials will be conducted in such a manner. As is indicated below, at present, all four HIV vaccine clinical trials taking place in South Africa are the result of such a collaborative effort.[107]

Internationally collaborative research takes many forms, and does not by definition have to involve clinical trials. A strict definition of internationally collaborative research requires no more than that researchers from different countries collaborate on the same project. Such collaboration may involve the sharing of ideas, the joint undertaking of literature studies or internationally comparative studies; and, as such, internationally collaborative research does not necessarily present ethical or legal difficulties.

However, where international collaboration involves clinical trials of a new intervention or drug in different countries, issues such as differing standards of care in different settings,[108] intellectual property rights, risk sharing and the fair distribution of the burdens and benefits of research become relevant. As a sub-species of international collaborative research, multi-centre studies have the potential to present a multitude of problems:[109]

> such collaborations pose unique and complex problems that must be addressed to ensure that international research is conducted with strict adherence to ethical principles, offers direct benefit to the research subjects, and has the potential or adoption of positive findings to other members of the population.

A multi-centred study is a study conducted simultaneously by several investigators at different centres or sites, with standardised methods and a standardised protocol.[110] These different sites may be situated in any number of countries, each with its own PI.

Much of international drug efficacy and safety research is undertaken by means of multi-centre studies. In these studies, the trial sponsor (a pharmaceutical company) is based in country A, and the clinical trials are conducted by PIs in countries A, S, T, U, V, X, Y and Z. The international collaborators in such research are host country institutions (usually the sponsors of research - the pharmaceutical company in country A), collaborating country institutions (academic institutions or

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107 See para 5.1 below.
108 See para 4.4.2 of ch 3.
109 Geller *et al* (n 106 above) 268.
110 Guideline 7 Good Practice guidelines.

research entities in countries A, S, T, U, and so on) researchers from both the host country and collaborating countries, research participants and their communities from the collaborating countries or from both the host and collaborating countries.

Much benefit may be derived from internationally collaborative research; however, in the past, multi-centre clinical trials have resulted in the exploitation of researchers and clinical trial participants.[111] Milford *et al* comment as follows:[112]

> Research in developing countries is often financed by well-resourced, developed countries and conducted in vulnerable host communities with diverse cultural backgrounds. Moreover, multinational research is frequently conducted according to the regulatory frameworks of wealthier sponsor countries, which may be inappropriate to host country conditions and raise ethical concerns about potential exploitation of host communities and participants, insensitivity to community ethos, the scope of sponsor-investigator obligations, and the appropriate communication of research results to participants.

Alternatively, international researchers have often been accused of 'changing their ethics at the customs desk'.[113] In order to protect the interests of South African researchers and trial participants in multi-centre trials, specific ethical guidelines have been drafted. Guideline 11 of the MRC guidelines and guideline 7 of the Good Practice guidelines deal with multi-centre trials and internationally collaborative research. A brief discussion of these guidelines follows.

Regarding the initial planning and design of multi-centre clinical trails:

The MRC guidelines prohibit research in a host country without local research collaboration in the design and conduct of that research.[114] It would therefore amount to a violation of the MRC guidelines for a sponsoring or collaborating country to conduct HIV vaccine research in South Africa without local researchers' input into, and collaboration on, the initial design of the research and the trial itself.

The Good Practice guidelines stress that the design of a multi-centre trial must ensure that local realities are considered and integrated into the design of the study.[115] In particular, the following must be addressed in the protocol:[116]

- inclusion and exclusion criteria must be appropriate for local realities;
- informed consent procedures must be tailored to local conditions;

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111 See eg paras 4.2.1 and 4.2.2 of ch 3.
112 Milford *et al* (n 72 above) 1.
113 McNeill quoted in Geller *et al* 268.
114 As above.
115 Guideline 7 Good Practice guidelines.
116 Guideline 7 Good Practice guidelines.

- study design differences between South African and other sites must be explained fully; and
- study extrapolations and conclusions potentially must be relevant to the South African context.

The MRC guidelines require that clear agreements on all aspects of the research are in place before submission of the research protocol to the relevant ethics committees. This includes agreements on intellectual property sharing, the management of the research process, the division of responsibilities, finances, the sharing of benefits and burdens, and any other appropriate aspects. [117]

In respect of the requirement that informed consent procedures be tailored to local conditions, Geller *et al* comment:[118]

> The Western concept of informed consent may not translate culturally to developing nations where individual rights and the patient-provider relationship may take on a different meaning than that of Western cultures. For example, the challenge of informed consent in cultures that may not accord self-determination, especially to young women, with the same importance as is the case in some Western societies calls into question some of the basic tenets of ethical research.

The view that informed consent is a peculiarly western notion is discussed in more detail in later paragraphs.[119]

Regarding the ethical review of multi-centre clinical trails:

The MRC guidelines stipulate that research ethics committees of all collaborating institutions approve the research protocol;[120] that, before granting approval, the South African ethics committee or committees consider whether the findings can, and will, be incorporated into the local healthcare system;[121] and that they ensure that proper informed consent will be obtained from all trial participants, their families and communities,[122] according to local custom.[123]

Furthermore, there must be a clear justification in the protocol of why the research is done in a particular country, a particular institution, with a particular

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117 Guideline 11.3.1 MRC guidelines.

118 Geller *et al* (n 106 above) 270. The writers comment that, in rural India, 'young women ... defer to their husband or senior family members and sometimes even village leaders for many important decisions including those of their own health' (270).

119 See para 5.4 below.

120 Guideline 11.4.1 MRC guidelines.

121 Guideline 11.4.1 MRC guidelines.

122 See para 5.4 below.

investigator, with a particular participant and in a particular community.[124] Unless there are compelling and acceptable reasons for the above, ethics committees are required to disapprove that research is done in a host country if it could as easily be carried out in a collaborating country.[125]

Of particular importance for HIV vaccine efficacy trials, the MRC guidelines require that ethics committees ensure that those involved in international research have some understanding of, and be sensitive to, the social, economic, and political milieu in which the research is taking place. This includes the protection of research participants who are subject to systematic deprivation as a result of poverty and other threats to freedom.[126] As pointed out above,[127] HIV vaccine efficacy trials need to take place in communities at high risk for HIV infection. Members of these communities are likely to be poor and vulnerable to exploitation. Research sponsors and PIs sensitive to these realities are better able to put in place safeguards that will protect trial participants and their communities.

The Good Practice guidelines require that the PI or overall project manager should be a South African-based scientist, in the case of collaborative projects with international research groups and multi-country studies as well.[128] The Good Practice guidelines further require that, in the case of multi-centre trials, a reasonable proportion of significant project team members (managers and technical experts) must be South African-based scientists.[129]

Regarding the potential for exploitation during multi-centre clinical trials:

The MRC guidelines prohibit the exploitation of one institution by another, or of any investigator, research participant or community.[130] Which actions, in particular, would amount to exploitation remain unclear.[131] The guidelines demand the respect, sharing and acknowledgement of the intellectual property rights of institutions, investigators, participants and communities before the research commences;[132] the equitable compensation of institutions, investigators, participants and communities

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123 Guideline 11.4.1 MRC guidelines.
124 Guideline 11.4.3 MRC guidelines.
125 Guideline 11.4.3 MRC Guidelines.
126 Guideline 11.4.3 MRC guidelines.
127 See paras 1 and 2.1 above. Also see para 2.3 below.
128 Guideline 7 Good Practice guidelines.
129 Guideline 7 Good Practice guidelines.
130 Guideline 11.4.2 MRC guidelines.
131 See also para 2.3.3 below.
132 Guideline 11.4.2 MRC guidelines.

(this compensation is to go beyond financial compensation);[133] and stress that sponsors and investigators have a moral obligation to assist indigenous peoples, traditional societies and local communities to protect their knowledge and resources; as well as that which is sacred and secret by tradition.[134]

Regarding the potential benefits which may flow from multi-centre clinical trials:
The MRC guidelines stress that the community in which the research is undertaken should benefit from such research, for example, by gaining access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.

Collaborative research should also be of benefit to the host country.[135] This may involve the development of the host country's health or research infrastructure or research capacity.[136]

The next section traces the epidemiologic and scientific, socio-economic and political contexts in which HIV vaccine efficacy trails are likely to take place in South Africa, highlighting the nature of the communities from which participants will be drawn and the potential risks they face. 'Vulnerability' is defined, and the importance of ensuring free and uncoerced informed consent in this context is outlined.

2. 3 The South African preventive HIV vaccine efficacy trial context

2.3.1 Epidemiological and scientific contexts

The HIV epidemic in South Africa shows no sign of declining.[137] UNAIDS estimates that in 2005, one in nine South Africans was living with HIV/AIDS.[138] In this context, and given the fact that alternatives such as microbicides and male circumcision do not provide a sustainable solution, it is imperative that a vaccine that curbs the spread of HIV is found.[139]

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133 Guideline 11.4.2 MRC guidelines.
134 Guideline 11.4.2 MRC guidelines.
135 Guideline 11.4.4 MRC guidelines; guideline 7 Good Practice guidelines.
136 Guideline 11.4.4 MRC guidelines; guideline 7 Good Practice guidelines.
137 UNAIDS (2006) *AIDS epidemic update* 17; also see para 3.3 of ch 2 above.
138 As above.
139 See para 3.5 of ch 2 for arguments on why a preventive HIV vaccine is necessary, eg viral resistance to HAART, its toxicity, poor drug compliance and the high cost of HAART. Also see Janse Van Rensburg (2002) 20 *CME* 577 – 579.

A successful preventive HIV vaccine should be effective, safe and affordable.[140] But what is an 'effective' vaccine and how is effectiveness measured? In response to these questions, the following goals or endpoints for preventive HIV vaccine development in South Africa have been outlined by vaccine scientists.[141] A preventive HIV vaccine will be considered successful if it succeeds either in preventing infection (known as sterilising immunity), or preventing disease.[142] If neither of the above is possible, a third possibility is that the successful vaccine will slow down or delay the progression of the disease from infection to death.[143] In other words, the vaccine will succeed in lowering the viral load in the blood of infected persons for a considerable period of time. This third possibility will indirectly decrease the transmission of the disease;[144] the vaccine thus will have a limited effect on the health of the vaccinated person (as she will become ill eventually), but a potentially significant effect on the epidemiology of HIV within the community.[145]

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140 Janse Van Rensburg (n 139 above) 577; Weidle *et al* (2002) 359 *The Lancet* 2264; Schoub (2002) 20 *CME* 561.

141 As above. See also para 4.3 of ch 2 above.

142 The endpoint of a *therapeutic* HIV vaccine trial is that the vaccine succeeds in ameliorating the disease by eliciting an immune response in the infected person (see Janse Van Rensburg (n 139 above) 580; Schoub (n 140 above) 561).
For most infectious diseases, sterilising immunity is the endpoint. In the case of sterilising immunity, the body is able totally to eliminate the virus, infection is thus prevented, and there are no signs and symptoms of the disease. Many scientists believe that it is not possible to develop a HIV vaccine that will prevent infection (see Janse Van Rensburg (n 139 above) 579; Weidle *et al* (n 139 above) 2264; Schoub (n 140 above) 561; Van Harmelen and Williamson (2000) 20 *CME* 568 569 – 570 569.
Once a person is infected with HIV, the virus remains in that person's body, as it integrates itself into the person's DNA.

143 Janse Van Rensburg 579; Weidle *et al* 2264; Schoub 561. The asymptomatic period of the disease will be prolonged, and there will be no or few symptoms (Janse Van Resburg 579 – 580).

144 A high viral load is a risk factor for HIV transmission – see paras 3.3 and 3.4 of ch 2 above.

145 This is known as a 'surrogate endpoint'. Janse Van Rensburg (n 139 above) 579; Weidle *et al* (n 140 above) 2264; Schoub (n 140 above) 561. The Meeting summary of AIDS vaccine trials: considerations for Phase III trial design and endpoints, held in 2001 in the USA, outlined the following as 'surrogate' or replacement endpoints in HIV preventive efficacy trials in a case where neither sterilising immunity, nor the prevention of disease is achieved by the candidate HIV vaccine (3):
Virologic endpoints: a) Decreased plasma viral load set-point, or b) decreased plasma viral load below some biologically significant set-point and, in addition, increased duration of the effect for a meaningful time period (eg more than one year).
Immunologic endpoints: a) Maintenance of the CD4 T-cell count (eg, >350 cells/μL), or b) decreased rate of CD4 T-cell decline.
Clinical endpoints:
a) Decrease in the number of HIV-infected vaccinated subjects requiring ARV treatment or b) increase in the time interval from infection to initiation of antiretroviral treatment.

Many challenges to HIV vaccine development exist; most notably, antigenic variation, the integration of the viral genome into the host cell, the substantial diversity in the virus subtype,[146] and the lack of a good animal model.[147] These challenges were discussed in detail in chapter 2 and will not be duplicated here.[148]

Vaccine efficacy is measured during Phase II and III vaccine trials.[149] Phase III vaccine efficacy trials are large-scale, double blind, placebo-controlled, randomised clinical trials.[150] Efficacy is measured statistically, but amounts to a situation in which those participants who received the HIV preventive vaccine have a significantly lower incidence of HIV infection than those receiving the placebo.[151]

During a Phase III efficacy trial, the possibility of adverse effects is also examined.[152] Large numbers of volunteers take part, usually more than a thousand.[153] As has been pointed out, because the efficacy of the candidate vaccine needs to be established, these volunteers should be at high risk for infection, and are drawn from communities with a high incidence of HIV.[154]

Abdool Karim outlines the factors at play in the selection of an ideal HIV vaccine trial site and its environment.[155] They are:[156]

Epidemiological endpoints: a) Decrease in sexual transmission rates by vaccinated subjects who become HIV-infected subsequent to vaccination, or b) decrease in maternal-infant transmission rates for women who become HIV-infected subsequent to vaccination. In these situations, the clinical benefit may be to others rather than to the vaccinated subject.
From the above it is clear that it will be necessary to keep track of vaccine trial participants over a long period of time to evaluate these surrogate markers. Also, should participants be treated with ARVs, this process of evaluation could be complicated.

146 South Africa has a predominantly subtype C HIV-1 epidemic; however, there is unending variety within the subtype in South Africa, and the implications of this diversity on the effective design of a HIV vaccine is unknown (see Abdool Karim (n 28 above) 590).

147 Janse Van Rensburg 579–580; Weidle *et al* 2264.

148 See para 4.5 of ch 2 above.

149 See para 5.4.1 of ch 2 above for more on the different stages in vaccine development.

150 See paras 5.2 and 5.3 of ch 2 for an exposition of terms such as 'double blind', 'placebo-controlled' and 'randomised'.

151 What is considered to be 'statistically lower' is a matter for debate. VaxGen's recently completed vaccine trials in Thailand and the USA were looking at a reduction in the level of HIV infection by at least 30% at a statistically significant level. This means that an efficacy of more than 30% would be seen 95 times out of 100 (Farham 'The trials of testing', on file with author).

152 Abdool Karim (n 28 above) 589.

153 The VaxGen Phase III trial involved 5009 volunteers.

154 In communities with a low HIV incidence rate, many more participants have to be enrolled in the trial in order to achieve statistical validity. Such trials are necessarily more expensive.

155 Abdool Karim (n 28 above) 589.

- an epidemiological situation with HIV incidence data on high-risk groups and evidence of high cohort retention rates over trials spanning three to five years (in everyday language this translates to sufficiently large number of high-risk HIV-negative individuals who can be enrolled and followed up for three to five years);
- an adequate clinical infrastructure (which includes facilities for counselling, the management and storing of the vaccine, facilities for data management and good laboratory management);
- investigators experienced in clinical research and clinical trial methodology and management; and
- the availability of an adequate cohort management, clinical and laboratory infrastructure.

The following tables represent various ongoing Phase I, II and III preventive HIV vaccine trials around the world (as of February 2007):[157]

Phase I clinical trials:

PROT #	START DATE	SPONSOR, FUNDER, DEVELOPER	TRIAL SITE(S)	VACCINE	# PRTCP	CLADE
VRC 011	April 2006	VRC	US	DNA vaccine with *gag, pol, nef + env* or Adenovirus vector with *gag, pol + env*	60	A, B, C
HVTN 065	April 2006	DAIDS, HVTN, VRC, GeoVax	US	Prime: DNA plasmid with *gag, pro, RT, env, tat, rev, vpu* Boost: Modified vaccinia Ankara (MVA) vector with *gag, pol, env*	120	B
IAVI D001	Febr 2006	IAVI, Therion	India	Modified vaccinia Ankara (MVA) with *env, gag, tat-rev, nef-RT*	32	C
HVTN 064	Jan 2006	DAIDS, HVTN, Pharmexa-Epimmune	US, Peru	Recombinant protein vaccine with *gag, pol, vpr, nef* and DNA	120	B

156 As above.

157 Adapted from AVAC (2006) *AIDS Vaccines:The Next Frontiers* 21-25. These tables do not account for vaccines presently in pre-clinical testing (see ch 2 para 5.3.2 for the single HIV vaccine that has completed Phase III trials (by VaxGen)).

				vaccine with protein containing T-helper epitopes from *env, gag, pol, vpu*		
HVTN 068	Feb 2006	DAIDS, HVTN, VRC	US	Adenovirus vector with *gag, pol + env* or DNA vaccine with *gag, pol, nef + env* B followed by adenoviral boost	66	A, B, C
HIVIS 02	Jan 2006	Karolinska Institute, Swedish Institute for Infectious Disease Control, WRAIR	Sweden	Modified vaccinia Ankara (MVA) viral vector with *env, gag,* and *pol* to volunteers from HIVIS 01	38	A, E
IAVI V001	Nov 2005	IAVI, NIAID, VRC	Rwanda, Kenya	Prime: DNA vaccine with *gag, pol, env* Boost: Adenovirus vector with *gag, pol, env*	104	A, B, C
RV 158	Nov 2005	WRAIR, NIH	US, Thailand	Modified vaccinia Ankara (MVA) viral vector with gp160, *gag* and *pol*	48	A, E
HVTN 063	Sept 2005	DAIDS, HVTN, Wyeth	US, Brazil	Prime: Genevax Gag-2692 +/- IL-15 DNA Boost: Genevax Gag-2692 + IL-12 DNA or IL-15 DNA	120	B
HVTN 060	Aug 2006	DAIDS, HVTN, Wyeth	US, Thailand	Prime: Genevax Gag-2692 +/- IL-12 DNA adjuvant Boost: DNA plasmids with gag or RC529-SE and GM-CSF with *env, gag, nef*	156	B
HVTN 054	Apr 2005	DAIDS, HVTN, VRC	US	Adenovirus vector with *gag, pol + env*	48	B A, B, C
VRC 008	Apr 2005	NIAID, VRC	US	Prime: DNA vaccine with *gag, pol, nef + env* Boost: Adenovirus vector with *gag, pol + env*	40	B A, B, C
N/A	Mar 2005	Changchun BCHT, Guangxi CDC	China	Prime: DNA vaccine Boost: recombinant adenovirus vector	49	C

HIVIS 01	Feb 2005	Karolinska Institute, Swedish Institute Sweden for Infectious Disease Control, Vecura	Sweden	Intramuscular or intradermal injections of plasmid DNA.with HIV genes *env, rev, gag,* and *RT*	40	A, B, C
EuroVacc 02	Feb 2005	EU, Imperial College London, UK MRC Clinical Trials Unit, EuroVacc	UK, Switzerland	Vaccinia vector with *gag, pol, nef, env*	40	C
N/A	Feb 2005	St Jude, NIH	US	Recombinant HIV-1 multi-envelope DNA plasmid vaccine with *env*	6	A, B, C, D, E
RV 156	Jan 2005	NIAID, HVTN, VRC, USMHRP, Makerere Univer	Uganda	Prime: DNA vaccine with *gag, pol, nef + env* Boost: Adenovirus vector with *gag, pol + env*		B A, B, C
IAVI C002	Jan 2005	IAVI, ADARC	US	Modified vaccinia Ankara (MVA) vector with *env/gag-pol, nef-tat*	48	C
HVTN 059	Oct 2004	HVTN, SAAVI, Alphavax	US, South Africa, Botswana	VEE (Venezuelan equine encephalitis) vector with *gag*	96	C
HVTN 055	Sept 2004	DAIDS, HVTN, Therion	US, Brazil	Prime: Modified vaccinia Ankara (MVA) viral vector with *env, gag, tat, rev, nef, pol* Boost: Fowlpox viral vector (FPV) with same genes as prime	150	B
HVTN 056	April 2004	DAIDS, HVTN, Wyeth	US	Conserved CTL epitopes from *gag, nef* and helper T epitopes from *env, gag* in adjuvant (RC329-SE), with or without cytokine (GM-CSF)	96	B
HVTN 050/ MERC 018	Jan 2004	NIAID, HVTN, Merck	Thailand, Brazil, Haiti, Puerto Rico, South Africa, US, Malawi, Peru	Adenovirus vector with *gag*	435	B

HVTN 049	Dec 2003	DAIDS, HVTN, Chiron	US	Prime: DNA vaccine with *gag, env* attached to microparticles Boost: Env protein (oligomeric gp140) + adjuvant (MF59)	96	B
HVTN 044	Dec 2003	DAIDS, HVTN, VRC	US	DNA vaccine with *gag, pol, nef + env* with or without cytokine (IL-2) adjuvant	70	B A, B, C
IAVI A001	Dec 2003	Columbus Children's Research Center, Indian Council of Medical Research, National AIDS Control Organization, IAVI, Targeted Genetics	Belgium, Germany, India	AAV2 (adeno-associated virus type 2) vector with *gag, pol,* □*RT* 50 C	50	C
B011; RV 138	July 2002	WRAIR	US	Canarypox viral vector with *env, gag, pol*	36	B

Phase I/II clinical trials:

PROT #	START DATE	SPONSOR, FUNDER, DEVELOPER	TRIAL SITE(S)	VACCINE	# PRTCP	CLADE
RV 172	May 2006	NIH, WRAIR, VRC	Kenya, Uganda, Tanzania	Prime: DNA vaccine with *gag, pol, nef + env* 324 B Boost: Adenovirus vector with *gag, pol + env* A, B, C	324	B A, B, C
C060301	Feb 2004	FIT Biotech, IAVI	Finland	DNA vaccine with *nef, rev, tat, gag, pol, env,* CTL epitopes	28	B

Phase II clinical trials:

PROT #	START DATE	SPONSOR, FUNDER, DEVELOPER	TRIAL SITE(S)	VACCINE	# PRTCP	CLADE

IAVI A002	Nov 2005	Children's Hospital of Pennsylvania, Columbus Children's Research Center, Indian Council of Medical Research, National AIDS Control Organization, Targeted Genetics Corp.	South Africa, Uganda, Zambia	AAV2 (adeno-associated virus type 2) vector with gag, pol, ÆRT	91	C
HVTN 204	Sept 2005	DAIDS, HVTN, VRC, Vical, GenVec	US, Brazil, South Africa, Haiti, Jamaica	Prime: DNA vaccine with *gag, pol, nef + env* Boost: Adenovirus vector with *gag, pol + env*	480	B A, B, C
ARNS VAC 18	Sept 2004	Arns, Aventis	France	5 lipopeptides with CTL epitopes from *gag, nef, pol*	132	B

Phase III clinical trials:

PROT #	START DATE	SPONSOR, FUNDER, DEVELOPER	TRIAL SITE(S)	VACCINE	# PRTCP	CLADE
RV 144	Oct 2003	USMHRP, MoPH Thailnd, Aventis, VaxGen	Thailand	Prime: canary pox viral vector with env and gag-pol; Boost: Env protein (gp120 subunits)	16 402	B, AVE
HVTN 502/Merck 023[158]	Dec 04	DAIDS, HVTN, Merck	US, Canada, Peru, DomRep, Haiti, Puerto Rico, Australia, Brazil, Jamaica	Adenovirus vector with gag, pol, nef	3 000	B

A guiding principle that all human subject research has to comply with in order to be considered ethical and legal is that there should be a favourable balance between risk and potential benefit.[159] The MRC guidelines define the term 'risk' as referring both to:[160]

158 This is a 'trial of concept'.

159 See ch 3 on the discussion of beneficence as a principle of research ethics, in para 3.4.2.

160 Guideline 9.12.4.1 MRC guidelines.

> the *probability* of a harm resulting from an activity and to its *magnitude*. Risk often stands for the combined probabilities and magnitude of several potential harms, whether they be psychological, sociological or physiological in nature. It should be noted that even inactivity may be associated with some risk and that every intervention, however simple it may be, involves some degree of risk.
>
> Risk includes the consequence of a breach of confidentiality and also risks to others, through the use of scarce resources for research that might otherwise be used for patient care.

Numerous writers have outlined the risks and benefits inherent in HIV vaccine trial participation.[161] For the sake of completeness, these risks are summarised below. The benefits of participation are outlined later.

a) Risks borne by participants

At the outset it should be remembered that the risks of HIV preventive vaccine efficacy trials differ according to vaccine design and trial design. Some vaccines are safer than others;[162] some trial designs may have more adverse effects than others, such as those using placebos.[163] The social and health status of the individual taking part in the trial also may contribute to the probability and magnitude of the risk.

Risks borne by participants of HIV preventive vaccine efficacy trials are physical, psychological and social in nature. As no Phase III HIV vaccine trial has yet been undertaken in South Africa, it is unclear which of these risks will materialise during these trials.

- *Adverse autoimmune reactions to the vaccine and the worsening of established infections*

Participation in HIV preventive vaccine efficacy trials expose participants to the risk of adverse autoimmune reactions to the vaccine and the possibility that the participant will suffer from a worse infection should she ever become infected with HIV.[164]

Fears with regard to adverse autoimmune reactions relate to the fact that HIV's gp160 contains several regions (such as HLA-DR and interleukin-2) with sequences homologous to that of cellular proteins (especially those found on human CD4

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161 See eg UNAIDS (2000) *Ethical considerations in HIV preventive vaccine research* 28; Graham and Wright (2003) 33 *N Engl J Med* 1335; Slack *et al* (2000) 96 *SA J Science* 293.

162 See para 4.4 of ch 2 above and see below.

163 See ch 3 above.

164 Graham and Wright (n 161 above) 1335.

cells).[165] It is feared that vaccination will stimulate autoimmune reactions against the body's own CD4 cells.[166] This theory is borne out by the fact that HIV-infected persons show a high incidence of autoimmune reactions.[167]

The possibility that HIV vaccination could worsen illness, if the trial participant should be infected with HIV subsequent to vaccination, has been mentioned as a possible risk to participation.[168] To date this risk has not materialised, although there is some evidence that this is the case in vitro.[169] Further, with regard to this risk there is the possibility that a trial participant may have a greater risk of developing an established infection upon being exposed to HIV than others.[170]

Someone already infected with HIV, when vaccinated, may develop a more serious and worse infection.[171] This may happen in cases where the participant is in the early stages of infection before sufficient antibodies are produced to show up on standard ELISA assays.[172] The person is diagnosed as HIV negative, whereas, in fact, she is HIV positive, and then inoculated.

- *Adverse reactions to the vaccine itself*

Other physical risks to HIV vaccination are adverse reactions to the vaccine itself,[173] pain, skin irritations, fever, and malaise.[174] HIV vaccination may require repeated inoculations, each in turn producing these adverse effects.

- *Live vaccines*

Live vaccines[175] carry the risk that the vaccine virus may mutate sufficiently to revert back to its virulent form and produce HIV infection. Although pre-clinical research is being done on live vaccines, there is no indication that these vaccines will be tested

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165 As above.
166 As above.
167 As above. So far, low levels of CD4-antibodies have indeed been detected in vaccine trial participants (see eg Key *et al* (1992) 8 *AIDS Research on Human Retroviruses* 1091). See also the commentary on the article by Veljkovic *et al* below.
168 Graham and Wright (n 161 above) 1335.
169 As above.
170 UNAIDS (n 161 above) 28.
171 Slack *et al* (n 161 above) 293.
172 See ch 2, para 3.3 above.
173 Such as an allergic reaction to one of its components.
174 UNAIDS (n 161 above) 28.
175 As their name indicates, live (attenuated) viruses are 'alive' and able to replicate in the vaccinated person.

on humans at present.[176] Should this occur, however, trial participants would be exposed to even more serious risk of harm.[177]

- *Immune tolerance*

Participation in a preventive HIV vaccine efficacy trial may result in immune tolerance which, in turn, will prevent the trial participant from being successfully immunised against HIV in the future.[178] This is a potentially serious risk, as it might mean that the participant will not be able to be given a subsequent, more effective vaccine.[179]

- *Stress, anxiety and depression*

Psychological risks to participants in HIV preventive vaccine efficacy trials include stress, anxiety and depression due to having to discuss intimate sexual matters with trial administrators, and the stress inherent in being subjected to repeat HIV testing.[180]

- *Sexual relationships may become strained*

Participation in HIV preventive vaccine efficacy trials might cause strain in the participant's sexual relations with others, especially when the participant's sexual partner (mistakenly) believes that the participant can infect others with the virus.[181]

- *Increased risk-taking behaviour*

Another potential risk of participating in HIV preventive vaccine efficacy trials is increased risk-taking behaviour by trial participants, caused by an (erroneous) belief that the candidate vaccine will protect them from infection.[182] This belief may be particularly dangerous in cases where trial participants belong to the placebo group.

- *Cultural isolation*

Trial participants from another culture and belief system who are exposed to alien scientific concepts may experience stress and anxiety.[183]

- *False-positive HIV test results*

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176 See n 175 above.
177 See para 4.4 of ch 2 above.
178 Slack *et al* 293.
179 As above.
180 UNAIDS 29.
181 As above.
182 See Celentano *et al* (1995) 9 *AIDS* 1079.
183 UNAIDS (n 161 above) 29.

After being vaccinated, participants will test HIV-positive on standard ELISA assays even though they are not infected with HIV. This could have serious consequences for participants' prospects of successfully taking out insurance, finding employment, and so on. Some writers have rejected these fears of discrimination based on positive HIV antibody tests. Their argument is that a standard immunoblot can easily discriminate real HIV infection (which should show antibodies to all HIV's proteins) from vaccine-induced HIV antibodies (to the envelope proteins alone).[184] However, as vaccine science progresses and vaccine designs become more complex, it is unlikely that immunity produced by the more complex DNA or vector vaccines will be easily distinguishable in antibody laboratory tests from real HIV infection.[185]

- *Negative perceptions and stigmatisation*

Not only will HIV preventive vaccine efficacy trial participants *test* positive on standard HIV-antibody tests, but they may be perceived by a misinformed public to *be* HIV positive. Participants in Phase III trials are usually high-risk individuals and this perception may cause them to be stigmatised and discriminated against. The communities from which these participants are drawn may be similarly stigmatised.

It is difficult to evaluate the seriousness of the risks mentioned above if one is not an expert in vaccine science; physical risks attendant upon HIV trial participation are especially difficult to assess. Nor is it easy to accurately estimate the chance of these risks materialising.

Although many vaccine scientists are quick to allay fears concerning the safety of vaccines, others are not so hasty, stressing the risks outlined above. For example, Veljkovic *et al*[186] raise serious concerns about preventive HIV vaccine safety (Veljkovic and colleagues are all well-respected scientists in the field of virology).

Veljkovic *et al* draw attention to the fact that, initially, the AIDS Research Advisory Committee in the USA commented in their report (about Phase III HIV-1 gp120/160 vaccine trials) that they 'should not be conducted at this time in this country'.[187] This decision not to conduct Phase III efficacy trials was based on the 'chance that tested HIV vaccines will compromise the immune system and make the

184 Francis *et al* (2003) 17(2) *AIDS* 151.
185 As above.
186 Veljkovic *et al* (2004) 23 *Intl Rev Immunology* 465-486.
187 As above, 466.

recipient more vulnerable to infection'.[188] Despite this, 'an advisory committee to WHO [...] recommended that large-scale Phase III of these HIV vaccine candidates should be allowed to proceed in developing countries'.[189] This recommendation was based on the argument that 'the desperate situation posed by the AIDS epidemic justifies acceptance of the so-called "small risks" involved'.[190]

When this specific gp120/160 vaccine later proceeded to Phase III trials in Thailand, the initial fears expressed about its safety were proven justified. Researchers reported that the vaccine 'acted as a decoy for the immune system ... increasing the likelihood of infection as well as disarming the immune system ... increasing the likelihood of rapid disease progression, which is seen in later-infected vaccinees'.[191]

Another widely used vaccine strategy, also criticised by Veljkovic *et al*, is the use of live recombinant vectors to carry vaccine proteins into the human body.[192] Veljkovic *et al* express fears that, when combined with HIV-1 gp 120/160, these recombinant vectors can mutate in the human body to cause dangerous infections.[193] Even if the probability of that happening is very low, it is not nil, posing a grave risk to HIV vaccine trial participants.[194]

Veljkovic *et al* further caution against the use of a VEE vector vaccine, such as the one used in the HVTN 059 / AlphaVax vaccine tested in South Africa.[195] Veljkovic *et al* express several reasons for concern about a VEE-based vaccine, not least of which is the fact that, according to reported data, the viral family to which VEE belongs is inherently recombinogenic in nature.[196]

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188 As above.
189 As above.
190 As above.
191 In this regard, see Locher *et al* 'Antibody and cellular immune responses in breakthrough infection subjects after HIV type 1 glycoprotien 120 vaccination' 71 (1999) *AIDS Research* 1685.
192 Veljkovic *et al* (n 186 above) 467. See para 4 of ch 2 above.
193 As above, 467.
194 As above.
195 See above.
196 Veljkovic *et al* (n 186 above) 472, quoting Weaver *et al* 'A comparison of the nucleotide sequences of eastern and western equinine encephalomyelitis viruses with those of other alphaviruses and related RNA viruses' (1993) 197 *Virology* 375 - 90 and Rumenapf *et al* 'Aura virus is a New World representative of Sindbis-like viruses' (1995) 208 *Virology* 621-633.
'Recombinogenic', as the term indicates, implies an ability to 'recombine'.

Moreover, Veljkovic *et al* caution against other viral vectors used in vaccines, such as the herpes simplex virus vector,[197] poxvirus (or vacinia) vectors[198] and HIV antigens found in plants.[199]

The question that needs to be answered is whether Veljkovic *et al* are being unnecessarily conservative, or even alarmist, advocating caution when everybody else is forging ahead with large-scale preventive HIV trials in high-risk populations, or whether their warnings indicate a real element of danger (however small). At present it is uncertain which of the perils they warn about, or the risks outlined above, if any, will materialise during HIV vaccine efficacy trials in South Africa. However, it is clear that at least some of these risks, potentially, are very serious – and that at least one of the virologists' warnings has manifested in harm to preventive HIV vaccine trial participants.[200] Inevitably, this example leads to the conclusion that the risks attendant upon preventive HIV vaccine trial participation in South Africa may be more serious than is openly admitted.

b) Benefits of participation

Risk should be balanced with the potential benefit that may accrue from HIV vaccine trial participation. A 'benefit' is defined as follows:[201]

> A benefit is the opposite of a harm, and refers to any favourable outcome of the research to society or to the individual. The outcome of research is never certain at the outset, and it is thus proper to consider the probability of benefit as well as its magnitude. In practice, 'benefit' often stands for the combined probabilities and magnitudes of several possible favourable outcomes.

Preventive HIV vaccine trial participation has the potential to benefit the individual participant and the community in a number of ways.

- *Increased feelings of self-worth because the trial participant is helping others*

This is one of the most important benefits derived from participation in non-therapeutic trials (where the participant does not suffer from the disease for which a therapy is being researched). The individual trial participant may not derive any personal benefit from participation, but knows that she is helping to find the answer

197 Veljkovic *et al* 472.
198 As above, 473.
199 As above, 476.
200 As described by authors referred to in n 191 above.
201 Guideline 9.12.4.5 MRC guidelines.

to a research question, and thus helping to increase knowledge that could benefit others in the future, be they identifiable or non-identifiable.[202]

During the VaxGen trial, IDUs, when asked why they took part, indicated that they wanted to do something to help stop the spread of the HIV epidemic.[203]

- *Increased access to health care and better quality health care*

This is an important benefit of participation, especially in resource-poor countries such as those in Africa where little is spent on health care. During preventive HIV vaccine trials, participants will have access to treatment for STDs, general medical examinations, HIV-testing with pre- and post-test counselling, and so forth.[204]

- *Counselling on risk-taking behaviours*

Preventive HIV vaccine efficacy trial participants are given extensive counselling to reduce high-risk behaviours which expose them to HIV infection. Initially it was debated that counselling will eliminate risk-taking behaviour totally, rendering the trial worthless, but this expectation has not materialised.[205]

- *Increased community awareness of scientific and epidemiological aspects of the HIV virus*

Through information campaigns and counselling, communities learn more about vaccine science and disease prevention. Although some communities may be well-informed already on these issues, others will benefit from additional knowledge.

- *An efficacious HIV preventive vaccine*

Most writers seem to forget the development of an efficacious preventive HIV vaccine as a potential benefit of trial participation. Such a vaccine will not only benefit the trial participant, but society in general. Such a benefit is immeasurable.

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202 They are identifiable if they belong to a specific group, such as pregnant women, new-born babies, and so on. They are unidentifiable if they belong to society in general, such as instances of research aimed at bettering our understanding of the risk factors for contracting a certain disease, research on blood or tissue samples of healthy volunteers, etc.

203 Francis *et al* (n 184 above) 153.

204 Whether trial participants who become HIV positive during a vaccine trial should have access to ARVs for the rest of their lives, is an important and much-debated issue, but lies outside the scope of this thesis. In this regard, see Tangwa (2001) *Developing World Bioethics* 156; Resnik (2001) *Developing World Bioethics* 11; Barry and Rawarth (2002) 16 *Ethics and Intl Affairs* 57.

205 See eg Francis *et al* (n 184 above).

The MRC guidelines instruct us to consider both the 'probability of benefit as well as its magnitude'. In the case of HIV vaccine efficacy trial participation, the first four benefits mentioned above at least are likely to occur or are 'probable'. It is probable that individuals and communities taking part in vaccine trials will benefit from increased medical attention, counselling on risk-taking behaviour and an increased knowledge about scientific concepts and knowledge about the epidemiological aspects of HIV.

In the case of the last potential benefit mentioned above, that of finding an effective vaccine for HIV, there is little doubt about the magnitude of the potential benefit. However, one should also consider the probability of the benefit. At best the probability of finding an effective vaccine is unknown at this stage; or worse, unlikely. In the case of an individual trial and an individual participant, such a probability cannot be very great, especially not during earlier trials, as many scientists predict that an effective HIV preventive vaccine is at least ten years in the future.

The above benefits reflect some of the reasons why preventive HIV vaccine trials are going ahead and are attracting participants, despite the precarious nature of the knowledge so far gained about the possible risks and side-effects of these trials.

c) Incentives for participation

A few studies have empirically analysed trial participants' motivations for participation in preventive HIV vaccine trials.[206] These are outlined below.

David Celentano *et al* identify the principal inducement to participate in a preventive HIV vaccine trial as being access to health insurance (62 per cent of the respondents in the questionnaire chose this as their primary reason for potential participation – framed in the questionnaire as a 'five-year family health insurance plan').[207] Almost 25 per cent of respondents, however, indicated that no incentive was needed, and that, even if no reward were offered, they would participate out of altruism.[208] Other participants indicated that they would participate in the hope of

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206 See eg Celentato *et al* (n 182 above) 1079; Mills *et al* (2004) 18 *AIDS* 2235 – 2242; Mills *et al* (2006) 3 *PLosMedicine* 309; and Strathdee *et al* (2000) 4 *AIDS and behaviour* 1079.

207 Celentato *et al* 1081.

208 As above.

'personal recognition'.[209] Interestingly, large financial incentives were selected by very few participants as a reason for their participation.[210]

d) Disincentives for participation

Disincentives for participation were identified. These were concerns about the safety of the candidate vaccine being tested,[211] fear of acquiring HIV through vaccination,[212] and concerns about the notions of 'voluntarism' in this context.[213]

Strathdee *et al* carried out research among HIV-negative IDUs and young gay and bisexual men in Vancouver, Canada. Their results show that a greater willingness to participate in HIV preventive vaccine trials is associated with a greater threat of possible HIV infection, higher depression scores and participation in needle exchange programmes.[214]

Mills *et al* investigated women's incentives and disincentives for participating. Barriers to women's participation in HIV vaccine efficacy trials are the following:[215]

- their fears about contracting HIV from the vaccine;
- testing positive for antibodies to HIV;
- the effect of the vaccine upon future pregnancies;
- appearing to distrust one's partner;
- mistakenly being viewed as HIV-infected;
- their partner refusing sex due to the women's involvement in the trial;
- discrimination against the participant;
- being refused entry into countries, or difficulties with immigration;
- potential job loss;
- the possibility of receiving a placebo;
- being unable to obtain insurance if they are infected during the trial; and
- the lack of convenient clinic hours for mothers, domestic workers, and sex workers.

An analysis of the socio-economic and political context of preventive HIV vaccine trials in South Africa is presented below.

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209 As above.
210 1081.
211 1080.
212 1081.
213 1081.
214 Strathdee *et al* (n 206 above) 1079. 83% of respondents were potentially willing to participate.

2.3.2 Socio-economic and political contexts

This section outlines the socio-economic and political contexts in which (specifically Phase III) preventive HIV vaccine efficacy trials are likely to take place in South Africa, highlighting the link between a high risk[216] of HIV infection and socio-economic factors such as poverty, gender discrimination, detrimental cultural practices and the stigmatisation of people living with the virus, in order to set the stage for a discussion of the implications of such a link for ethical guidelines and human rights on informed consent in HIV vaccine trials in later paragraphs.[217]

a) Socio-economic context

Public health campaigns which proclaim that HIV 'knows no boundaries such as wealth, race, colour, gender or social status' are misleading (though, perhaps, not intentionally). Whether a person is at risk for HIV infection depends, not only on if that person practices safe sex, but, to a certain extent, be it indirectly, on the society and culture in which that person finds him or herself.[218]

Several studies have shown a correlation between poverty and HIV infection.[219] Poor people become infected not because they are poor, but because of the structural inequalities pervasive in the societies and cultures in which they live.[220] Anton Van Niekerk sums up the situation:[221]

> Viral diseases, as we know, do not all become epidemics. To become an epidemic, a niche or social context is required. In Africa ... poverty is the main aspect of this niche or social context.

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215 Mills *et al* (n 206 above) 309.

216 'Risk' is used here as an attribute of an environment, not of a group of people. See n 9 above on how the term is used in popular language to indicate a distinction between those 'at risk' and those 'not at risk'; between 'us' and 'them'.

217 See paras 3 and 4 below.

218 In this regard, see eg Over 'The Effects of Societal Variables on Urban Rates of HIV infection in Developing Countries: An Exploratory Analysis' in Ainsworth *et al* (2000) who remarks that 'social, cultural and economic conditions will influence the frequency of risky sexual behaviour'.

219 See eg Barnett and Whiteside (n 30 above) 124 - 156, 159 - 181, 182 – 195; Van Niekerk in Van Niekerk and Kopelman (n 35 above) 53 - 70; Benatar in Van Niekerk and Kopelman 71 - 83. Barnett and Whiteside comment: 'Thus relative wealth reduces vulnerability at all levels from the individual to the nation. These resources are not purely financial; they may include skilled labour, or access to care; even a strong, cohesive and compassionate civil society' (167).

220 There is a correlation – but poverty is not the cause of HIV-infection, it is the economic context in which HIV thrives. President Mbeki (mistakenly) regards poverty as the cause of HIV/AIDS (in this regard, see Van Niekerk 'Moral and social complexities of AIDS in Africa' in Van Niekerk and Kopelman 53 - 54.

221 Van Niekerk in Van Niekerk and Kopelman 55.

After infection the progression of the disease is an expression of economic and / or social inequality. The rich can afford ARVs, the poor cannot. The rich stay healthy longer because of better access to health care, better nutrition and better living standards. This is not only true for the individual, but also for communities, countries, regions and continents. Judge Edwin Cameron comments as follows:[222]

> I can take these tablets, because on the salary I earn as a judge, I am able to afford their cost ... In this I exist as a living embodiment of the iniquity of drug availability and access in Africa ... My presence here embodies the injustices of AIDS in Africa, because, on a continent in which 290 million Africans survive on less than one US dollar a day, I can afford monthly medication costs of about US $400 per month. Amidst the poverty of Africa, I stand before you because I am able to purchase health and vigour. I am here because I can afford to pay for life itself.

In the case of women the divide between rich and poor is even more marked: in developed countries, generally, women living with HIV/AIDS are able to stay healthy longer and enjoy a better quality of life. In pregnancy, they have access to Nevirapine and other antiretrovirals which prevent the transfer of HIV to their child. In less developed countries, women on the whole lack access to health care, also to HAART. They get ill sooner, and inevitably die of AIDS. In pregnancy, their chances are one in three of passing HIV on to their children: '[t]hus relative wealth reduces vulnerability at all levels from the individual to the nation'.[223]

HIV infection is both a cause and a consequence of poverty. Poverty increases the conditions which lead to an increased risk of HIV infection, while HIV infection increases vulnerability[224] to poverty. For example, poverty increases vulnerability to HIV infection due to poor nutrition, lack of access to health care (which would, for example, treat STDs which are risk factors for HIV infection), greater exposure to (sexual and other) violence, the necessity of engaging in transactional sex and the lack of knowledge about preventive methods, and so on. HIV infection, on the other hand, increases poverty because it results in long periods of illness, the death of breadwinners, job loss, lack of access to education, discrimination in the labour market, young children becoming orphans, the increase in single-parent families, and the like.

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222 Cameron (2000) First Jonathan Mann Memorial Lecture: 'The deafening silence of AIDS' XIII International AIDS Conference, Durban, 7-14 July.

223 Barnett and Whiteside (n 30 above) 167.

224 'Vulnerability' is used here as indicating those features of an individual or a society which make it more or less likely to become infected with HIV.

The HRC's 'South African national HIV prevalence, HIV incidence, behaviour and communication survey 2005' (HSRC's survey or survey) bears out the link between poverty and HIV infection rate.[225] The survey distinguishes between HIV prevalence rates for people living in formal and informal settlements, and in rural and urban settings. The HRC's survey shows that people living in informal settlements (and therefore belonging to a lower socio-economic group) have a much higher HIV prevalence rate than those in formal housing (urban informal settlements 25.8 per cent prevalence, rural informal settlements 17.8 per cent; compared to 13.9 per cent for both rural and urban formal housing).[226]

Anton Van Niekerk comments that poverty:[227]

> has accompanying side-effects, such as prostitution, (ie the need to sell sex for survival), poor living conditions, education, health and health care, that are major contributing factors to the current spread of HIV/AIDS.

The 'side-effects' of poverty pointed out by Van Niekerk have important implications for the design and conduct of clinical trials in these communities. In poor and desperate communities, where resources are scarce and opportunities even scarcer, where there is limited access to health care, and where unemployment and poverty are the order of the day, research participants may be especially vulnerable to exploitation.[228]

South African women are worse hit by the epidemic than men, not only because of the socio-economic factors above, but also because of biological factors.[229] The HRC's survey shows that women between the ages of 15 and 49

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225 HSRC (n 25 above) 40. Different HIV prevalence studies yield different results. In 2004, the Department of Health published the 2004 National HIV and Syphilis antenatal sero-prevalence survey, which, based on a sample of 16 061 women at antenatal clinics across the country, the survey estimated that in 2004, 29.5% of pregnant women in South Africa were HIV positive and that a total of 6.29 million South Africans were living with HIV. These results are higher than the results obtained by the HSRC's survey, but there may be explanations for this discrepancy (see n 231 below).

226 As above.

227 Van Niekerk in Van Niekerk and Kopelman (n 35 above) 55.

228 Ruth Macklin defines exploitation as occurring 'when wealthy or powerful individuals or agencies take advantage of the poverty, powerlessness, or dependency of others by using the latter to serve their own ends without adequately compensating benefits for the less powerful or disadvantaged individuals or groups' Macklin (2003) 17 *Bioethics* 475.

229 'Several anatomical and physiological characteristics of women and girls play a role in the transmission and acquisition of HIV. Since the female genital tract has a greater exposed area than the male genital tract, women may be prone to greater per exposure risk of HIV-infection. Coercive or forced sex can lead to microlesions (very small tears in the vagina) that facilitate entry of the virus. Young women, in

have a HIV positive prevalence rate of 20.2 per cent (the antenatal survey of 2004 showed a prevalence rate of 29.5 per cent[230]), while men in the same age group have a prevalence rate of 11.7 per cent.[231] Women show a prevalence rate almost twice that of men.[232]

Adolescent girls and young women are also worse affected than adolescent boys and young men. In the HSRC's survey of youth between the ages of 15 and 24, females show a prevalence rate of 16.9 per cent, males only 4.4 per cent. The overall situation for youth between the ages of 15 and 24 living in informal settlements is dire – they show a prevalence rate of 25.8 per cent.[233]

It is not only poverty which increases the conditions which lead to an increased risk of HIV infection; in societies in which women are (considered) unequal to men, unequal power relations between men and women have a similar effect. These relations of unequal power are often the result of women's calamitous socio-economic status:[234]

> Women's relative powerlessness in heterosex is largely determined by material inequalities that obtain between women and men ... material inequalities that give rise to and are in turn supported by cultural and ideological constructions of gender.

In societies where women are denied access to education they are forced to find menial, low-paying jobs, or they make a living from selling sex to infected partners.[235] In such societies women become infected with HIV because they are

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particular, who have less mature tissue, are more susceptible to infection, as well as more susceptible to coercive sex' (IAVI (2004) 'Gender in HIV vaccine trials: Addressing challenges in developing countries' 2).

230 See n 231 below.

231 HSRC's survey 38. Incidentally, the HSRC's survey shows a lower overall prevalence rate than other surveys. This could be explained by the fact that other surveys base their statistics on results obtained from women attending antenatal clinics. On the whole, it is African women who attend public health facilities such as antenatal clinics, and they show a much higher prevalence than other race groups which are also included in the HSRC's survey (Africans show an overall HIV prevalence rate of 19.9%, whites 0.5%, coloureds 3.2% and Indians 1.0%) (see HSRC's survey 40). The HSRC's survey also compares the prevalence rate of African females to the 2004 results obtained from the Department of Health's antenatal survey. The results correspond closely – see HSRC's survey, 42.

232 There are biological / scientific reasons for this higher prevalence rate, such as women's anatomy making them more susceptible to the virus. See n 229 above.

233 HSRC's survey (n 25 above) 40. The situation is the same in other countries in Southern Africa. Hence the concern to include the youth in HIV vaccine efficacy trials.

234 Alexander and Mbali 'Beyond 'bitches and prostitutes': Folding the materiality of gender and sexuality into rights-based HIV/AIDS interventions' quoting Wilson (1997) *EnGendering AIDS* 29 in Viljoen (ed) (2005) 51.

235 See eg Karim *et al* (1995) 85 *American J Public Health* 1521.

unable to insist upon safe-sex practices or because of their poor state of nutrition and general health.

Traditional cultural practices, such as dry sex and polygamy[236] expose women to HIV infection;[237] even monogamous marriage may put women at risk. Virginia Van der Vliet comments as follows on expectations of married African women and their risk of HIV infection:[238]

> ... raised in [a] strongly patriarchal society, with a tradition of polygamy, macho ideas of masculinity, and an emphasis on her duty to bear children to ratify bridewealth contracts, [the married woman's] rights to demand fidelity or the use of condoms, or to refuse sex, are, for most women, not negotiable. Economic dependency on her partner weakens her position further.

Other factors exacerbate women's risk of contracting HIV. Anton Van Niekerk remarks:[239]

> ... the grim evidence of a rapid increase in so-called 'sugar daddy' relationships, in which older men seek out younger sexual partners (often mere children) – partly because of their (the men's) perception that young girls might not be infected, while they themselves, of course, often are – and a scary picture of the moral depravity of sectors of South African society emerges. This is an environment very conducive to the flourishing of the AIDS epidemic.

Women who live with HIV/AIDS are stigmatised (sometimes they are even blamed for spreading HIV):[240]

> Moreover, HIV-positive women in these communities [Hammanskraal and Temba] are stigmatised as being prostitutes, or 'loose women', or as having 'invited' HIV infection to claim access to social grants.

Occasionally, women living with HIV/AIDS are killed when they reveal their status, as in the well-publicised case of Gugu Dlamini who was stoned to death by her neighbours.

Stigmatisation leads to discrimination and a violation of equality:[241]

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236 See eg Pieterse 'Beyond the reach of law? HIV, African culture and customary law' (2000) 3 *J SA L* 431.

237 Eg dry sex and female genital mutilation (FGM). According to Marelise Richter, in her paper on 'Customary law, gender and HIV/AIDS in South Africa' (delivered on 4 August 2003, AIDS Law Project, Centre for Applied Legal Studies), many traditional cultural practices in Africa display an attitude toward women's reproductive ability as a legal object that can be bought and sold. This attitude, in turn, severely limits women's ability to refuse sex or unsafe sex, increasing women's risk of contracting HIV.

238 Van der Vliet (1999) July *Pulse Track* 3, quoted by Van Niekerk in Van Niekerk and Kopelman 62.

239 Van Niekerk in Van Niekerk and Kopelman (n 35 above) 62.

240 Alexander and Mbali in Viljoen (n 234 above) 51.

> The rights of people living with HIV/AIDS are often violated because of their presumed or known HIV status, causing them to suffer both the burden of the disease and the burden of discrimination. Stigmatisation and discrimination may affect the uptake of [antiretroviral] treatment, and may also affect employment, housing and other rights.

Even worse - women's (and men's) stigmatisation encourages the spread of HIV; because they fear stigmatisation, they do not get tested for HIV, persist in unsafe sexual practices, and the epidemic continues:[242]

> [t]his, in turn, contributes to the vulnerability of others to infection, since HIV-related stigma and discrimination discourages (*sic*) individuals infected with and affected by HIV from contacting health and social services.

It is important to emphasise the point made in the quote above: not only do poverty, women's inequality and stigmatisation create greater vulnerability to HIV infection, but they also compound a vicious circle whereby people who are infected with HIV are further stigmatised and discriminated against, creating greater poverty and inequality, and, in turn, causing the exposure of others to the disease. This self-perpetuating circle epitomises the relationship between poverty, gender inequality and stigmatisation and HIV infection. Poverty, gender inequality and stigmatisation increase the risk for HIV infection, and the impact of HIV infection deepens poverty, stigmatisation and gender inequality; putting others at risk of infection, and resulting in further impoverishment.

The MRC's vaccine trial guidelines explain this complicated interrelationship between poverty, women's inequality and stigmatisation, and its implications for HIV vaccine trials: [243]

> HIV/AIDS is a condition that is both highly feared and stigmatised, largely because it is associated with blood, sex, and illegal activities such as commercial sex. As these issues are difficult to address openly, people affected by HIV/AIDS in South Africa experience stigma, discrimination, and even violence. Vulnerability to HIV infection is greater *where people are marginalised* due to their *social or legal status*. These factors *increase the risk of social and psychological harm* for people participating in HIV vaccine trials. Additional efforts must be made to minimise these risks, and to ensure that risks are justified by the benefits. *Meaningful community participation and authentic informed consent are critical safeguards*.

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241 Zuberi ' "If you (be)come HIV positive, you will lose your human rights" - HIV/AIDS stigma and human rights: A localised investigation of Hammanskraal communities' in Viljoen 13.

242 As above.

243 Book V, 'Context' 4. My emphasis.

The socio-economic status of a community, thus, has important implications for the design and conduct of clinical trials, and for obtaining informed consent from participants.[244] Zion remarks:[245]

> ... in an environment where the majority can neither read or write and is wallowing in poverty and sickness, hunger and homelessness, and where the educated, the powerful, the rich, or the expatriate is a semi—god, how can you talk of informed consent?

b) Political context

Clinical research to find cures and treatments does not take place in a political vacuum. The selection of issues as 'research priorities' is determined by political agenda,[246] as is the funding of specific research.[247] HIV/AIDS vaccine research, especially, is unlikely to escape political point-scoring and bickering; particularly in South Africa, HIV/AIDS is a highly politicised issue.

The HIV/AIDS epidemic in South Africa has often met with silence, denial, and apathy on the part of the government. At the outset, President Mbeki denied or downplayed the existence of the epidemic.

> No-one has sounded the alarm where I work daily in the Presidency and nobody has said there is a particularly alarming tendency of people dying. There has not been any indication ... in the Presidency nobody has said we are losing 10 per cent of our staff every year because of AIDS.[248]

The President's stance on the causes of AIDS, and the insistence by the Minister of Health, Dr Manto Tshabalala-Msimang, on the efficacy of dietary treatment of the disease, internationally, have caused alarm. In effect, attitudes such as these

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244 These implications are discussed in paras 3 and 4 below.

245 Zion quoted by Moodley in Van Niekerk and Kopelman (n 35 above) 174.

246 For example, the controversy surrounding stem-cell research in the USA and in other countries.

247 Powerful political lobbies advocate cancer research, and even the supply of expensive drugs to people suffering from cancer (eg the demand by activists that Herceptin, an expensive breast-cancer drug, be supplied to women on Britain's National Health system).

248 President Thabo Mbeki, in an interview with *City Press*, quoted by Mark Heywood. President Mbeki has also denied the very existence of a causal link between HIV and AIDS. See eg, TAC 'Statements by South African President Thabo Mbeki on the subject of HIV/AIDS' available at <http://www.tac.org.za/Documents/Other/Mbeki-on-HIVAids-Updated.doc> (5 October 2006).
On possible reasons for this denial, see Van Niekerk in Van Niekerk and Kopelman (n 35 above) 58.

denigrate legitimate attempts by scientists to develop treatments such as ARVs or an effective vaccine. Nicoli Nattrass pointedly observes:[249]

> Dr Manto Tshabalala-Msimang has fought a rear-guard action by resisting the introduction of antiretrovirals for mother-to-child transmission prevention (MTCTP) – until she was forced to do so by a Constitutional Court ruling – and by resisting the introduction of highly active antiretroviral therapy for AIDS-sick people until a cabinet revolt in late 2003 forced her to back down on this too.

Nattrass claims further that the Minister of Health personally has continued to undermine the rollout of ARV treatment in the public sector, *inter alia* by supporting the use of unproven substances and by couching her position in a dissident discourse that highlights the side-effects of antiretrovirals, portraying them as 'poison'.[250]

In a paper entitled 'HIV/AIDS and South Africa's war on science',[251] Jonathan Berger outlines a 'state-sponsored campaign [by President Mbeki and Dr Tshabalala-Msimang] of promoting untested remedies coupled with an attack on evidence-based medicine'.[252] He concludes the campaign is a consequence of a failure to deal decisively with the aftermath of President Mbeki's public embrace of AIDS denialism and results in the promotion of untested medicines, traditional, 'complementary' or 'alternative'.[253] Berger cites instances of what he terms an indirect attack on evidence-based medicine and its expression in South African policy and law;[254] as well as a law-making agenda which seeks to expand the powers of the executive.[255]

Berger quotes Natrass to the effect that scientists have been portrayed by the government in its campaign 'as, at worst, biased spokespeople for the

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249 Nattrass (2006) 'AIDS, science and governance: The battle over antiretroviral therapy in post-apartheid South Africa' available at <http://www.aidstruth.org/nattrass.pdf> (30 September 2006).

250 As above. Also see Fourie (2006) 164 - 166.

251 Berger 'HIV/AIDS and South Africa's war on science' Paper delivered at the XVI International HIV/AIDS Conference, Toronto, Canada, 13 -18 August 2006.

252 As above, 2.

253 The campaign misrepresents and/or distorts the available evidence; raises legitimate concerns regarding the pharmaceutical industry and its pursuit of profit at (almost) all costs; and appeals to sensitivities regarding culture, tradition and colonialism's assault on traditional knowledge systems (n 251 above, 2 – 4).

254 For example, by failing to take decisive action against those who act in defiance of the provisions of the Medicines and Related Substances Act, 1965 and its regulations; and actively facilitating unlawful activity in contravention of the Medicines Act (n 251 above, 2 – 4).

255 For example, reducing Parliament's Portfolio Committee on Health to a rubber-stamp body without oversight authority; undermining the independence of regulatory authorities under the guise of 'transformation'; and centralising control in the hands of the Minister of Health by investing her with unguided, overly broad (and frequently inappropriate) discretionary powers. (n 251 above, 2 – 4).

pharmaceutical industry, and at best, as promoting scientific protocols that are inappropriate for traditional or alternative medicines'.[256] Natrass is outspoken on the consequences of discrediting legitimate science and scientists:[257]

> Once science is discarded as the best yard-stick of efficacy, patients are at the mercy of charlatans selling unproven substances. Responsible governments should not place them in this position – especially in this age of AIDS when so many people's lives are at stake.

Pieter Fourie in *The political management of HIV and AIDS in South Africa*, outlines three consequences of the administration's (in)actions: the specific policy problem of treatment has been monetarised; civil society has had to resort to litigation to enforce citizens' rights; and the artificial separation of prevention from treatment policy response strategies have become increasingly politised and entrenched.[258] He remarks that despite evidence that it is more expensive *not* to treat people living with HIV with ARVs, the administration remains steadfast in its refusal to purchase and distribute these drugs.[259]

This position is not that of everyone in government, or of officials within the Department of Health, nevertheless, it is influential in establishing public opinion. In South Africa an 'attack upon science' manipulates the environment in which HIV vaccines are tested, is decisive in determining if HIV vaccine trials are regarded as worthwhile and a public good, and undermines clinical research which seeks to establish HIV vaccine efficacy. If the scientific basis of medicine and medical research is publicly cast into doubt by the powerful, then vaccine trial participants will feel mislead and confused.

Roy Mugerwa *et al* in 'First trial of the HIV-1 vaccine in Africa: Ugandan experience', demonstrate how the trial in Uganda was hijacked by politicians in order to win votes, and indicate the effect on the trial.[260]

Despite extensive efforts to prepare host communities for the trial, according to Mugerwa *et al* the first HIV vaccine trial on African soil was mired in difficulties. First, misconceptions arose about the purpose of the trial among the general public and trial participants;[261] these ranged from the belief that the vaccine would protect

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256 See Natrass (n 249 above) quoted by Berger 3.
257 As above, 25.
258 Fourie (n 250 above) 163.
259 As above, 164.
260 Mugerwa *et al* (2002) 324 *British Med J* 226-229.
261 Mugerwa *et al* 226.

against unsafe sex or that participants were to be injected with HIV to the conviction that participants would be exposed deliberately to persons with HIV.[262] Most of the misinformation originated in false and conflicting rumours and media reports on the vaccine.[263] Media writers, reporters and editors failed to perceive the fundamental distinction between a vaccine and a drug and confused the vaccine with HAART,[264] resulting in a demand that the vaccine be given to as many people as possible.[265] The Ugandan government's polio vaccine campaign was disrupted by allegations that the vaccine was contaminated with HIV.[266]

Over and above such misunderstanding, the situation of misinformation and confusion was used by Ugandan government officials and politicians to win political points; fears were expressed that Ugandans were being used as guinea pigs for experiments that could not be done in the West.[267] The safety of participants became a much-debated public issue. Prominent Ugandan scientists claimed that the virus used in the manufacture of the vaccine might replicate in humans and cause wide-spread disease.[268] Such disagreements among scientists added to the public's confusion.[269]

Not only HIV-related scientific research and HIV-related health care, but health care in general in South Africa suffer as a result of government inaction, misguided policy and the mismanagement of resources. Despite a commitment to combat HIV, exemplified in policies such as the HIV/AIDS/STD strategic plan for South Africa 2000-2005,[270] the government has allowed delays in the provision of ARVs,[271] with the loss of many lives.

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262 As above.

263 As above.

264 Mugerwa *et al* (n 260 above) 226.

265 As above.

266 As above.

267 As above, 227. In the Ugandan Parliament, the following remark was made by a Minister:
'This vaccine should be tried on animals in the National Park. President Museveni has sanctioned its use on Ugandans in exchange for money to finance his war in the Congo'.

268 As above.

269 Mugerwa *et al* (n 260 above) 227. Furthermore, the lack of an adequate national regulatory and control body in Uganda to approve the research delayed the research considerably. Six different local committees, one on ethics, science, technology, etc, had to be convened to approve the protocol.

270 Issued in 2000, and intended as a broad national strategic plan to guide the South African response to the HIV/AIDS epidemic. The strategic plan is based on an integration of STD, HIV/AIDS and TB care and responses. It centres on the strategies of prevention, management and care.

In November 2003, the Operational Plan on Comprehensive Care and Treatment for HIV and AIDS (Operational Plan) was adopted in Cabinet. The Operational Plan stipulates, among other requirements, that the Department of Health works together with the Department of Correctional Services to implement the Operational Plan in prisons, giving prisoners access to ARVs. The case of *EN and Others v Government of the Republic of South Africa and Others*[272] arises from the failure of the Department of Correctional Services to implement the operational plan and ensure access to ARVs in prisons. The action was brought by fifteen inmates living with HIV and AIDS at the Westville Correctional Centre. The Department of Correctional Services alleges that it is unable to supply ARVs to prisoners because it is not accredited to provide such medication to prisoners, and because of security concerns surrounding ARV roll-out centres located off-site.[273]

The Durban High Court granted the relief sought by the applicants in ordering the Department of Correctional Services to remove the restrictions that prevented the applicants and similarly situated prisoners from accessing ARV treatment.[274] This matter did not end here as the government appealed the decision. In consideration of the prisoners' health, an application was brought to compel the Department to provide these prisoners with ARVs in the interim (while the outcome of the *appeal* was awaited). The Court granted an interim execution order. The government appealed the interim execution order as well. Judge Nicholson (the judge in the application for the interim execution order) has this comment on the appeal:[275]

> These have taken place – I gather – on extremely rare occasions. It is somewhat ironic and sad that both occasions relate to the government seeking to avoid the effect of court orders for the provision of ARVs.[276]

Civil society repeatedly has had recourse to the courts in an attempt to force fulfilment of the government's constitutional duty relating to the supply of ARVs.

In contrast Fourie points to official attempts to undo some of the damage done.[277] In the (national) Department of Health newly-appointed officials appear

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271 See *MEC for Health, KwaZulu-Natal v Premier, KwaZulu-Natal: In re Minister of Health and Others v Treatment Action Campaign and Others* 2002 (5) SA 717 (CC), 2002 10 BCLR 1033 (CC).

272 Case 4576/2006 (Durban High Court) (unreported).

273 Prisoners would have to be transported to these sites by the already short-staffed prison staff (see Muting and Mbazira (2006) 7 *ESR Review* 14).

274 Muting and Mbazira 15.

275 Judgement by Judge Nicholson, 28 August 2006, at para 15, quoted in Hassim (2006) 2 *Intl J Prisoner Health* 157.

276 Judge Nicholson is referring here to the *TAC* case, n 271 above).

277 Fourie (n 250 above) 188.

willing to speed up delivery of ARVs and other essential services to combat AIDS.[278] The Deputy Minister of Health has sponsored efforts to integrate HIV into the areas of health care and AIDS treatment and seems to view civil society as an ally rather than an enemy.[279] Amy Patterson sees as hopeful the understanding that HIV and AIDS pose the greatest threat to society:[280]

> The masses understand that AIDS, rather than recalcitrant whites, uncaring overseas corporations, or leftwing critics, threatens most menacingly to wipe out the gains of the liberation struggle. This realization, and its manifestation in renewed citizen activism, provides some hope for the long-term fight against AIDS in South Africa's new democracy.

At present, 80 per cent of South Africa's population relies on the public health care system.[281] Charles Ngwena writes as follows about the effects of transformation upon equity and the development of the South African health care system:[282]

> Given the phenomenal scale of transformation that has been taking place since the demise of apartheid, constraints and even contradictions are inevitable. Whilst the trajectory towards a health care system that embraces egalitarianism [and] equity is clear, so are the attendant problems and detracting factors. Providing universal health care is costly to a middle income country that does not have a national health insurance system.

Reports abound of the inability of the South African public health care system to cope with the demands made upon it. According to Benatar, in 1994, there was an opportunity[283]

> to develop a strong public health system offering balanced primary, secondary and tertiary services. Such a system would have been aided and strengthened by a small and strong private sector with many private medical practitioners also doing part-time work in public hospitals. But the pace and the extent to which privatisation has been allowed has largely destroyed this potential.

If we combine a divisive political environment with a health care system in which resources are stretched and HIV/AIDS is not a priority, then doubts arise if South Africa is really such an 'ideal setting for clinical trials to establish HIV vaccine efficacy'.[284]

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278 As above.
279 As above.
280 Patterson (2005) 146.
281 Van Niekerk in Van Niekerk and Kopelman (n 35 above) 56.
282 Ngwena (2003) 9 *Fundamina: A J Legal History* 132.
283 Benatar 'The lost potential of our health system' *The Cape Times* 14 January 2005 9, quoted in Van Niekerk and Kopelman 56.
284 See the discussion in the introduction to this section of the thesis, and n 28 where Abdool Karim is quoted as saying: 'South Africa is well-placed to play a valuable role in the global effort to find an HIV vaccine because the country has a well-established clinical trial infrastructure and capability in the midst of one of the world's worst HIV epidemics'.

2.3.3 Vulnerability of subjects to exploitation

Often poverty, a lack of resources, gender inequality and a lack of access to health care are the order of the day in communities with a high incidence of HIV infection. Because of the presence of these factors, such communities are vulnerable to exploitation in research.

It is certainly not true that communities in which these factors are present are at all times vulnerable to exploitation in research, or that communities which display the opposite characteristics are immune to exploitation. Vulnerability in this context is rather a matter of degree. Some communities, because of their characteristics, are more vulnerable to exploitation than others. The UN guidance document entitled 'Ethical considerations in HIV preventive research', in a similar context, points out that the usefulness of the 'developing/developed' terminology for assessing risk of harm and exploitation is limited, as it refers primarily to economic considerations which are not the only relevant factors in HIV vaccine research.[285] It is therefore important to identify the *particular* aspects of a social context that create conditions for exploitation or increased vulnerability for participants. The UN guidance document outlines characteristics which are considered to create the 'conditions for exploitation or increased vulnerability'.[286] They are governmental, institutional or social stigmatization or discrimination on the basis of HIV status (which is present to some extent in South Africa);[287] an inadequate ability to protect HIV-related human rights, and to prevent HIV-related discrimination and stigma, including those arising from participation in a HIV vaccine trial (which, again, may be present to some degree in the South African context);[288] social as well as the legal marginalization of groups from which participants might be drawn, such as women, IDUs, MSM and sex workers (to some extent present in South Africa); the limited availability, accessibility and sustainability of health care and treatment options;[289] the limited capacity of individuals or groups in the community to understand the research process, to understand the informed consent process;[290]

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285 UNAIDS (n 161 above) 23.

286 As above.

287 As above, 23 - 24. See guidance point 7 (and its commentary) of the Declaration of Helsinki (2000 rev) and guideline 13 of the CIOMS guidelines which outline similar characteristics. Also see para 2.3.2 above.

288 See para 2.3.1 above.

289 See para 2.3.2 above and ch 6 below.

290 See para 5 below.

and to be able to give freely their informed consent in the light of prevailing class, gender, and other social and legal factors.[291]

As indicated above,[292] most, if not all, of these characteristics may be present at potential Phase III preventive HIV efficacy trial sites in South Africa, some to a greater extent than others. However, the presence of these characteristics does not altogether rule out the possibility of ethical research taking place – they merely point to the *potential* for exploitation.[293]

A failure to include in research individuals or groups in this category necessarily will result in their being denied access to the benefits which obtain from research conducted in their community. In the case of HIV vaccine efficacy trials, these benefits include the important one of developing a clade C HIV vaccine to be used in South Africa, and other benefits, such as counselling on risk-taking behaviours or increased access to medical care.[294]

Ruth Macklin warns that efforts to protect vulnerable communities may amount to paternalism.[295] She points to the 1993 version of the CIOMS guidelines which read that 'Phase I and II vaccine studies should be conducted only in developed communities of the country of the sponsor'.[296] This guideline was criticised very strongly by developing countries. They argued that:[297]

> it is paternalistic and demeaning to developing country researchers and subjects alike, as it presumes an inability either to conduct the research properly or to ensure that subjects are adequately informed and not coerced or deceived into enrolling.

Macklin remarks further: '[t]his recommendation – designed to protect vulnerable populations from harm in biomedical research – was resented by developing country researchers and health advocates in these regional consultations'.[298]

To sum up, in seeking to protect vulnerable communities from exploitation, one should remember the following:

- Research in vulnerable communities is not by definition exploitative and unethical.

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291 As above.
292 Para 2.2.2.
293 Ruth Macklin expresses a similar view, see Macklin (n 228 above) 477: 'being vulnerable to exploitation need not result in being exploited'.
294 For a complete outline of these benefits, see para 2.2.1 above.
295 Macklin (n 228 above) 480. Also see Macklin (2004) 1 – 4; 95.
296 Macklin (n 228 above) 480.
297 As above.
298 As above. Also see Macklin (n 295 above) 4.

- Measures may be taken in vulnerable communities to exclude or limit exploitation.
- One should not deny vulnerable communities the opportunities which accompany research participation.
- Paternalistic attitudes should be avoided.

Vulnerability, however, is not only limited to the vulnerability of a society to being exploited during research. In the context of HIV/AIDS in South Africa, vulnerability also refers to the likelihood that a 'society will suffer adverse consequences resulting from increased illness and death'[299] if the research to find a vaccine for HIV does not go ahead. In other words, the risk of exploitation may be offset by the potential rewards that may be gained by research which helps to find a vaccine. Exploitation in research should thus be seen as one of many potential dire fates that may befall a vulnerable community. If no research is undertaken it may result in 'increased illness and death'. In this context, informed consent has a very important role to play.

The outline above of the socio-economic and political context in South Africa, contributing to the vulnerability of preventive HIV vaccine efficacy trial participants, is presented to contextualise issues of informed consent in HIV vaccine efficacy trials, which are discussed later.[300]

It should be evident that, because of the socio-economic and political environment in which preventive HIV vaccine trials take place, participants are especially vulnerable to exploitation.

2.3.4 The capacity of research ethics committees to assess the ethics of HIV vaccine research

The primary responsibility for the protection of the interests of research participants lies with the relevant research ethics committee.[301] However, as is mentioned in an earlier section, the ability of a REC to judge the potential for harm to research participants, to some extent at least,[302] depends on the knowledge of its members about the scientific field from which the specific clinical trial protocol originates.

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299 Barnett and Whiteside (n 30 above) 47.

300 See paras 3, 4 and 5 below.

301 See above, para 2.2.2.

302 It also depends on many other factors, such as the number of 'lay' members on the committee (the sensitivity of the committee to the community), the extent to which the committee is representative of South African society (the race and gender

In the case of HIV vaccine efficacy trials, it may very well be that the research ethics committee lacks knowledge in particular areas of vaccine research. In such a case, it becomes very difficult to protect participants from exploitation, especially in situations where participants are already at risk for exploitation because of their socio-economic or political circumstances.

Concern regarding the capacity of African research ethics committees to deal with research protocols, and in specific their ability to deal with HIV/AIDS-related protocols, has been raised before. For example, Hyder *et al* point out that many researchers in developing countries believe that members of RECs are more concerned about politics than with their role in protecting the interests of research participants.[303] Other problems faced by African RECs include their perceived lack of independence, problems related to conflicts of interest of committee members, problems in finding suitably qualified members to serve on RECs, their lack of financial and other resources, and so on.[304]

In South Africa, numerous initiatives have been started to build the capacity of RECs to assess the ethics of HIV vaccine trial protocols, such as SARETTI[305] and IRENSA.[306] Although they are undoubtedly of great value, it is as yet unclear what these initiatives have achieved.

A recent study by Milford *et al* sets out to empirically assess the resources and needs of RECs in Africa to evaluate HIV vaccine efficacy trial protocols.[307] Milford *et al* identified 71 RECs in fifteen African countries which potentially will evaluate HIV vaccine trial protocols.[308] Self-administered questionnaires were sent to each of these research ethics committees. A 61 per cent response rate was achieved.[309] The results of the questionnaire indicate the following:

- When asked to rate their capacity to review protocols for HIV vaccine trials, only one REC reported that it had excellent capacity in reviewing such protocols.[310]

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composition of the committee) and so on. In this regard, see Moodley and Myer (2007) 8 *J Med Ethics* 1.

303 Hyder *et al* (2004) 30 *J Med Ethics* 69 - 70.

304 See eg Loff *et al* (2002) 359 *The Lancet* 956; Benatar (2002) 54 *Social Science & Med* 1131-1141; London (2002) 92 *American J Public Health* 1079-1084; Milford *et al* (n 72 above) 1; Kasper (2002) 8 *Haemophilia* 166 - 169.

305 South African Research Ethics Training Initiative.

306 International Research Ethics Network for Southern Africa.

307 Milford *et al* (n 72 above).

308 As above, 2.

309 As above, 2 - 3.

310 As above, 3.

- All other RECs that responded to the questionnaire admitted that their lack of ethics training in HIV vaccine research was a challenge. Only 6 per cent of members of ethics committees had received *any* training in the assessment of HIV vaccine trial protocols.[311]
- 90 per cent of respondents considered the following training needs as crucial: scientific aspects of HIV vaccine trials; the determination of run phases; potential risks of HIV vaccine research; appropriate risk reduction strategies; post-trial access to benefits; placebo-controlled trials; monitoring and oversight; and a vaccine product not meeting the prevailing sub-type.[312]
- 97 per cent of RECs agreed that committee members had inadequate training in the assessment of HIV vaccine trial protocols.[313]
- 80 per cent agreed that they had inadequate resources and ability to monitor such protocols.[314]

Milford *et al* comment that 'the general finding from this study is that African RECs view their capacity to review HIV vaccine trial protocols as 'moderate to limited'.[315] '[T]raining in scientific aspects of vaccine research' was identified as the most pressing training need,[316] and RECs 'expressed the need for training in potential risks of HIV vaccine trials and appropriate harm minimization measures'.[317] The following table represents the responses of the RECs that agreed that certain issues were a challenge (taken from Milford *et al*):[318]

Agreed that issue was a challenge	***Overall***	***Had reviewed HIV vaccine protocols***
Lack of training: HIV vaccine trial ethics	97%	91%
Lack of ongoing training: Health research ethics	87%	73%
Lack of training: Health research ethics	87%	80%
Inadequate ability to monitor approved protocols	80%	91%
Competence to review HIV vaccine trial protocols	75%	64%

311 As above.
312 As above, 5.
313 As above.
314 As above.
315 As above, 5.
316 As above.
317 As above, 7.
318 As above.

Significantly, regarding the funding of RECs, Milford *et al* remark that:[319]

> [u]nderfunding suggests that ethical review may not be regarded as a core component of research. For ethics to be taken seriously, REC funding should be proportional to the funding of the scientific costs of the trials under review.

Should Milford *et al* be correct in their view that the lack of adequate funding for ethical review indicates that ethical review is not an important or core aspect of the research endeavour, it points towards a general lack of concern for the welfare of research participants. As ethical review is primarily aimed at protecting the interests of the participants in research, its neglect may lead to disastrous results.

Worse still, even though by their own admission this study is only a preliminary investigation and is not validated statistically, Milford *et al* have uncovered a serious lack of capacity of RECs to deal adequately with HIV vaccine research protocols. Research participants in Africa could thus be at the mercy of unscrupulous researchers who have their own interests to consider, which seldom include the welfare of research participants. As the guardians of the interests of participants in research, ethics committees have to have the ethical and scientific expertise to function adequately when assessing HIV vaccine research protocols.[320]

2.4 Conclusion

It is extremely urgent that HIV vaccine efficacy trials be undertaken.[321] Ironically, the very factors which promote the spread of HIV make certain communities in South Africa ideal candidates for HIV vaccine efficacy trials ultimately aimed at halting the spread of the disease.

This section outlines the economic, social and political context of HIV vaccine efficacy trials in South Africa, as well as a number of methodological and practical aspects of clinical trials, such as review procedures and investigator responsibilities. As such, the section functions to provide a background against which the protection extended to vaccine trial participants by ethical guidelines and the law on informed consent may be considered.

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319 As above, 8.

320 Unfortunately, it is impossible to ascertain information about specific instances in which RECs, due to a lack of expertise in HIV vaccine science, were unable to competently assess the scientific merits of a trial, as this is not information they readily share. However, the fact that 75% of the respondents in the study mentioned above felt that they lacked competence in the area is an indication that they feel themselves lacking in the necessary knowledge.

321 See para 3.5 of ch 2 for a discussion on the urgency of the need for an effective HIV preventive vaccine.

The discussion shows how aspects of the South African economic, social and political contexts, such as dire poverty, women's inequality, stigmatisation, poor access to health care and political denial and inaction not only increase certain communities' vulnerability to HIV infection, thereby accelerating the spread of the disease, but increase those communities' vulnerability to exploitation and abuse during HIV vaccine efficacy trials.

The examination of the different procedures, roles and responsibilities in human subject research in South Africa establishes the background against which methodological and procedural aspects of HIV vaccine efficacy trials should be viewed. As most HIV vaccine efficacy trials will involve internationally collaborative research efforts, an examination of the local guidelines governing such research is included to show the potential for exploitation existing in multi-centre trials.

The discussion in the last section, centring on the perceived lack of capacity of African RECs to deal adequately with HIV vaccine trial protocols, focuses on a cause for concern. The interests of research participants who are at risk for exploitation because of their socio-economic and political situation need to be protected by RECs; when those RECs feel that they are not adequately equipped to deal with HIV vaccine trial protocols, the question needs to be asked whether HIV vaccine trials in Africa and South Africa could ever be considered ethical and legal.

With that question in mind, the next section studies national and international ethical guidelines on informed consent that are relevant to preventive vaccine efficacy trial participation in South Africa.

3 ETHICAL GUIDELINES ON INFORMED CONSENT WITH REFERENCE TO PREVENTIVE HIV VACCINE EFFICACY TRIAL PARTICIPATION IN SOUTH AFRICA

3.1 Introduction

Because of their vulnerable situation, the potential exists that participants in HIV vaccine efficacy trials in South Africa may be exploited. Informed consent is regarded as one of the primary ways of ensuring that research participants are protected against exploitation. In this section, international and national ethical principles and guidelines relevant to informed consent in preventive HIV vaccine efficacy trials are discussed.

First, the international system is outlined. The Nuremberg Code and the World Medical Association's Declaration of Helsinki are discussed in so far as they pertain to informed consent in HIV vaccine efficacy trials in South Africa. The ethical guidelines on informed consent in the Belmont Report are outlined, as are the Council for International Organizations of Medical Sciences' (CIOMS) International Ethical Guidelines for Biomedical Research involving Human Subjects. The focus moves to the local system of ethical guidelines relevant to HIV vaccine efficacy trial participation, and the MRC Guidelines on ethics for medical research and its Guidelines on HIV preventive research are investigated. As well, the Department of Health's Good Practice Guidelines and HIV/AIDS research guidelines are investigated. Throughout the emphasis is on informed consent within the context of preventive HIV vaccine efficacy trials in South Africa.

For purposes of comparison each set of guidelines is discussed under the following headings:

i) Authority or legal force
ii) Capacity to consent
iii) *Informed* consent
iv) *Free* consent
v) Clear, unequivocal and comprehensive consent
vi) Revocable consent
vii) Prior consent
viii) Formalities

However, before attention turns to the actual ethical guidelines, the interaction between international and national ethical guidelines is discussed.

3.2 Interaction of international and national ethical guidelines on informed consent in South Africa

International and national systems of ethics co-exist in South Africa, as they do in many parts of the world. RECs in South Africa consider both international ethical guidelines and national guidelines as binding upon them.[322] This is despite the fact

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322 See Van Oosten, who holds the view that South African ethics committees regard the Declaration of Helsinki as binding upon them. Also, see the web-pages of several Schools of Health in South Africa. For example, the University of Pretoria's School of Health Sciences webpage proclaims that the Ethics Committee respect the

that international ethical guidelines, on the whole, are promulgated by different medical societies such as the World Medical Association (WMA) and the Council for International Organizations of Medical Sciences (CIOMS), and in theory are binding only upon the members of these societies.

Some international and local guidelines give guidance as to their authority and interaction with other local and international guidelines and principles. For example, the Declaration of Helsinki requires that researchers *consider* their own local legal and ethical guidelines, as well as international guidelines on ethics.[323] There is, in this case, no absolute duty on the researcher to follow local ethical and legal guidelines – she merely has to *consider* them. The Declaration states in principle A.9: 'No national ethical, legal or regulatory requirement should be allowed to *reduce or eliminate* any of the protections for human subjects set forth in this Declaration'.[324] The Declaration, therefore, considers itself the minimum standard that should be adhered to.

The above statement is controversial as, although considered an important international document dealing with ethics, the Declaration of Helsinki is a *declaration* of ethics and is without binding legal force. It certainly cannot have more force than local legislation as it is not a binding treaty, signed and ratified by member states. The only way in which the Declaration of Helsinki has binding force in a local legal system is if it is considered part of customary international law, and thus is binding on all states.[325] This possibility is discussed in detail below.[326]

The Nuremberg Code,[327] published as part of the judgment in the Nuremberg trials of war criminals before the Nuremberg Military Tribunals, is, similarly a declaration and does not have the force of law. Various opinions argue that the Nuremberg Code is part of customary international law and, as such, has binding legal force throughout the world. These arguments are also dealt with later.

The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research 1979 (Belmont Report)[328] was published by the

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Declaration of Helsinki, the CIOMS Guidelines, and other documents of ethics. See <http://www.up.ac.za/academic/healthsciences_old/ethics/> (31 July 2006).

323 Principle A.9. My emphasis.

324 My emphasis.

325 See para 3.4 in ch 4 above.

326 See below.

327 From the Trials of war criminals before the Nuremberg Military Tribunals under Control Council Law 10, Vol II Nuremberg, Germany, October 1946 – April 1949.

328 FR Doc 79-12065 (filed 17 March 1979); <http://ohrps.osophs.dhhs.gov/humansubjects/guidance/belmont.htm>;

American National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research[329] as a report in the Federal Register of the United States of America. Publication in the Federal register gives the Belmont Report official status as a statement of policy, and is not a set of binding legal rules or principles and guidelines.[330]

The International Ethical Guidelines for Biomedical Research involving Human Subjects (CIOMS Guidelines)[331] was published by the Council for International Organizations of Medical Sciences (CIOMS), a NGO founded under the auspices of the World Health Organization and the United Nations Educational, Scientific and Cultural Organization (UNESCO). CIOMS's task in the formulation the CIOMS Guidelines was to 'indicate how the ethical principles that should *guide* the conduct of biomedical research involving human subjects, as set forth in the Declaration of Helsinki, could be effectively applied, particularly in developing countries, given their socio-economic circumstances, laws and regulations, and executive and administrative arrangements'.[332] Again the CIOMS Guidelines are mere guidelines, as indicated by the use of the word 'guide', and are intended to be 'of use' in defining 'national policies on the ethics of biomedical research involving human subjects'.[333] Meier comments: 'International ethical guidelines, often drafted by the same suspect medical organisations discussed above, have proven to be illusory tenets in the practice of medicine. They are not widely accepted or followed by physicians'.[334]

The UNAIDS's Ethical considerations in HIV preventive vaccine research ethical guidelines (UNAIDS vaccine trail guidance document or guidelines), though relating to HIV vaccine efficacy trials, likewise, are guidelines – they do not have the force of law, even though they are comprehensive in their guidance.

At the local level, it appears as if the MRC Guidelines on ethics for medical research (MRC Guidelines) are the sole ethical guidelines in South Africa which have the force of law, as they have been promulgated in terms of a statute.[335] The MRC

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329 Established in 1974 by the National Research Act (Levine (n 2 above) 15).

330 See the official summary of the Belmont Report, para 3, available at <http://ohrp.osophs.dhhs.gov/humansubjects/guidance/Belmont.htm>.

331 The CIOMS Guidelines were published by the Council for International Organizations of Medical Sciences (CIOMS) in conjunction with the World Medical Association (WMA) in 1982, and were updated in 1993 and 2002.

332 CIOMS 'Background' to the CIOMS Guidelines, para 1. My emphasis.

333 As above, para 12.

334 Meier (2004) 30 *American J L & Med* 434.

335 See ch 3 above.

Guidelines govern all research carried out by or on behalf of the MRC, and research funded by the MRC and approved by its ethics committee.[336]

The Department of Health's Guidelines for good practice in the conduct of clinical trials on human participants in South Africa (Good Practice guidelines) state that the principles should be 'read in the context of the Declaration of Helsinki, October 2000, and the ICH Harmonised Tripartite Guidelines for Good Clinical Practice'. The Preamble declares that 'the Good Practice Guidelines are produced as *a reference text* for researchers, research sponsors, the general public and all those who have an interest in clinical trials research in South Africa'.[337] As a 'reference text' it is unlikely that the Guidelines have binding legal force. They 'provide *guidance* on minimum standards that are *acceptable* for conducting clinical trials in South Africa'[338] and aim to provide South Africa with 'clearly articulated standards of good clinical practice in research that are also relevant to local realities and contexts'. Though these are laudable objectives, they do not confer upon the Good Practice guidelines any more force than that of guidelines on ethics.[339]

The Good Practice guidelines are 'applicable to both academic and contract clinical research'. As they are not legal rules, however, there is little that the research participant can do if the Good practice guidelines are violated.

It has been argued that some *basic* ethical principles and guidelines, such as informed consent in the Nuremberg Code and the Declaration of Helsinki, have obtained the status of customary international law norms, and are binding on states irrespective of whether they have entered into a treaty.[340] It is submitted that this

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336 Van Oosten (n 11 above) 7.

337 My emphasis.

338 My emphasis.

339 Although the Good Practice guidelines 'are closely related to the regulatory requirements of the Medicines Control Council and those of the National Department of Health's legislative and regulatory framework' (Preamble, Good Practice guidelines) they do not go beyond 'ensur[ing] a standardised and ethical approach to clinical trial activities in South Africa'.

340 Various authors have commented on the possibility that ethical guidelines and rules may constitute customary international law. See eg Fidler (2001) 42 *Harvard Intl L J* 299; Bassiouni *et al* (1981) 72 *The J Criminal L and Criminology* 1597; Ford and Tomossy (2004) 1 *L, Social Justice and Global Development J*, available at <http://elj.warwick.ac.uk/global/issue/2004-1/fordtomossy.html> (31 July 2006); Teubner (2006) 69 *The Modern L Rev* 327; Kelleher (2004-2005) 38 *Columbia J L and Social Problems* 567; Todres (2000) 16 *New York L School J Human Rights* 737; Meier (n 334 above).
See also ch 4 above, paras 5.1 – 5.4.
To become a rule of customary international law, an ethical principle must be supported by general and consistent state practice; and there must be evidence that

view cannot be supported. First, the Nuremberg Code has received limited attention in domestic courts, making it unlikely that its contents - even its first principle - are widely recognised and practiced by states.[341] Second, the Declaration of Helsinki, while broadly endorsed around the world, remains an ethical code promulgated by a professional association (the World Medical Association). It is thus very limited in its scope of application.[342] Therefore, the status of either document as a source of customary law has yet to receive 'authoritative judicial consideration'.[343]

Keeping in mind their non-binding nature, the following paragraphs outline the international and national guidelines on ethics related to informed consent.

3.3 International ethical guidelines on informed consent in research

3.3.1 Nuremberg Code

As indicated,[344] the application of the Nuremberg Code is understood to be limited to non-therapeutic research.[345] The focus of the Nuremberg Code is on the individual. The individual is placed ahead of the results of any potential research project; the good of the majority does not take precedence over the well-being of the individual.

The first principle of the Nuremberg Code - the lengthiest - states that the voluntary consent of the human subject is 'absolutely essential'.[346]

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the general and consistent state practice is followed out of a sense of legal obligation, called *opinio juris*. See para 4.4.2 of ch 4 above.
It is argued that ethical principles 'have no inherent legal authority but are referred to by many regulatory bodies involved in formulating ethical guidelines or regulations for biomedical research' (Nuffield Council on Bioethics (1999) 6). Thus, it is argued, there is evidence of consistent state practice; also, that many national systems of law require adherence to the principles of ethics.

341 Ford and Tomossy (n 340 above) 3; Meier (n 334 above) 532.

342 As above.

343 Ford and Tomossy (n 340 above) 6.

344 See para 3.1.1 of ch 3 above.

345 This understanding of the reach of the Nuremberg Code is attributable to its origins – the atrocities committed by the National Socialist Government in Germany during World War II upon prisoners of war, and other, 'undesirable', persons.

346 The principle states:
The voluntary consent of the human subject is absolutely essential.
This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion, and should have sufficient knowledge and comprehension of the elements of the subject matter involved so as to enable him to make an understanding and enlightened decision. The latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and

After the initial broad statement that the voluntary consent of the individual is absolutely essential, the principle sets down the specifics regarding the nature of the informed consent and the specifics with which it has to comply. The following statements are important to the present study.[347]

i) Authority or legal force

Some have argued that the Nuremberg Code is an international legal document[348] and that the principle of informed consent as articulated in the Nuremberg Code forms part of customary international law.[349] This argument is discussed above.

ii) Capacity to consent

The principle states that the person who is consenting should have the 'legal capacity to give consent'. However, legal capacity is not defined, leaving the determination of legal capacity to the local legal system.

The Nuremberg Code does not make provision for proxy consent (in the case of minors and incompetent adults); as a result it is unclear whether the omission implies that proxy consent should never be allowed.

iii) Informed *consent*

She should have '*sufficient* knowledge and comprehension of the elements of the subject matter involved so as to enable her to make an understanding and enlightened decision'.[350] Note that it is not required by the Nuremberg Code that *all* information is shared, merely that the research participant has 'sufficient knowledge'. The Nuremberg Code is silent with regard to the nature of 'sufficient knowledge' which enables the participant to reach an informed consent.

The Nuremberg Code can be interpreted to allow 'sacrifice' of the individual with their consent in cases where the objective of the research project is important enough. That is, the code could be read as allowing experiments that would otherwise not be considered ethical. For example, because the search for an effective vaccine for HIV is of such importance, the Nuremberg Code may be read as

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hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.
The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

347 Principle 1 Nuremberg Code.

348 See Annas (1992) 2 *Health Matrix* 119.

349 See n 340 above.

allowing the sacrifice of the research subject for the greater good of society, provided the subject consents to participate in the research.

iv) Free *consent*

The person who is consenting[351] should be '*so situated* as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion'. Though comprehensive, the exact situational requirements that must be met before a research participant can be regarded as able to exercise 'free power of choice' are not detailed. The result is a value judgment on the part of the person initiating the research.

v) Clear, unequivocal and comprehensive consent

The principle makes it clear that the responsibility for making sure with respect to the 'quality of the consent' rests upon everyone who 'initiates, directs or engages in the experiment'; and is 'a personal duty and responsibility which may not be delegated to another with impunity'.

Full information has to be provided regarding 'all inconveniences and hazards reasonably to be expected', as well as 'the effects upon his health or person which may possibly come from his participation in the experiment'. The participant consents to all aspects of the proposed research.

vi) Revocable consent

The Nuremberg Code does not expressly require an awareness on the part of the research participant that her consent may be revoked.

vii) Prior consent

The Code expressly requires that, 'before the acceptance of an affirmative decision by the experimental subject' there should be made known to [her] the nature, duration, and purpose of the experiment' and 'the method and means by which it is to be conducted'. Prior consent is thus a requirement under the Nuremberg Code.

ix) Formalities

The Nuremberg does not prescribe any formalities that consent has to comply with.

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350 n 346 above; my emphasis.

351 The Nuremberg Code uses the male pronoun 'he' throughout.

3.3.2 Declaration of Helsinki

Guideline 20 of the WMA Declaration of Helsinki (2000)[352] requires that 'the subjects [of research] must be volunteers and informed participants in the research project'.

Guideline 22 sates:[353]

> In research of human beings, each potential subject must be *adequately* informed of the *aims*, *methods*, *sources of funding*, any possible conflicts of interest, institutional affiliations of the researcher, the *anticipated benefits* and *potential risks* of the study and the *discomfort* it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After *ensuring that the subject has understood the information*, the physician should then obtain the subject's *freely-given informed consent*, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

i) Authority or legal force

The Declaration of Helsinki is a code of ethics, and has no binding force in law. However, it is widely referred to by ethics committees and researchers.

ii) Capacity to consent

The Declaration of Helsinki does not give guidance regarding who has the legal capacity to give valid informed consent. This aspect is determined by local ethical and legal rules. However, the Declaration determines that where a person is legally incompetent to give informed consent, due to psychological and physical illness or minority, proxy consent should be obtained as prescribed by 'applicable law'.[354] However, the Declaration states that these groups should not be included in research unless the research is necessary to promote the health of the population represented and the research cannot be performed on legally competent persons.[355]

Further, should the legally incompetent persons be capable of understanding and agreeing, their consent, in addition to that of the authorised representative, is required.[356]

Research on individuals from 'whom it is not possible to obtain consent, including proxy or advance consent' should be performed only if the physical and / or mental condition that prevents obtaining informed consent is a necessary

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352 Reprinted in Levine (n 2 above) 427.
353 My emphasis.
354 Guideline 24.
355 As above.
356 Guideline 25.

characteristic of the research population.[357] It appears from this that under the Declaration of Helsinki non-therapeutic research is not permitted on mentally incompetent persons.

iii) Informed *consent*

Guideline 22 states that 'each potential subject must be *adequately* informed of the *aims*, *methods*, *sources of funding*, any possible conflicts of interest, institutional affiliations of the researcher, the *anticipated benefits* and *potential risks* of the study and the *discomfort* it may entail'.

It is not clear what the description 'adequately informed' entails. It is possible for the researcher (the Declaration is after all aimed at the members of the WMA) to pass judgment on or ignore the point of view of the research participant.

iv) Free *consent*

In guidelines 20 and 22 the Declaration of Helsinki requires that consent should be given freely. Apart from these requirements, Guideline 23 requires that when obtaining informed consent 'the physician should be particularly cautious if the subject is in a dependent relationship with the physician' or she 'may consent under duress'. If the subject is in a 'dependent relationship', the informed consent should be 'obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship'.[358] Persons who are poor, uneducated, or belong to a lower socio-economic group, who are open to coercion, are protected by this principle.

v) Clear, unequivocal and comprehensive consent

From the phrase, '[a]fter *ensuring that the subject has understood the information'*, responsibility for ensuring that these aims are achieved clearly rests with the individual researcher. Although it is not stated what makes consent comprehensive, the subject should be 'informed of the *aims*, *methods*, *sources of funding*, any possible conflicts of interest, institutional affiliations of the researcher, the *anticipated benefits* and *potential risks* of the study and the *discomfort* it may entail'.[359]

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357 Guideline 26.
358 Guideline 23. Also see Meier (n 334 above) 525.
359 Guideline 22.

vi) Revocable consent

According to guideline 22, the subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal.

vii) Prior consent

Prior consent is implied (by the fact that the consent is sought after the information on the project is given) but it is not expressly stated as a requirement in the Declaration of Helsinki.

viii) Formalities

Guideline 22 requires that the 'physician [...] obtain the subject's *freely-given informed consent*, preferably in writing'. Written consent is thus not an absolute requirement by the Declaration of Helsinki, but is strongly advised: 'If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed'.

3.3.3 The Belmont Report

The Belmont Report summarises the three ethical principles (respect for persons, beneficence, justice) that are fundamental to the specific ethical rules formulated in documents such as the Nuremberg Code. It is the sole international code of ethics that expresses the ethical framework for the various guidelines and principles. On informed consent, the Belmont Report determines in Part C as follows:

> Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards of informed consent are satisfied.
>
> While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

The Belmont Report then proceeds to describe each of the elements.

i) Authority or legal force

The Belmont Report is a document containing ethical principles and has no binding legal force. It is regarded as authoritative in the USA, but its status in the rest of the

world is variable. Research sponsored by any agency of the American state has to comply with the Belmont Report.[360]

ii) Capacity to consent

The Report does not specify who has the capacity to consent, leaving it to the legal system of the individual country to determine; but it does take notice of the fact that:[361]

> not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental ability, or circumstances that severely restrict liberty.

iii) Informed *consent*

With regard to the information requirement, the Belmont report notes, '[e]ven when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation'.

With regard to comprehension, the Belmont Report declares: '[b]ecause the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities'.

iv) Free *consent*

'Voluntariness' is viewed as essential and valid consent is obtained only when that consent is given 'free from coercion or undue influence'. The Report notes in this regard that the situation in which the research participant finds herself is vital in determining undue influence: 'inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable'.

v) Clear, unequivocal and comprehensive consent

The Belmont Report requires that the research procedure, the purpose of the research, risks and anticipated benefits, and alternative procedures (should the research involve therapy) should be clearly explained: 'investigators are responsible for ascertaining that the subject has comprehended the information'.

vi) Revocable consent

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360 Such as research sponsored by the National Institutes of Health, and so on.

361 Basic principles, I Respect for persons.

A statement offering the subject the opportunity to ask questions and to withdraw at any time from the research is required.[362]

vii) Prior consent

Prior consent is not explicitly required by the Belmont Report.

viii) Formalities

No formalities are required by the Belmont Report.

3.3.4 The CIOMS Guidelines

In Guideline 1 (of the CIOMS Guidelines)[363] there is the requirement that:

> [f]or all biomedical research involving human subjects, the investigator must obtain the informed consent of the prospective subject or, in the case of an individual who is incapable of giving informed consent, the proxy consent of a properly informed representative.

i) Authority or legal force

The CIOMS Guidelines have no binding force. Like the other international codes of ethics, it is a guidance document containing ethical principles which aim to direct behaviour.

ii) Capacity to consent

The CIOMS Guidelines do not give guidance as to who is capable of consenting to participate in research, leaving it to the legal system of the individual country to determine. Guideline 1 makes provision for proxy consent; 'in the case of an individual who is incapable of giving informed consent, the proxy consent of a properly informed representative' should be obtained. However, the CIOMS Guidelines do not declare when proxy consent is allowed; again it is left to the local ethical and legal system.

iii) Informed *consent*

With regard to the information requirement, Guideline 2 of the CIOMS Guidelines deals with 'essential information for prospective research subjects' that must be shared 'in a language that he or she is capable of understanding' before informed

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362 Part C Application, para 1.

363 The CIOMS Guidelines were published by the Council for International Organizations of Medical Sciences (CIOMS) in conjunction with the World Medical Association (WMA) in 1982, and updated these guidelines in 1993 and 2002.

consent is obtained. This information includes the following of relevance to the present study:[364]

- that the individual is invited to participate in research and the nature of the research;
- the expected duration of participation;
- benefits that might reasonably be expected to accrue to the subject or others;
- any foreseeable risks or discomfort to the subject, associated with participation in research;
- the extent to which confidentiality of records in which the subject is identified will be maintained; and
- the therapy that will be provided for research-related injuries.

iv) Free *consent*

The CIOMS Guidelines require that the research participant should be told that she is 'free to refuse to participate and free to withdraw from the research at any time without penalty or loss of benefits to which he or she would otherwise be entitled'.[365] It is the responsibility of the investigator to exclude the possibility of unjustified deception, undue influence and intimidation.[366]

Guideline 4 clearly prohibits undue inducement to participate in research. Guideline 8, which deals with research in 'underdeveloped communities', requires that every effort should be made 'to secure the ethical imperative that the consent of individual subjects be informed' and that the research proposals are reviewed and approved by an ethical review committee that has amongst its members 'persons who are thoroughly familiar with the customs and tradition of the community'.

v) Clear, unequivocal and comprehensive consent

Guideline 3 deals with the obligations of investigators with regard to obtaining informed consent from participants. The investigator has a duty to communicate to the prospective subject all the information necessary for adequate informed consent: give the subject an opportunity to ask questions; exclude the possibility of unjustified deception, undue influence and intimidation; and seek consent only after the

364 Guideline 2 CIOMS Guidelines.
365 Guideline 2 CIOMS Guidelines.
366 Guideline 3 CIOMS Guidelines.

prospective subject has adequate knowledge of the relevant facts and of the consequences of participation. [367]

vi) Revocable consent

A statement indicating that the participant is free to refuse to participate and free to withdraw from the research at any time without penalty or loss of benefits to which he or she would otherwise be entitled is required by the CIOMS Guidelines.[368]

vii) Prior consent

The researcher should seek consent 'only after the prospective subject has adequate knowledge of the relevant facts and of the consequences of participation'.[369]

viii) Formalities

The CIOMS Guidelines demand that, 'as a general rule' the investigator should 'obtain from each prospective subject a signed form as evidence of informed consent and renew the informed consent of each subject each time if there are material changes in the conditions or procedures of the research'. [370]

The requirement that the informed consent of the research participant is sought 'each time [...] there are material changes in the conditions and procedures of the research' does not appear in any of the other international guidelines. This requirement is an important aspect of informed consent and ensures the continuing consent of the research participant and protects the research participant in circumstances in which serious adverse effects are noticed during a clinical trail.

3.3.5 UNAIDS' Ethical considerations in HIV preventive vaccine research

The last of the international guidelines to be discussed is the UNAIDS' Vaccine trial guidance document. These guidelines are the most comprehensive of the international ethical guidelines examined so far, and deal with all aspects of HIV vaccine efficacy trials. The UNAIDS' vaccine trial guidance document demonstrates an awareness that trials take place in communities which may be vulnerable to exploitation, and makes context-specific recommendations.[371]

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367 Guideline 3 CIOMS Guidelines.
368 Guideline 2 CIOMS Guidelines.
369 Guideline 3 CIOMS Guidelines.
370 Guideline 3 CIOMS Guidelines.
371 See below.

Informed consent is covered in guidance point 12.

> Independent and informed consent based on complete, accurate, and appropriately conveyed and understood information should be obtained from each individual while being screened for eligibility for participation in an HIV preventive vaccine trial, and before s/he is actually enrolled in the trial. Efforts should be taken to ensure throughout the trial that participants continue to understand and to participate freely as the trial progresses. Informed consent, with pre- and post-test counselling, should also be obtained for any testing for HIV status conducted before, during, and after the research.

There are a number of important aspects of point 12 to be considered.

i) Authority or legal force

The UNAIDS' vaccine trial guidance document, as its name indicates, is not legislation or a binding regulation.

However, because of its practical applicability to the situation of HIV vaccine efficacy trials, the document will be relied upon extensively by research ethics committees. This is confirmed by Milford *et al* in their study on the resources and needs of research ethics committees in Africa in evaluating HIV vaccine efficacy trial protocols:[372] of all the international and local guidelines and guidance documents, 67 per cent of the members of research ethics committees who responded to the questionnaire rated the UNAIDS' vaccine trial guidance document the most appropriate when having to make a decision on the ethics of a proposed HIV vaccine-related clinical trial.[373] Respondents who had previously reviewed HIV vaccine trial protocols gave the UNAIDS' vaccine trial guidance document the highest rating; with a single exception.[374]

ii) Capacity to consent

The UNAIDS' vaccine trail guidance document does not prescribe who is capable of consent. However, the informed consent process, in the terms of reference of the explanatory notes, though acknowledging the difficulty, reinforces the *status quo* in the local community and unquestioningly follows local custom, regardless of whether it is repressive towards women:

> Other situations which make individual informed consent difficult include those in which an individual requires approval of another person or group in order to make decisions, where there is coercion, and where there is a cultural tradition of sharing risks and responsibilities, e.g. in some cultures where men hold the prerogative in marital relationships, where there is parental control of women, and/or where there

372 Milford *et al* (n 72 above).
373 Milford *et al* 4.
374 As above.

are strong influences by community and/or religion or hierarchy (see Guidance Point 13).

The explanatory notes do not condemn these practices, but insist that 'such authorization or influence must not be used as a substitute for individual informed consent. Nor should trials be conducted where truly individual and free consent cannot be obtained'.

iii) Informed *consent*

The guidance point stresses 'independent and informed consent', based on 'appropriately conveyed and understood information'. Guidance point 12 places the responsibility on the researcher to convey the information in an 'appropriate' manner. What is 'appropriate' will depend on the context in which the information is conveyed, and on the level of understanding of the trial participant. The information should be linked to what is *understandable* in the circumstances (particularly the level of education and literacy) of the individual trial participant. In the context of HIV vaccine efficacy trials in South Africa, it is submitted that an 'appropriate manner' implies that the possible risks and benefits and other important aspects of the trial be communicated in lay person's terms, that is, language that is non-scientific and non-technical – and easy to understand.

The explanatory notes emphasise that consent is 'informed', requiring that prospective are participants provided with the information:

- that they have been chosen as prospective participants because they are at relatively high risk of HIV infection;
- that they will receive counselling and access to the means of risk reduction (in particular, male and female condoms, and clean injecting equipment, where legal) concerning how to reduce their risk of infection; and
- that in spite of these risk reduction efforts, some of the participants may become infected, particularly in the case of Phase III trials where large numbers of participants at high risk are participating.

Further, participants should be informed of the experimental nature of the trial, that some of the participants will be receiving a placebo, and about the risk of physical harm, as well as psychological and social harm, of the types of treatment and compensation that are available in the case of harm and of services to which they may be referred should harm occur.

Prospective participants of Phase I, II or III trials should also be informed of the nature and duration of the care and treatment that are available, and how these are to be accessed if they become infected with HIV during the course of the trial.

The UNAIDS' vaccine trial guidance document provides the most context-specific requirements and these are accompanied by explanatory notes:

> A process of consultation between community representatives, researchers, sponsor(s) and regulatory bodies should be used to design an effective informed consent strategy and process. Issues such as illiteracy, language and cultural barriers, and diminished personal autonomy should be addressed in this consultative process.

This note ensures that informed consent is contextualised; that is, it is adapted to the specific circumstances that the trial participant finds herself in. An ethical and legal principle – informed consent – has been adapted to accommodate local circumstances, so that is relevant to local conditions but still ensures participant autonomy.

Another explanatory note reads:

> In some communities, special efforts may be required to achieve adequate understanding of 'cause and effect', 'contagion', 'placebo', 'double blind', and other concepts involved in the scientific design of the research.

The translation of scientific terms into the local languages of communities in which these terms are not familiar is required. In order to obtain consent that is 'informed', the explanatory notes make provision for cultural differences to be accounted for with reference to the agent that authorises the research:

> In some communities, it is customary to require the authorization of a third party, such as a community elder, in order for investigators to enter the community to invite individual members to participate in research.

Note the use of 'authorization ... to enter the community ... to invite individual members'. The wording indicates an understanding, although elders and other figures of authority in the community do not replace the need for individual informed consent, that, out of respect for local customs, researchers may approach them first to gain their consent to approach the members of 'their' community. This process of being 'cleared' by local authorities has been likened by one researcher to obtaining a visa to visit another country.[375]

iv) Free *consent*

The UNAIDS guidance document stresses that the '*independent* and informed consent'[376] of the participant should be sought. 'Independent' consent indicates that it is free from the influence of factors that limit autonomy and coerce participants.

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375 See Molyneux *et al* (2005) 61 *Social Science & Medicine* 433.

376 Guidance point 12.

In this regard it should be remembered, however, that an explanatory note refers to the role of community elders in providing 'authorization .... to enter the community ... to invite individual members' to consent. Although such authorisation does not replace individual informed consent, the fact that that elders have duly 'authorised' the research may place pressure, however subtle, on members of that community to participate. This potential problem is discussed in more detail above.[377]

v) Clear, unequivocal and comprehensive consent

Guidance point 12 places the responsibility on the researcher to convey the information in an 'appropriate' manner.

The UNAIDS' vaccine trial guidance document understands informed consent to be a process – hence the use of the phrase 'throughout the trial'. It is not only at the beginning of the trial that the participant is informed of the relevant issues concerning the trial, but the process of communication between the participant and the researcher should be ongoing. The responsibility is on the researcher continuously to make sure that the participant is still 'informed' and 'consenting'.

Guidance point 12 reiterates that the consent should be comprehensive: '[t]hroughout all stages of the trial and consent process, there should be assurance by the investigator that the information is understood before consent is given'; and '[e]fforts should be taken to ensure throughout the trial that participants continue to understand and to participate freely as the trial progresses'.

vi) Revocable consent

Guidance point 12 makes no reference of the need to inform participants that they may withdraw their consent and withdraw from the study at any time.

vii) Prior consent

Informed consent should be obtained at the beginning of the process, 'while being screened for eligibility for participation in an HIV preventive vaccine trial, and before s/he is actually enrolled in the trial'. Informed consent clearly is to be obtained in advance. 'Screened for eligibility' in this context refers to pre-enrolment screening which determines eligibility for participation; in other words, a negative HIV-antibody test result.

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377 This issue is discussed in greater detail in another context; see para 5.4 below.

The guidance point re-iterates that HIV-antibody testing should be accompanied by informed consent and pre- and post-test counselling: 'Informed consent, with pre- and post-test counselling, should also be obtained for any testing for HIV status conducted before, during, and after the research':[378]

> Informed consent, with pre- and post-test counselling, should also be given for any repeated tests for HIV status. Throughout all stages of the trial and consent process, there should be assurance by the investigator that the information is understood before consent is given.

The participant's consent given before the trial is not all-encompassing and excludes consent to repeated HIV-testing. Although this requirement places a heavy burden on the researcher, who has to ensure that the infrastructure for the necessary counselling is in place, it ensures an important benefit to the participant – counselling on risk-taking behaviour.

viii) Formalities

The UNIAIDS's Guidance document does not lay down any formalities with which the informed consent needs to comply.

South African RECs consider themselves bound by international documents of ethics.[379] In a study by Millford *et al* on the resources and needs of RECs in Africa (discussed above),[380] respondents to the questionnaire were asked to rate the appropriateness of a list of international ethical guidelines for use in their country when evaluating HIV vaccine research. The ratings that were used were 'very appropriate', 'somewhat appropriate', 'not really appropriate', or 'very inappropriate'.[381] The UNAIDS Guidance document was rated as very appropriate by 67 per cent of the respondents.[382] Of the RECs that had actually reviewed HIV vaccine protocols, all but one gave the UNAIDS guidelines the highest rating. 58 per cent of respondents said the Declaration of Helsinki was very appropriate, and 48 per cent rated the CIOMS guidelines as very appropriate.[383] According to the responses, the Belmont Report ranked lowest.[384] As well, all committees that in the past had

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378 Guidance point 12.
379 See para 3.2 above.
380 Millford *et al* (n 72 above) 4.
381 As above.
382 Millford *et al* (n 72 above) 4.
383 As above.
384 As above.

actually reviewed HIV vaccine trial protocols felt that all the guidelines that were listed were very appropriate for use in their countries.[385]

It will seem that, on the whole, RECs consider all international documents of ethics of use in evaluating HIV vaccine efficacy trial protocols, but the UNAIDS Guidance document is considered the most appropriate.

Important for the current study, an overwhelming percentage of ethics committees regarded it as a priority to develop appropriate national ethical guidelines.[386] The variable use of ethical guidelines across committees, insensitivity to local conditions, and the difficulty of adapting international guidelines to local conditions were all rated as important challenges to the use of guidelines by 70 per cent of respondents.[387] A total of 28 RECs from thirteen countries indicated that they would value assistance in adapting the UNAIDS HIV vaccine trial guidelines to fit local conditions.[388] It will thus seem as if RECs feel the need to 'localise' or contextualise international ethical guidelines for local circumstances. I return to this point later.

This concludes the discussion of international ethical guidelines on informed consent; below, national ethical guidelines are examined.

3.4 National ethical guidelines on informed consent in research

3.4.1 MRC Guidelines on ethics for medical research, specifically Book 5, which deals with HIV preventive vaccine research

Book I of the MRC Guidelines, which provides general principles on informed consent, proposes that informed consent is the moral and legal justification of research;[389] supplies extensive guidance on the capacity to consent;[390] describes the informational requirement of consent;[391] participant autonomy;[392] and the nature, scope and limitations of the investigator's duty to disclose;[393] and states that consent to participation should be free and voluntary.[394]

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385 As above.
386 As above.
387 As above.
388 As above.
389 Para 5 MRC Guidelines.
390 Para 5.3.1.
391 Para 5.3.2.
392 Para 5.3.2.2.
393 Para 5.3.2.3.
394 Para 5.3.2.4.

The general guidelines on informed consent contained in Book 1 will not be discussed further here, as Book 5 of the MRC Guidelines, entitled Guidelines on Ethics for Medical Research: HIV Preventive Vaccine Research (MRC vaccine trail guidelines) extensively covers informed consent in the specific context of HIV vaccine trail participation in South Africa. Nonetheless, the general guidelines will be referred to on occasion in the discussion of the MRC vaccine trial guidelines.

The MRC vaccine trail guidelines deal with informed consent in guidelines 12 and 13.[395] Guideline 12 declares:

> Independent and informed consent for participation, based on complete, accurate, and appropriately conveyed and understood information as well as its consequences, should be obtained from each individual who is legally competent to give consent. Consent should be obtained for screening for eligibility for participation in an HIV preventive vaccine trial, and before a participant is actually enrolled in a trial. Throughout the trial efforts must be made to ensure that participants continue to understand the consequences of participation and that they participate freely as the trial progresses. Informed consent, with pre- and post-test counselling, should also be obtained for testing HIV status before, during, and after the research.

Guideline 12 is followed by eleven explanatory notes which cross-reference other sections of the vaccine trial guidelines, Ethics Book 1, as well as the Good practice guidelines.

i) Authority or legal force

As pointed out at the beginning of this section, the MRC Guidelines are the only ethical guidelines in South Africa which have the force of law, having been promulgated in terms of a statute.[396] Van Oosten comments:[397]

> Obviously, all medical research undertaken by employees of the MRC and persons acting for or on behalf of the MRC, or with the assistance of the MRC, must be performed in accordance with the *Guidelines.* But medical research undertaken by employees of academic or other institutions and persons acting for or on behalf of academic or other institutions, or with the assistance of academic or other institutions, must conform to the ethical guidelines of the institution concerned. If no such guidelines exists in a given instance, it is submitted that the MRC's Guidelines should be followed ...

At present, researchers working for and on behalf of the MRC have several vaccine candidates in the pipeline, and because they are bound by the MRC guidelines, the

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395 Guideline 13 will not be discussed here as it is dealt with extensively in the section on informed consent in para 5 below.

396 See ch 3 above.

397 Van Oosten (n 11 above) 8.

MRC Guidelines Books 1 and 5 play an important role in guiding HIV vaccine research in South Africa.

ii) Capacity to consent

Guideline 12 should be read together with the section on capacity to consent in Ethics Book 1, which deals with general ethical requirements on capacity to consent.[398] Guideline 12.7 requires that 'legal requirements for capacity to consent must be met'. Guideline 12.7 does not give any guidance on where these legal requirements are to be found, or what should be done if these requirements are in conflict with each other,[399] or if there are conflicts between legal rules and ethical guidelines, such as Guideline 12.7. Guideline 12.7 lays down its own general rules regarding informed consent: persons above the age of 18 who are of sound mind may give valid consent to vaccine trial participation; if the person is below the age of 18 proxy consent by a parent or legal guardian is required; '[i]n certain circumstances persons below the age of 18 years are considered able to give their own consent'.

Guideline 18.7.1 reiterates the requirements laid down in Guideline 12.7, restating that persons above the age of 18, 'who are of sound mind, are generally considered capable of giving independent informed consent for participation in research',[400] and that, when persons below the age of 18 are to be involved in research, proxy consent from a parent or legal guardian must be obtained.

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398 Para 5.3.1.

399 See para 4.1.1 below for a discussion on the conflicting requirements regarding consent under South African law.

400 This is so even while inconsistency prevails in South African law regarding the age at which capacity to consent is presumed to be obtained. Various laws prescribe different ages for the individual consent of children. In terms of the new Children's Act, children over the age of 12 years are competent to consent, without the assistance of parent or guardian, to any 'medical treatment' and a person over the age of 18 years is competent to consent to an operation. In terms of the Human Tissue Act of 1983, a person of 14 years may donate blood; and in terms of the Termination of Pregnancy Act of 1996 a woman, that is a female person of any age, can consent to an abortion. See also fn 407 below.

In South African law, in a few defined circumstances, persons *under* the age of 18 are considered able to have full legal capacity to give their own consent to participate in research. So called "emancipated minors" include persons under the age of 18 years who are married, widowed or divorced, or who have applied for emancipation and it has been deemed by a court that they are competent to administer their affairs, and that their best interests are served by anticipating majority. As this is a complex and emerging area in the law, legal advice should be sought.

Regarding the capacity of children to consent to HIV vaccine trial participation, Guideline 18.7.11 determines as follows:

> Therefore, the enrolment of children in HIV vaccine research in South Africa requires informed consent from a parent or legal guardian, and assent from the child, according to his or her evolving capabilities.

Several elements are worth mentioning here. First, it seems as if the MRC vaccine trial guidelines regard children as persons below the age of 18. This view is in line with the Constitution[401] and the new Children's Act.[402] Second, Guideline 18.7 states that if children are to participate in HIV vaccine research they will need the proxy consent of their parents or legal guardian. The confusion that exists whether HIV vaccine research may be classified as therapeutic or non-therapeutic research is evident in Guidelines 18.7.2.1 and 18.7.3:

> If a research ethics committee classifies an entire HIV vaccine trial protocol as "therapeutic research" it is possible that *independent* consent for participation could be secured from children who are *14 years and older*. However the permission of the parents or legal guardian is *still highly desirable*. The participation of children who are under 14 years would require parental consent as well as assent from the child according to his or her evolving capabilities.[403]
>
> - and -
>
> If a research ethics committee classifies an entire HIV vaccine trial protocol as "non-therapeutic research", parents must provide proxy consent for participation and the child must assent (according to his or her evolving capabilities), provided that the risks are no more likely and no greater than the risk attached to routine medical or psychological examination of children, or the risk that is normally encountered in the daily lives of people in a stable society (see Point 18.6.1). Where there is an over-riding medical or scientific rationale, such risks may be slightly increased (see Point 18.6.1.1).[404]

Guidelines 18.7.2.1 and 18.7.3 contrast sharply with the conditions laid down by the National Health Act[405] in section 71[406] and by the Children's Act, in sections 129(1) to 129(10).[407] For example, the National Health Act makes no distinction between

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401 Constitution of South Africa 1996.

402 Act 38 of 2005.

403 Guideline 18.7.2.1. My emphasis.

404 Guideline 18.7.3.

405 n 27 above.

406 Section 71 distinguishes between therapeutic and non-therapeutic research, laying down a different threshold in each case for minor's participation in research. In the case of therapeutic research, the consent of the parent or guardian of the child is required **and,** if the minor is capable of understanding, the consent of the minor is also required (s 71(2)(c) - (d). In the case of non-therapeutic research, the Act requires the consent of the Minister of Health, the consent of the parent or guardian of the child, and if she is capable of understanding, the consent of the minor (section 71(3)((a)(ii) - (iv).

407 Secs 129(1) - (10) of Act 38 of 2005:
129(1) Subject to section 5(2) of the Choice on Termination of Pregnancy Act, 1996

(Act 92 of 1996), a child may be subjected to medical treatment or a surgical operation only if consent for such treatment or operation has been given in terms of either subsection (2), (3), (4), (3, (6) or (7).
(2) A child may consent to his or her own medical treatment or to the medical treatment of his or her child if-
(a) the child is over the age of 12 years; and
(a) the child is of sufficient maturity and has the mental capacity to understand the benefits, risks, social and other implications of the treatment.
(3) A child may consent to the performance of a surgical operation on him or her or his or her child if-
(a) the child is over the age of 12 years; and
(b) the child is of sufficient maturity and has the mental capacity to understand the benefits, risks, social and other implications of the surgical operation; and
(c) the child is duly assisted by his or her parent or guardian.
(4) The parent, guardian or care-giver of a child may, subject to section 3 1, consent to the medical treatment of the child if the child is-
(a) under the age of 12 years; or
(b) over that age but is of insufficient maturity or is unable to understand the benefits, risks and social implications of the treatment.
(5) The parent or guardian of a child may, subject to section 3 1, consent to a surgical operation on the child if the child is-
(a) under the age of 12 years; or
(b) over that age but is of insufficient maturity or is unable to understand the benefits, risks and social implications of the operation.
(6) The superintendent of a hospital or the person in charge of the hospital in the absence of the superintendent may consent to the medical treatment of or a surgical operation on a child if-
(a) the treatment or operation is necessary to preserve the life of the child or to save the child from serious or lasting physical injury or disability; and
(b) the need for the treatment or operation is so urgent that it cannot be deferred for the purpose of obtaining consent that would otherwise have been required.
(7) The Minister may consent to the medical treatment of or surgical operation on a
(a) unreasonably refuses to give consent or to assist the child in giving consent;
(b) is incapable of giving consent or of assisting the child in giving consent;
(c) cannot readily be traced; or
(d) is deceased.
(8) The Minister may consent to the medical treatment of or surgical operation on a child if the child unreasonably refuses to give consent.
(9) A High Court or children's court may consent to the medical treatment of or a surgical operation on a child in all instances where another person that may give consent.
(10) No parent, guardian or care-giver of a child may refuse to assist a child in terms of subsection (3) or withhold consent in terms of subsections (4) and (5) by reason only of religious or other beliefs, unless that parent or guardian can show that there is a medically accepted alternative choice to the medical treatment or surgical operation concerned.

In terms of s 39(4) of the previous Act, the Child Care Act 74 of 1983, children over 14 were legally capable of consenting to medical treatment for themselves and their children. Children over the age of 18 years were legally capable, in addition, of consenting to medical operations upon themselves. Such consent is valid only where the minor is sane and sober.
The consent of a parent or legal guardian was required by the Act for treatment if the minor is under 14, and for an operation if the minor is under 18. In the event of conflicting views between the child's father and mother, the child's best interest settles the matter.

children above and below the age of 14; the Health Act requires the consent of the Minister of Health in the case of non-therapeutic research on children.

iii) Informed *consent*

Guideline 12 requires that informed consent of participants 'based on complete, accurate, and appropriately conveyed and understood information as well as its consequences, should be obtained from each individual who is legally competent to give consent'.

Guideline 12.5.2 requires that trial participants have an adequate understanding of the aims, procedures, duration, potential risks, expected benefits, and personal implications of trial participation. They should also understand their rights as participants.

The MRC vaccine trial guidelines refer the reader back to the general requirements of the informational requirement of informed consent and the disclosure duties of the investigator in the MRC Guidelines, Book 1, guideline 5.3.2.3. On top of the general requirements contained in Book 1, Guideline 12.4.1 requires that each prospective participant is extensively 'counselled, using appropriate language and techniques', and in a position to understand:

> i. that they will receive counselling and access to the means of risk reduction but that in spite of these efforts, some may become infected with HIV;
> ii. that it is not known whether the experimental vaccine will prevent HIV infection or disease, and that some of the participants will receive a placebo instead of the candidate HIV vaccine (when such is the case). Therefore, they cannot assume that trial participation will afford them protection from HIV infection [...];
> iii. that participants in Phase II and III trials have been selected because they are at relatively high risk of HIV infection;
> iv. the potential specific risks for physical, psychological and social harm; how these will be minimised, and the types of treatment, compensation and services that will be available should harm occur [...];
> v. the nature and duration of care and treatment that is available if they become infected with HIV during the course of the trial, and any benefits to them personally or to their community that might be expected from participating in the trial [...];

'Medical treatment' was not defined in the Act, but would probably exclude non-therapeutic medical research. Therapeutic research, therefore, may be undertaken with the consent of a minor over 14 if it takes the form of treatment, and with the consent of a minor over 18 if it involves an operation. This competence to consent of minors was held to extend to health research which is tantamount to treatment or an operation and, hence, to therapeutic research only.
Non-therapeutic research on minors was generally not permissible, except where parental consent (and the assent of the minor concerned) was obtained for observational research of a non-therapeutic and non-invasive nature and observational research of a non-therapeutic and invasive nature, provided that normally no more than negligible risk is foreseeable or known from routine clinical practice, and that the distress or discomfort is negligible.

> vi. the confidential nature of their participation, and the limits of confidentiality where these apply [...];
> vii. that they are free to participate, or to withdraw at any time without adverse consequences; and
> viii. the expected time when results will be made available to them.

The information delineated above is far-reaching, and encompasses most issues that should be covered in the information component to informed consent in HIV vaccine trials. It is the most extensive guidance of all the ethical guidelines and legal rules on informed consent; probably because the MRC vaccine trial guidelines, unlike most of the other guidelines, cover a specific topic (HIV vaccine research), and because they are applied within a very specific geographic, social-economic and legal context. International guidelines, on the whole, are more general in nature (with the exception of the UNIADS vaccine trial guidance document) and other local ethical guidelines cover a wider range of research.

The fact that the information must be conveyed using 'appropriate language and techniques' shows an awareness of the circumstances in which HIV vaccine trial participants may find themselves, and that the language may have to be adapted to take account of differing levels of education and literacy, different cultural views on research and so on. In this light, Guideline 12.5 further discusses the transfer of information and requires that the transfer of information be viewed as a bilateral process between investigators/counsellors and prospective participants. Investigators and counsellors should make every effort to apprise themselves of the life circumstances, expectations and motivations of prospective participants. Guideline 12.6.1 notes that true understanding requires that trial information is understood 'in terms of the participant's personal, or religious and cultural values'.

The MRC vaccine trial guidelines include commentary regarding the measures to be taken to assess the comprehension of participants. Guideline 12.6.2 notes that participants' short-term recall of technical information about trials is not an adequate indication of understanding; Guideline 12.6.3 requires the use of a range of procedures 'to assess both understanding of technical terms (e.g. placebo) and understanding of the personal implications of participation (e.g. possible stigma or discrimination)'. Assessment procedures include check-lists of understanding of technical information, as well as responses to narratives or vignettes related to participation. Furthermore, Guideline 12.6.4 requires that procedures to assess understanding be developed in consultation with community representatives.

iv) Free *consent*

The MRC vaccine trial guidelines require that consent be given freely in Guidelines 12.8 to 12.9. Guideline 12.8 reminds researchers that 'respect for autonomy and self-determination are the foundation of informed consent'; consent must be 'voluntary and freedom of choice must be safeguarded'.

Guideline 12.8.1 places the responsibility upon investigators to 'assess conditions that may threaten the autonomy of participants'. Participants may attempt to win the favour, and avoid the disapproval, of investigators because of real or perceived differences in the power relation among investigators and participants, and the real or perceived benefits of trial participation. This 'social desirability' factor may lead participants to express socially desirable views rather than views based on personal needs and values, for example, about the acceptability of trial procedures.[408]

It is the responsibility of the investigator to introduce measures to reduce potential threats to autonomy and free consent, such as trial counsellors or community representational structures.[409]

Guideline 12.8.3 deals with undue inducement and requires that offers that persuade participants to volunteer against their better judgement or to assume risks that they would not otherwise have assumed, should be avoided. Investigators again should consult community representatives for assistance in making appropriate distinctions with regard to local conditions between legitimate benefits and undue inducements.

v) Clear, unequivocal and comprehensive consent

This aspect is implied but not expressly stated by the MRC vaccine trial guidelines. The responsibility for ensuring consent lies with the investigator.

Guideline 12.10 notes that informed consent is required during specific stages in the trail; and that informed consent should be obtained for each stage. The stages are the following: when candidates are screened for eligibility to participate; when an HIV test is performed; and when the person is judged eligible for enrolment.[410] Consent in viewed by the MRC vaccine trial guidelines as an ongoing process during the course of the trial.

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408 Guideline 12.8.1.1.
409 Guideline 12.8.2.
410 Guideline 10.2.2.

vi) Revocable consent

Guideline 12.10.2.2 stipulates that participants understand that they are not obliged to participate and that they are entitled to withdraw from the trial at any time without suffering any loss of benefits to which they would otherwise have been entitled. After enrolment, investigators must give participants 'ongoing explicit assurance that their continued participation is based on free consent and understanding'.[411]

vii) Prior consent

Informed consent should be given at each of the different stages where consent is required (see paragraph vi) above).

viii) Formalities

The MRC guidelines are very specific as to the nature and extent of the formalities they prescribe for the documentation of informed consent. Guideline 12.9 remarks that 'after careful consideration of the implications of trial participation, prospective participants will decide whether to participate or not'; if they 'choose to participate, a *record of their explicit consent should be obtained, through the signing of the informed consent form*'.[412]

Guideline 12.9.1 states that 'while the formal record of consent is important, it can never substitute for the process of informed consent'. In cases where participants are illiterate alternative procedures may be negotiated, such as providing a thumbprint in the presence of approved witnesses.

Guideline 12.9.3 stresses that informed consent forms must contain sufficient information about the trial procedures and their consequences for participants to ensure a clear understanding of relevant considerations, without being complicated by excessive information.

When prospective participants refuse to have a formal record of participation, *written* informed consent may be waived.[413] However this waiver is limited to 'certain compelling circumstances'.[414] The 'necessary protections and regulatory requirements' must be met.[415]

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411 Guideline 12.10.3.
412 My emphasis.
413 Guideline 12.9.4.
414 As above.
415 Guideline 12.9.4.

To ensure that participants do not consent without due consideration of the information about the trial, Guideline 12.9.5 requires a 'cooling-off' period of an 'appropriate interval ... between counselling and obtaining explicit formal consent'.

3.4.2 Good Practice guidelines

The Good Practice guidelines are more general in nature than the MRC guidelines, as they do not focus specifically on HIV vaccine research, but on research in general. The Good Practice guidelines mention the ethical principles of respect for persons, beneficence and non-maleficence and justice in the foreword, and comment that the principles should be 'read in the context of the Declaration of Helsinki, October 2000 and the ICH Harmonised Tripartite Guidelines for Good Clinical Practice'.[416] Guideline 3.5 deals with informed consent.

i) Authority or legal force

As pointed out at the beginning of this section, the MRC's Guidelines are the only ethical guidelines in South Africa which have the force of law, as they have been promulgated in terms of a statute,[417] the Good Practice guidelines are not legally binding.

ii) Capacity to consent

The Good Practice guidelines do not say who has the capacity to consent to research; this is to be determined by law.

iii) Informed *consent*

With regard to the informational aspect of informed consent, guideline 3.5 of the Good Practice guidelines states that '[t]he PI is responsible for ensuring that an adequate information package, in an acceptable format, is available for use in the process of seeking informed consent from participants to participate in the study'. The guidelines do not explain what 'an adequate' information package entails. This is a weak point in the guidelines, as unscrupulous investigators may provide only limited information on the risks of a potential study, thus negating the consent given by the participant.

Guideline 3.5 further requires that in the case of multi-site trial or a multi-country study, the site PI must 'ensure that informed consent procedures take

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416 Foreword Good Practice guidelines.

417 See ch 3 above.

cognisance of the characteristics of the site participants and tailor the informed consent content and procedures accordingly'. Unlike the MRC vaccine trial guidelines, the Good practice guidelines do not give any guidance on this subject – we do not know how the PI will go about tailoring the informed consent process so that it takes cognisance of local realities.

iv) Free *consent*

The Good Practice guidelines do not expressly require freely-given consent, but consent in accordance with the 'principles outlined in the Declaration of Helsinki'[418] is assumed to be freely given.

v) Clear, unequivocal and comprehensive consent

The responsibility of ensuring consent lies with the principle investigator or designated person. Guideline 3.5 determines that the 'PI, co-investigator, or designated person as defined in the protocol, should then seek the participant's informed consent to participate in the study in accordance with the principles outlined in the Declaration of Helsinki, and in these guidelines'.

The Good Practice guidelines do not specify that the consent should be comprehensive in nature.

vi) Revocable consent

They also do not require a statement of understanding that the participant may revoke her consent at any stage during the course of the trial.

vii) Prior consent

The Good Practice guidelines do not require prior consent; however, consent in accordance with 'the principles outlined in the Declaration of Helsinki' will presumably be prior consent.

viii) Formalities

The Good Practice guidelines state that 'in all instances both written and verbal informed consent should be obtained'. Furthermore, in cases where the participant is illiterate, verbal consent 'should be obtained in the presence of and countersigned by a literate witness'.

3.4.3 Ethical considerations for HIV/AIDS clinical and epidemiological research

Guideline 9 of the Good Practice guidelines, entitled 'Ethical Consideration for HIV/AIDS Clinical and Epidemiological Research' ('Good Practice guidelines: HIV research') describes informed consent. The description of informed consent is in greater detail than in the Good Practice guidelines, as these guidelines are more specific in nature.

i) Authority or legal force

As is the case with other ethical guidelines, these guidelines do not have the force of law.

ii) Capacity to consent

No guidance is given on who has the capacity to consent to research.

iii) Informed *consent*

The Good Practice guidelines: HIV research, provide extensive information on what is included in the information provided to participants. They should be made aware of the following:

- that the trial involves research;
- the purpose of the trial;
- the trial treatment(s) and the probability for random assignment to each treatment (where appropriate);
- the trial procedures to be followed, including all invasive procedures;
- the subject's responsibilities;
- the fact that participation in the trial is voluntary and refusal to participate or withdrawal from the trial will not prejudice the ongoing care of the person in any way;
- those aspects of the trial that are experimental;
- the foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, foetus, or nursing infant;
- the expected benefits (when there is no intended clinical benefit to the subject, the subject should be made aware of this);

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418 Guideline 3.5.

- the alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks;
- the compensation and/or treatment available to the subject in the event of trial related injury;
- the anticipated *pro rata* payment, if any, to the subject for participating in the trial; and
- the anticipated expenses, if any, to the subject for participating in the trial.

This list is extensive as the guidelines deal specifically with HIV/AIDS clinical and epidemiological research. However, no mention is made of the language, terminology or cultural appropriateness of the information that is provided, nor of any necessity that the participant understand the information – the participant must merely be 'made aware' of the information'. It seems as if the requirement for informed consent in the Good Practice guidelines: HIV research are lower than those in the MRC vaccine trial guidelines.

iv) Free *consent*

Guideline 9(f) requires that the participant 'be made aware' that 'participation in the trial is voluntary and refusal to participate or withdrawal from the trial will not prejudice the ongoing care of the person in any way'.

v) Clear, unequivocal and comprehensive consent

Guideline 9(o) does not explicitly state that the responsibility for ensuring informed consent rests with the PI, but does require that a contact name and number of the PI and a directly responsible investigator be provided to the participant.

No statement is made regarding the possibility that informed consent may include consent for different stages of the trial; this is probably due to the general nature of the guidelines.

vi) Revocable consent

Guideline 9(f) provides that the participant should be made aware that 'withdrawal from the trial will not prejudice the ongoing care of the person in any way'.

vii) Prior consent

No such requirement is included.

viii) Formalities

A 'written informed consent form' is referred to by the Good practice guidelines: HIV research.

3.5 Conclusion

This section highlights international and national ethical guidelines on informed consent that may be appropriate to the protection of participants in HIV vaccine trials in South Africa. It establishes that the international and national systems of ethical guidelines co-exist in South Africa.

Informed consent is a well-established requirement for the ethical conduct of research. It is extensively dealt with in both national and international ethical guidelines. Although these guidelines vary in respect of the detail that is included regarding the nature of the consent that is required, generally, they provide more detail than is given by the broad statement of a standard laid down by human rights law.[419] In ethical guidelines, the broad guarantee of informed consent is, on the whole, given content.

International and national ethical guidelines which focus specifically on HIV vaccine trials, or HIV-related research, are more appropriate to the situation of HIV vaccine trial participants. It can therefore be expected that RECs will prefer to rely on those guidelines in making their assessment on the ethics of vaccine research.

The different international and national guidelines discussed above vary in terms of their requirements for informed consent. The different headings used in the discussion (such as 'free consent', 'formalities' and 'prior consent') show that each set of guidelines emphasises different aspects of consent in research, and that each set of guidelines sets a slightly different standard that has to be met. For example, the Nuremberg Code, the CIOMS Guidelines, UNAIDS' vaccine trial guidance document and the MRC vaccine trail guidelines make mention of the requirement that consent should be given *prior* to the research being undertaken.

It is very important to note that emphasis is placed in international and local ethical guidelines on *procedural requirements* for informed consent, so much so that many ethicists refer to informed consent in ethical guidelines as the 'consent *procedure*'. Ethics committees tend to concentrate on whether the correct *procedure* has been followed in obtaining consent – whether consent forms have been adequately translated into local languages, whether all the formalities have been met, and so on. This concern is typical of both international and national ethical

guidelines.[420] Yet, the impression is created that informed consent is viewed by the drafters of (international and local) ethical guidelines as a *procedural requirement*, rather than a substantive means of protecting patients and research participants from abuse. Of all the ethical guidelines on informed consent considered, the Good Practice guidelines alone refer to the substantive principle of respect for persons or autonomy that underpin the guidelines,[421] avoiding the impression that as long as the *procedure* is complied with, all is well.

Jonathan Montgomery comments as follows on this emphasis on the procedural aspect of informed consent:[422]

> Consent forms, particularly for pharmaceutical research, can become so long and detailed that they are as likely to confuse people as to assist them making choices. The purpose of these forms is not so much to enhance the quality of decision making as to transfer the risks involved in trials to the research subjects. This is as if to say that 'the participants knew this might happen, because we told them, so they willingly ran the risks and we cannot be blamed if they materialise' [...] Consent in the hands of these legal advisers is not about promoting the moral value of autonomy but about removing the need for health professionals to take responsibility for treatment being in the interests of their patients by transferring that responsibility to them. The moral value of autonomy is not, in fact, promoted and the moral purpose of healthcare is obscured.

In these circumstances, informed consent is seen as a procedure to be complied with so as to protect researchers and research sponsors from legal action, and not as a manifestation of the research participant's decision after a full appreciation of the possible consequences.[423]

The emphasis upon procedure over substance erodes the meaning of informed consent with the result that informed consent no longer is an exercise of

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419 See para 5.5 below.

420 See eg the Good Practice guidelines: HIV research which provides extensive information on what should be included in the information provided to participants; the MRC Guidelines which, in guideline 12.9.3, stress that informed consent forms must contain sufficient information about the trial procedures; the UNAIDS vaccine trial guidance (the most elaborate context-specific requirements of all the international guidelines discussed above) which require that:

> A *process* of consultation between community representatives, researchers, sponsor(s) and regulatory bodies should be used to design an effective informed consent strategy and *process*. Issues such as illiteracy, language and cultural barriers, and diminished personal autonomy should be addressed in this consultative process.

421 See para 3.4.2 above.

422 Montgomery (2006) 26 *Legal Studies* 185, 188 - 189.

423 See generally, in a different context and with a rather more philosophical outlook, Duncan Kennedy's excellent (and lengthy) exposition entitled 'Form and substance in private law adjudication' (1975-1976) 89 *Harvard L Rev* 1685 – 1778.

autonomy, but is an empty gesture - the rules are obeyed but the meaning of the act is neglected.

It is essential to note that most of the international and local ethical guidelines examined above fail to acknowledge the importance and role of 'difference' in the research endeavour generally, and its importance in obtaining the informed consent of HIV vaccine trial participants in South Africa. In general, no mention is made in these guidelines of the fact that certain groups tend to be exploited more often in research due to their vulnerable social, political or economic situation. By and large, ethical guidelines display no awareness of the role of context in determining susceptibility to exploitation.

The only documents to have taken cognisance of the importance of context in ensuring informed consent are the UNAIDS' vaccine trial guidance document (to a lesser extent), and the MRC vaccine trial guidelines (to a greater extent). Mostly because they are specific to a certain situation (HIV vaccine efficacy trials) and situated within a definite social, economic and political context, these documents display an awareness of the research participant, not as a disembodied or abstract being, but as a relational being within a society. This point is expanded upon at a later stage.[424]

4 HUMAN RIGHTS LAW ON INFORMED CONSENT WITH REFERENCE TO PREVENTIVE HIV VACCINE EFFICACY TRIALS PARTICIPATION IN SOUTH AFRICA

4.1 Introduction

The focus on international and national ethical guidelines on informed consent in South Africa has been an attempt to assess the extent to which these guidelines protect the interests of HIV vaccine trial participants in South Africa. As pointed out in paragraph 2 above, participants are vulnerable to exploitation due to the socio-economic and political contexts in which these trials take place.

Informed consent, as a primary way of ensuring that research participants are protected against exploitation, is both an ethical and human rights imperative. In this section international and national human rights relevant to informed consent in preventive HIV vaccine efficacy trials in South Africa are discussed. First, the interaction between the international and national or domestic systems of human rights is described. A short summary is provided of the role of international law in

the local sphere of human rights protection, illustrating that international law and national law, in some respects, are one system of law. Second, the international human rights system is delineated, and the discussion examines instruments at both the universal and at the regional level. Third, the national human rights law system is examined, and case law as well as common law are reported on as an introduction to the jurisprudence of the Constitutional Court in terms of section 12(2)(c) of the Constitution. The section concludes with a discussion of the interrelationship between socio-economic rights and civil and political rights and the implications of this interrelationship for HIV vaccine trials in South Africa which are likely to take place in settings where participants are predominantly poor or destitute. The notion of exploitation in research is revisited. The section concludes with an evaluation of the contribution of human rights law to the protection of HIV vaccine efficacy trail participants in South Africa.

As international law provisions tend to be part of larger, less specific instruments than documents containing ethical guidelines and, therefore, lack specificity, it is not possible to rely on the same sub-headings that were used in the section above on ethical guidelines. Where possible, however, aspects, such as authority or legal force and capacity to consent, are discussed, as well as the formalities that are required in the process.

4.2 Interaction of international and national human rights law on informed consent in South Africa

The international and national (or 'domestic' or 'local') systems of ethics co-exist in South Africa in the sense that both direct the actions of ethical review committees and researchers - no specific 'action' is needed to incorporate international ethical guidelines into the South African system of ethical guidelines. South African research ethics committees regard international ethical guidelines as binding.[425] This situation corresponds to that of international customary law, which is regarded as binding and is followed throughout the world.

In the case of international human rights law in the form of treaties, the situation is slightly different. International and national or domestic[426] human rights

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424 See below and ch 6.
425 See para 3.2 above.
426 In international law referred to as 'municipal'.

law do not just coexist – in general, human rights treaties have to be 'domesticated' before they can have the force of law in South Africa.

As indicated in chapter 4, effective national human rights systems, in which enforceable remedies are available, exist in many countries. In these instances the protection offered under the international system is subsidiary to national human rights protection. It is only when domestic remedies are exhausted, do not exist or are inaccessible, that the victim of a human rights violation may turn to a regional or UN forum.[427]

In South Africa, the international and national systems of human rights protection do not coexist as 'equals'. In most instances,[428] it can be said that international human rights law (in the form of treaty law) has the *potential* to apply in the South African domestic system of law, as international human rights law has to be 'domesticated' before it can be applied locally and before it can be said to enjoy the force of law (unless it may be regarded 'self-executing'). Chapter 4 dealt with the theories regarding the status of international law in domestic systems of law as well as the steps that have to be taken before a treaty is part of national law; these issues will not be revisited.[429] However, a few points need to be borne in mind for the discussion below.

Chapter 4 demonstrates that customary international law and international treaty law have different force and effect in South African law. The South African Constitution treats customary international law as part of national law, as one system of law,[430] but with a very important proviso: section 232 states that '[c]ustomary international law is law in the Republic *unless it is inconsistent with the Constitution or an Act of Parliament*'.[431] Thus, according to section 232, customary international law is lower in status than specific national law (an Act of Parliament) and the Constitution.[432] However, subordinate legislation, common law and case law (other than case law emanating from the Constitutional Court which interprets the Constitution) are lower in status than international customary law.

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427 However, the role of international human rights law is to provide not only an alternative forum, but also normative guidance according to which the law develops.

428 Unless the specific rule on international human rights law can be regarded a international customary law.

429 See para 5.2.2 of ch 4.

430 Dugard (2001) 51.

431 My emphasis.

432 See Dugard 52.

International treaty law is different because treaties have to be incorporated into South African law by legislative action; they are not immediately part of domestic law. The Constitution directs the incorporation or domestication of international human rights law in the form of treaties in sections 231 to 233. The legislature does not conclude treaties,[433] but in the case of treaties that require ratification, the legislature should pass a resolution to transform them into national or municipal law.[434]

It is important to again mention here the notion of self-executing provisions, which was discussed in chapter 4.[435] Self-executing provisions are rules of international law which are considered to apply directly in domestic legal systems, or, stated differently, they are treaty provisions or a treaty which of their own force constitute rules of municipal law which municipal courts must apply in deciding cases involving the rights of individuals.[436] The South African Constitution allows for the self-execution of treaty provisions in section 231(4):

> Any international agreement becomes law in the Republic when it has been enacted into law by national legislation; but a *self-executing provision* of an agreement that *has been approved by Parliament* is law in the Republic *unless it is inconsistent with the Constitution or an Act of Parliament.*
> [My emphasis.]

In the discussion of international human rights treaty provisions relevant to the position of HIV preventive vaccine trial participants below, treaty provisions which potentially are self-executing will be identified.

In chapter 4 it was emphasised that international human rights law is important when it comes to the interpretation of the South African Bill of Rights. Section 39(1)(b) of the Constitution demands that, when interpreting the Bill of Rights, a court, tribunal or forum 'must consider international law'; thus compelling the use of international law as an interpretive tool when interpreting the Bill of Rights. Guidance has to be sought from international human rights declarations, treaties, conventions and covenants.[437] International agreement of a technical,

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433 sec 231(1).

434 Sec 231(2) states that international agreements bind the Republic only after they have been approved by resolution in both the National Assembly and the National Council of Provinces, unless they are of the type of agreement referred to in subsection (3) (Dugard (n 430 above) 56 – 57).

435 See para 6.3 of ch 4 above.

436 Olivier (2002) 27 *SA Ybk Intl L* 99.

437 Whether these treaties have been signed or ratified by South Africa is not significant as no qualification to that effect is included in section 39(1) – see ch 4 above, para 5.2.2.

administrative or executive nature, becomes law if it meets the requirements in section 231(3).

Another aspect of sub-section 39(1)(b) is mentioned; the sub-section requires a court, tribunal or forum to *consider* international law. It does not provide that a court, tribunal or forum will be *bound by* international law, but that it should consider such law when interpreting the rights in the Bill of Rights. [438]

To sum up: according to section 232, although customary international law forms part of national law, it is lower in status than specific national law and the Constitution, but subordinate legislation, common law and case law are lower in status than international customary law. International agreements or treaties are not law in the Republic unless they have been approved by resolution in Parliament.[439] When they have been approved by a resolution in Parliament, international agreements or treaties are part of national law, but are lower in status than the Constitution and an Act of Parliament, according to sections 231 and 232 of the Constitution. From the above, it is clear that international and national human rights law are *one system* - it is therefore important to remember in the discussion below that the two systems should not be treated as two separate systems, but as one system of law under the Constitution.

Section 39 of the Constitution compels the use of international law in the interpretation of the Bill of Rights – but does not bind the judiciary in their interpretation to international law; it should merely consider such law.

It appears that international customary law and treaties that are incorporated into national law (or 'domesticated') alone have any value in the safeguarding of HIV vaccine efficacy trial participants (such as article 7 of the ICCPR). Nevertheless, article 27 of the Vienna Convention declares that a state 'cannot [consequently] plead provisions of its own law or deficiencies in that law' in response to a claim that it is in breach of a treaty obligation. South Africa, therefore, cannot invoke domestic legislation, or its constitutional provisions, to evade treaty obligations. International human rights law and national human rights law both play a valuable role in the protection of the interests of research participants in HIV vaccine efficacy trials.

The following sections examine the extent of the protection offered by national and international human rights law on informed consent.

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438 My emphasis.

439 Unless they are of a self-executing nature; see above.

4.3 International human rights law on informed consent in research

4.3.1 The UN system

a) The Universal Declaration of Human Rights

The Universal Declaration is not a treaty - it is a resolution of the UN General Assembly and, in theory, has no binding force of law.[440] However, the Universal Declaration has been transformed into a normative instrument that creates at least some legal obligations for member states of the UN, and parts thereof are regarded by many to be binding as customary international law.[441] Dugard remarks that not all the provisions of the Universal Declaration are part of customary international law but the right to non-discrimination, the right to a fair trial and the prohibition on torture, and cruel, inhuman or degrading treatment, 'undoubtedly belong to the corpus of customary law today despite the fact that they may not always be observed. Their status as custom is assured by both *opinio juris* and *usus*'.[442]

The Universal Declaration of Human Rights does not mention informed consent explicitly. Nevertheless, in article 3 it guarantees the right of everyone to 'life, liberty and security of person', and in article 5 it guarantees that '[n]o one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment'.

Either article 3 or article 5 may be used to argue that participants in clinical research should provide informed consent to participation. The right to individual autonomy is usually regarded as included in the right to security of the person, and thus, the right not to be subjected to medical experimentation without informed consent, as well.[443] Similarly, as the International Covenant on Civil and Political Rights (ICCPR) includes medical experimentation as part of the right not to be subjected to torture, cruel, inhuman or degrading treatment in article 7, one may argue that the right not to be subjected to medical experimentation without informed consent is part of the same right in the Universal Declaration. However, the opposite argument may also be made: since it is not explicitly mentioned in the Universal Declaration, while it is mentioned in the ICCPR, the equivalent right in the Universal Declaration does not contain a prohibition on medical experimentation without free and informed consent.

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440 Buergenthal (1995) 33.
441 See para 3.2.1 of ch 4 above.
442 Dugard (n 430 above) 241.
443 Eg as in the South African Constitution 1996.

Although there is consensus regarding the view that freedom from torture may be regarded as part of international law,[444] there is no evidence in the literature that any international law scholar is of the opinion that a right to free consent to medical or scientific experimentation may be 'read into' the protection against torture offered by the Universal Declaration. That is unfortunate, inclusion would have meant that informed consent becomes a rule of customary international law and is immediately enforceable in all countries.

The position in South Africa, however, is not dependant on this argument, as South Africa has ratified the main UN treaty on the topic, the ICCPR, to which the discussion now turns.

b) The treaty-based system

i) ICCPR

The ICCPR is the sole UN human rights treaty to include an express provision on informed consent, thus establishing informed consent as a principle of international law and conferring enforceable rights on research participants.[445] Non-compliance with the prohibition on experimentation without free consent in the ICCPR is thus a matter for international concern.

Article 7 of ICCPR reads: 'No one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment. In particular, no one shall be subjected without his free consent to medical or scientific experimentation'.

The wording of the first part of article 7 of the ICCPR mirrors article 5 of the Universal Declaration (widely considered to be binding customary international law),[446] therefore, article 7 (as customary international law) would be binding on states not party to the ICCPR. This means that the protection offered against torture or inhuman and degrading treatment is available even against countries that have not signed and ratified the ICCPR.

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444 Dugard 241 - 242; Nowak (2005) 157.

445 Article 2(2) of ICCPR states 'each State party to the present Covenant undertakes to take the necessary steps, in accordance with its constitutional processes and with the provisions of the present Covenant, to adopt such legislative or other measures as may be necessary to give effect to the rights recognized in the present Covenant'. Article 2(2) gives effect to the rights in the Convention, and ensures their enforcement as it requires governments to 'adopt such laws or other measures as may be necessary to give effect to the rights recognised in the present Covenant'. According to article 3(a), state parties must further ensure that 'any person whose rights or freedoms as herein recognized are violated shall have an effective remedy'.

446 See above.

Significantly, article 7 prohibits experimentation without 'free consent', not that which lacks *informed* consent. This distinction is attributable to the fact that the article was drafted in the late 1940s,[447] and, as indicated above,[448] at this time the model for informed consent was paternalistic, emphasising the person's consent and not the information provided, or her understanding of that information.

The phrasing of article 7 suggests that scientific experimentation is seen as a sub-class or even as an *example* of 'torture' or 'cruel, inhuman or degrading treatment or punishment' – because of the use of the words '[i]n particular'. This proposal may be explained by the drafting history of the ICCPR – according to the *travaux préparatoires*, drafting on article 7 started in 1948 soon after the Nuremberg Trials, and article 7 was so phrased in response to the atrocities committed by representatives of the National Socialist German government in the concentration camps under the guise of medical experimentation.[449] The aim stated in the second sentence of the article is to 'prohibit criminal experiments on human beings such as those committed in Nazi concentration camps'.[450]

Nowak comments that it follows from the structure of the article (that is, the fact that it appears that medical experimentation is an *example* or instance of cruel and inhuman treatment) that 'only experiments that by their very nature are to be deemed torture or cruel, inhuman or degrading treatment are prohibited'.[451] Thus, according to Nowak, the prohibition in the second sentence of art 7 does not extend to experiments of which the interference with personal integrity does not reach the degree of 'degrading or inhuman treatment'.[452] For example, according to Nowak, the clinical testing of pharmaceuticals without the knowledge and/or consent of the person concerned falls within the scope of article 7 *only if its effect* constitutes degrading or inhuman treatment.[453] It will seem as if Nowak interprets article 7 to mean that ordinary research experiments, which do not impose the type of harm that may be classified as 'cruel', 'degrading' or inhuman, are not protected by article

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447 See Nowak (n 444 above) 188, where he points out that, as early as 1948, art 6 of the draft International Bill of Rights contained a similar provision, prohibiting scientific experimentation against a participant's will.

448 See para 1 above.

449 Nowak 188.

450 Nowak 190. For general information on the *travaux préparatiores* of ICCPR, see Bossuyt (1987) *Guide to the 'travaux préparatiores' of the International Covenant on Civil and Political Rights*.

451 Nowak (n 444 above) 191.

452 As above.

453 As above. My emphasis.

7, *even if* no informed consent to participation was given. Consequently, experimentation is allowed when a person gives his free consent, or, 'when the very nature of the experiment makes it clear that the experiment cannot be deemed torture or cruel inhuman or degrading treatment'.[454]

If this view were held to be correct, it would mean that the article holds 'free consent' to experimentation as optional in some cases, rather than prohibiting *all* scientific experimentation without informed consent. Nowak's interpretation of article 7 is not supported by the Human Rights Committee in General Comment 20.[455] The Human Rights Committee states, without adding any qualification regarding the nature of the experimentation: 'Article 7 expressly prohibits medical or scientific experimentation without the free consent of the person concerned'.[456] Even though such experimentation may not be deemed as 'cruel' or 'degrading', the very fact that no consent was given contravenes article 7. Further, Nowak admits, if regard be had to the *travaux préparatoires*, the lack of free consent is considered as a 'sign' of the inhuman character of the medical experiment.[457]

The drafting history of article 7 was marked by problems regarding phrasing: article 7 had to protect against Nazi-like atrocities but still allow for legitimate experimentation.[458] France proposed the current phrasing of article 7, replacing the phrase 'against his will' in a previous version with 'without his free consent'.[459] Nowak stresses that, in contrast to the phrase 'against his will', it is not sufficient that the person 'merely remains passive' – 'consent' requires an action or an agreement from the person.[460] The phrase '*free* consent' implies not only that the research participant agrees to the study, but that she does so without any coercion.

Nowak further comments that article 7, when interpreted in the light of the *travaux préparatoires,* reveals that 'the article refers only to interference that may be termed medical or scientific "experimentation"'.[461] This view may be supported, as the aim of the prohibition was clearly to protect against illegal 'experimentation'.

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454 As above.
455 Issued by the Human Rights Committee on 3 April 1992.
456 General Comment 20, para 7 <http://www.unhchr.ch/tbs/doc.nsf/0/6924291970754969c12563ed004c8ae5?Opendocument> (31 January 2007). General Comments are so-called 'soft' law, and are not binding, but they do represent an authoritative interpretation of 'hard' law. See para 2.9 of ch 4 above.
457 As above.
458 188.
459 Nowak (n 444 above) 189.
460 See Nowak 190, fn 187.
461 Nowak 188.

Normal medical interventions or treatment do not fall within the ambit of the protection offered by article 7.

Nowak is of the view that proxy consent is not provided for under article 7.[462] According to Nowak, the use of 'without *his* free consent' makes it clear that the person herself must give informed consent.[463] Whether Nowak's view can be supported depends on the interpretive strategy to be followed. A strict, literal interpretation of the article supports Nowak's view; a more purposive or value-orientated interpretive approach does not. In this regard the Human Right Committee has commented that '... special protection in regard to such experiments is necessary in the case of persons not capable of giving valid consent, and in particular those under any form of detention or imprisonment. Such persons should not be subjected to any medical or scientific experimentation that may be detrimental to their health'.[464] It seems as if the Human Rights Committee does not support Nowak's literal reading of the article.[465] In his study on whether research subjects of clinical trials in developing countries are in a position to sue investigators for human rights violations, Jonathan Todres remarks that 'it is unlikely that [article 7] intended to ban new therapies for children or others who are unable by law to give informed consent'.[466]

Article 7 prohibits not only experimentation which causes physical suffering, but also that which causes psychological distress. General Comment 20 states, 'article 7 relates not only to acts that cause physical pain but also to acts that cause mental suffering to the victim ... It is appropriate to emphasise in this regard that article 7 protects, in particular, children, pupils and patients in teaching and medical institutions'.[467] General Comment 20 additionally states that the aim of the provisions of article 7 'is to protect both the dignity and the *physical and mental integrity* of the individual. It is the duty of the State party to afford everyone protection through legislative and other measures as may be necessary against the acts prohibited by article 7 ...'[468]

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462 Nowak 191.
463 Nowak 191.
464 General Comment 20 para 7.
465 Also see below, for commentary on the interpretation of sec 12(2)(c) of the South African Constitution, 1996, where similar phrasing is used.
466 Todres (n 340 above) 745 fn 25.
467 General Comment 20 para 5.
468 General Comment 20, para 2. My emphasis.

Article 7 of ICCPR is 'non-derogable', as is stated by the UN Human Rights Committee: 'The text of article 7 allows of no limitation. The Committee reaffirms that, even in situations of public emergency such as those referred to in article 4 of this Covenant, no derogation from the provision of article 7 is allowed and its provisions must remain in force ... No justification or extenuating circumstances may be invoked to excuse a violation of article 7 for any reasons, including those based on an order from a superior officer or public authority.'[469]

General Comment 20 requires that 'States Parties should indicate how their legal system effectively guarantees the immediate termination of all acts prohibited by article 7 as well as appropriate redress. The right to lodge complaints against maltreatment prohibited by article 7 must be recognized in the domestic law'.[470] The General Comment further requires that '[c]omplaints must be investigated promptly and impartially by competent authorities so as to make the remedy effective'.[471] Although the General Comment appears to be focussed on situations of detention, this paragraph of the Comment is more general in its reach, and places clear duties on state parties to prevent experimentation without free consent. State parties must enact legislation which 'effectively guarantees the immediate termination of all acts prohibited by article 7 as well as appropriate redress'. In South Africa the required legislation (in the form of the National Health Act) has been passed, prohibiting experimentation without free consent, but it does not provide 'appropriate redress' for violations of article 7. This omission should be addressed by the South African legislature.[472]

A number of cases dealing with violations of the first part of article 7, prohibiting cruel, inhuman and degrading treatment or punishment, have reached the Human Rights Committee.[473] The second part of article 7, relating to experimentation without free consent, has elicited only one communication to the Human Rights Committee. In this case, *Viana Acosta v Uruguay*,[474] the author of the

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469 General Comment 20 para 3.

470 General Comment 20 para 14.

471 As above.

472 See ch 6 below, para 5.4.

473 See eg Communication 11/1977 *Grille Motta v Country*; Communication 74/1980 *Angel Estrella v Country*; Communication 464/ 1991 *Ng v Canada* 464/1991 (inhuman and/or cruel treatment); Communications 623-627/1996 *Domukovsky and Other v Georgia* 623-627/1996 (conditions of detention); and so on.

474 Communication 110/1981 *Viana Acosta v Uruguay*, available at <http://www.unhchr.ch/tbs/doc.nsf/0/658ade4b795d348ac1256ab8004f9b9c?OpenDocument> (31 January 2006).

communication alleges that he was subjected to psychiatric experiments by a doctor[475] and that for three years, against his will, he was injected with tranquillisers every two weeks. He alleges, also, that in May 1976, when resisted being injected, Captain X[476] ordered a group of soldiers to subdue him forcibly in order to inject the drug and that he was subsequently held incommunicado in a punishment cell for 45 days. On 14 and 15 April 1977 he was interrogated and subjected to torture at Libertad prison. He lists the names of several Uruguayan officials who practised torture. However, the Committee in response did not consider in detail free consent as such, but merely found that the treatment of Acosta during his detention was inhuman within the meaning of articles 7 and 10.[477]

In his study of whether the Ugandan AZT-trials[478] violated any international human rights norms, Fidler states that 'there are no precedents [which] assist international legal analysis'.[479] The lack of case law dealing with the second sentence of article 7 is unfortunate, as no authoritative determination has been given on exactly what standards of free consent are accepted universally as binding. Although the general prohibition in article 7 may be taken as an international norm, because of the lack of case law it lacks substance and specificity; it is not known for certain what constitutes sufficient free consent nor which actual circumstances would constitute a violation.

A major problem with the ICCPR is that, unlike the European and Inter-American systems, it does not establish an international court of human rights.[480] The decisions of the Human Rights Committee are not legally binding, so that, in practice, it has become a quasi-judicial monitoring body for state reporting and individual complaints procedures.[481] However, the Human Rights Committee reports to the General Assembly, which to some extent is able to enforce the Human Rights Committee's decisions through political measures.[482]

The ICCPR is regarded as applying to state actors only. For individuals to access the remedies under the treaty, the states to which they belong need to have

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475 The name of the doctor is not included in the communication.
476 No actual name is given in the communication.
477 *Viana Acosta v Uruguay* paras 2.7; 14 - 15.
478 See ch 3 above.
479 Fidler (n 340 above) 338.
480 Nowak 79.
481 Nowak 80.
482 South Africa has not yet submitted its initial report under ICCPR, which was due on 9 March 2000.

signed the Optional Protocol on the Convention on Civil and Political Rights.[483] South Africa has signed and ratified the Optional Protocol in November 2002.[484]

Finally, it is submitted that article 7 of the ICCPR is a self-executing provision. In the case of self-executing provisions, it is not necessary for countries to incorporate the treaty into their domestic law for it to bestow enforceable rights upon individuals. Article 7 of ICCPR, if it were a self-executing provision, would be directly applicable (of course, it depends on the provisions regarding international treaties in the constitutions of countries).

Article 7 meets the 'pointers' set out above[485] for it to qualify as a self-executing provision. First, it is clear from the *travaux préparatoires* that drafting on article 7 started in 1948 soon after the Nuremberg Trials, and that the article was drafted in response to the atrocities committed by representatives of the National Socialist German government in the concentration camps under the guise of medical experimentation.[486] The aim stated in the second sentence of the article is to 'prohibit criminal experiments on human beings such as those committed in Nazi concentration camps'.[487] Second, article 7 is phrased in relatively precise language – medical experimentation without the participant's free consent is prohibited.[488] Third, the article (and the ICCPR) establishes negative obligations or prohibitions which are generally regarded as self-executing, as no further measure of implementation is required.[489] Finally, article 7 benefits individuals, which is one of the 'requirements' for it to qualify as a self-executing provision (where a provision creates private rights, it is assumed to be directly applicable).[490] It employs the words 'no one' twice, giving the article an individual character.

ii) International Covenant on Economic, Social and Cultural Rights

The International Covenant on Economic, Social and Cultural Rights (ICESCR) recognises a wide range of second generation rights which are not immediately enforceable. A state party undertakes, only, to 'take steps ... to the maximum of its

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483 See ch 4 above, para 3.2.2.

484 See http://www.unhchr.ch/tbs/doc.nsf/22b020de61f10ba0c1256a2a0027ba1e/802564040 04ff315802564610078e734?OpenDocument (31 January 2007).

485 See para 4.2 above and para 6.2 of ch 4.

486 Nowak (n 444 above) 188; see above.

487 Nowak 190; see above.

488 As above.

489 Olivier (n 436 above) 107.

490 See Olivier 107 and above.

available resources ... with a view to achieving the full realisation of the rights...'[491] The wording of article 2(1) refers to 'obligations of conduct', rather than 'obligations of result'.[492]

Although the ICESCR does not contain a provision regarding informed consent, article 12 establishes 'the right of everyone to the enjoyment of the highest attainable standard of physical and mental health'.[493] The Committee on Economic, Social and Cultural Rights (CESC) mentions that the right to health 'contains both freedoms and entitlements',[494] such as the right 'to be free from non-consensual treatment and experimentation'. General Comment 14 reads:[495]

> The right to health contains both freedoms and entitlements. The freedoms include the right to control one's health and body, including sexual and reproductive freedom, and the right to be free from interference such as the right to be free from torture, non-consensual treatment and experimentation. By contrast, the entitlements include the right to a system of health protection which provides equality of opportunity for people to enjoy the highest attainable level of health.

General Comment 14 observes that the right to health is 'related to and dependent upon the realization of other human rights as contained in the International Bill of Rights'[496] as well as dependant upon access to the 'underlying determinants of health'.[497] The determinants include access to adequate sanitation, an adequate supply of safe food, nutrition, housing, healthy occupational and environmental conditions, and access to health-related education and information, including sexual and reproductive health. The population of state parties to the Convention should participate in all health-related decision-making at the community, national and international levels.[498]

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491 Art 2(1)

492 Nowak (n 444 above) 81. States are merely obliged to achieve progressive realisation of these rights.

493 The inclusion of the word 'attainable' stresses that the right to health as guaranteed by article 12 is not unqualified – only the best 'attainable' health is guaranteed, by obligating state parties to 'take steps ... to the maximum of its available resources ... with a view to achieving the full realisation of the rights ...' (art 2(1)).

494 General Comment 14 para 8.

495 General Comment 14 para 8. My emphasis.

496 General Comment 14 para 3.

497 General Comment 14 para 11.

498 As above. Also see General Comment 3 para 10 (UN Doc E/C12/1990/8), in which the CESC Committee states:
'a State party in which any significant number of individuals is deprived of foodstuffs, of essential primary health care, of basic shelter and housing, or of the moist basic forms of education is, prima facie, failing to discharge its obligations under the Covenant'.

Article 12, as relates to its content of the right to be free from non-consensual medical experimentation, has not yet been litigated under international human rights law.

Although South Africa has not ratified the ICESCR, the Convention is not without relevance to the situation of HIV vaccine efficacy trial participants in South Africa. Section 39(1)(b) of the Constitution orders the judiciary to consider international law in the interpretation of the rights in the Bill of Rights. In the case of *Government of the Republic of South Africa v Grootboom,*[499] the Constitutional Court made explicit reference to General Comment 3 of the Committee on Economic, Social and Cultural Rights, including its concept of minimum core obligations. General Comments of the Committee thus have persuasive force in South Africa, despite the country's non-ratification of the ICESCR.

iii) CEDAW

Like the ICESCR, CEDAW does not make explicit reference to the protection of the right to free and informed consent. However, article 5(a) obliges states parties to:

> take appropriate measures to modify the social and cultural patterns of conduct of men and women, with a view to achieving the elimination of prejudices and customary and all other practices which are based on the idea of the inferiority or superiority of either of the sexes or in stereotyped roles of men and women.

It is not too far-fetched to use the subsection to ensure that consent to participation in HIV vaccine trials is an individual informed consent of a woman taking part in the trials, and that customary practice whereby a woman's father or husband or the headman of the community takes a decision on her behalf, is not allowed. The obligation is placed on the states parties to CEDAW to fulfil the right under the subsection, this obligation could also be interpreted to include protecting a woman's right to give individual consent.

The application of the subsection in this way should be viewed in the light of General Recommendation 24 which deals specifically with women and health, issued by the Committee on the Elimination of Discrimination against Women (CEDAW Committee).[500] General Recommendation 24 notes that women and girls do not

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499 2000 11 BCLR 1169 (CC).

500 Committee on the Elimination of Discrimination against Women *General Recommendation 24 Women and Health* <http://www.unhchr.ch/tbs/doc.nsf/(Symbol)/77bae3190a903f8d80256785005599ff >(1 April 2006).

have sufficient power to refuse sex or insist on safe sexual practices, and that they are often subjected to marital rape and polygamy, exposing them to HIV infection.

South Africa has submitted its first state report under CEDAW. It was considered by the Committee on 24 and 29 June 1998.[501] The requirement of informed consent is mentioned not at all in the Committee's Concluding Observations.[502]

iv) CRC

In Chapter 4, CRC is discussed at length; including its relevance to clinical research in children, and that discussion will not be repeated here.[503] CRC reflects a realisation that the specific needs and rights of children require specialised recognition and protection, but does not mention informed consent explicitly.

v) CAT

In the Convention Against Torture and Other Cruel, Inhuman or Degrading Treatment or Punishment (CAT),[504] 'torture' is defined as 'any act by which severe pain or suffering, whether physical or mental, is intentionally inflicted on a person for *such purposes as obtaining* from him or a third person *information or a confession*, *punishing him* for an act he or a third person has committed or is suspected of having committed, or *intimidating or coercing him or a third person*, or for any reason is based on discrimination of any kind, when such pain or suffering is inflicted by or at the instigation of or with the consent or acquiescence of a public official or other person acting in an official capacity'.[505] The aim of CAT is therefore to prevent and punish torture that is inflicted by a person who is acting in his personal capacity or a person acting with the consent or acquiescence of another public official. Article 1 states that the term torture 'does not include pain or suffering arising only from, inherent in or incidental to lawful sanctions'.

Article 16 of CAT requires that each state party 'undertake[s] to prevent in any territory under its jurisdiction other acts of cruel, inhuman or degrading

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501 See CEDAW/C/SR.387, 388 and 393, < http://www.unhchr.ch/tbs/doc.nsf/(Symbol)/A.53.38.Rev.1,paras.100-137.En?Opendocument> (31 January 2007).

502 As above.

503 See para 4.3.5 of ch 4 above.

504 Adopted by the General Assembly on 10 December 1984 and entered into force on 28 June 1987 after the twentieth instrument of ratification required to bring it into force, was deposited.

treatment or punishment *which do not amount to torture* as defined in article I, when such acts are committed by or at the instigation of or with the consent or acquiescence of a public official or other person acting in an official capacity'.[506] In particular, the article asserts the obligations contained in articles 10, 11, 12 and 13 apply to other forms of cruel, inhuman or degrading treatment or punishment'. Although CAT, therefore, is aimed not only at 'torture', but also 'inhuman or degrading treatment or punishment', it is submitted that experimentation without informed consent does not fall within the scope of the definition: though clinical research, in a sense, may be described as 'obtaining ... information', there is no match with the other particulars in the definition: clinical research is not carried out by someone acting in an official capacity (unless the research is carried out by a police, military or prison doctor); or on the orders of someone acting in an official capacity.

4.3.2 The African regional system

a) The African Charter of Human and Peoples' Rights

There is no mention in the African Charter on Human and Peoples' Rights (African Charter) of free and informed consent to medical experimentation. However, article 4, which states that 'human beings are inviolable', and that 'every human being shall be entitled to respect for his life and integrity of his person', is relevant to the situation of HIV vaccine trial participants in South Africa. Furthermore, article 6 ensures that every 'person shall have the right to liberty and to the security of his person'. Even though informed consent to research participation is not mentioned, these articles of the African Charter can be used in support of the notion that HIV-related clinical research participants give free and informed consent to research participation. Research without such consent violates the integrity and security of the person.[507]

b) African Bioethics Resolution

A Resolution on Bioethics was adopted by the Assembly of Heads of State and Government of the OAU at its 32nd ordinary session (African Bioethics Convention).[508] In paragraph 2, the African Bioethics Resolution endorses the priority placed upon informed consent by the ICCPR and in paragraph 3 stresses the 'obligation to obtain

505 My emphasis.
506 My emphasis.
507 Also see discussion in ch 4 above.

the free and enlightened consent' to research, and makes provision for 'the definition of rules to protect vulnerable populations, the incapacitated, persons deprived of freedom as well as the sick under emergency conditions'.

The African Bioethics Resolution introduces a new term in referring to consent, namely, '*enlightened* consent'. It is unlikely that the word 'enlightened' is used here in the context of 'liberal', 'free-thinking' or 'free from prejudice';[509] as in other human rights and ethics documents, it is used as a synonym for 'knowledgeable'; in the sense of being informed about a subject. In all probability the drafters of the Resolution did not intend to establish a higher standard in other documents. It is submitted that the term 'enlightened' in this context is a literal translation of '*éclairé*', the term in the French version of the document: *consentement libre et éclairé*.[510] The word 'enlightened' should be understood to mean no more than 'informed consent'.

The African Bioethics Resolution displays an awareness of factors which influence individuals or groups in their ability to give free consent, as well as an understanding of the context in which research is taking place. It requires the definition of rules to protect vulnerable populations, the incapacitated, persons deprived of freedom as well as the sick under emergency conditions - so that they may freely consent. The Resolution does not explain who is in the category of 'vulnerable' populations; it is submitted that 'vulnerable' in this context equates with vulnerable to exploitation in research.

The African Bioethics Resolution does not create any binding obligations upon state parties, and is an example of 'soft law'. It is one of the least known resolutions under the regional system.[511]

c) African Charter on the Rights and Welfare of the Child

Although the African Charter on the Rights and Welfare of the Child[512] (African Children's Charter) does not protect a child's right not to be subjected to medical

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508 AHG/Res 254 (XXXII) 1996; also reprinted in 4 *African Ybk Intl L* (1996) 375.

509 See definition given in 1987 edition of The Concise Oxford Dictionary of Current English, 320.

510 See definition Mansion (ed) (1964) *Harrap's French and English Dictionary* 209.

511 It was very difficult to obtain any meaningful information on the Resolution's drafting history, signatories, etc.

512 Adopted in by the 26th ordinary session of the Assembly of Heads of State and Government in Addis Ababa on 11 July 1990 and entered into force on 29 November 1999 upon ratification by 15 member states (OAU Doc CAB/LEG/153/Rev 2, reprinted in Heyns (ed) *Human rights law in Africa* 1997 (1999) 38. It has 29 state parties.

experimentation without their informed consent, it does protect the child's right to survival and development in article 5, which includes the child's right to life; her right to health in article 14 and her right to protection against child abuse and torture in article 16. Under article 16, 'States parties ... shall take ... measures to protect the child from all forms of torture, inhuman and degrading treatment and especially physical or mental injury or abuse'. This article could be interpreted as pertaining to the informed consent of children in research.

d) Protocol to the African Charter on Human and Peoples' Rights on the Rights of Women in Africa

The Protocol to the African Charter on Human and Peoples' Rights on the Rights of Women in Africa[513] (Women's Protocol) refers to women's informed consent in article 4 which deals with the rights to life, integrity and security of the person. Article 4(2) provides that '[s]tates parties shall take appropriate and effective measures to: ... (h) prohibit all medical or scientific experiments on women without their informed consent'. Apart from article 7 of the ICCPR, the Women's Protocol is thus the only human rights instrument which contains a provision which mentions informed consent explicitly, and which is applicable to the situation of HIV vaccine trial participants in Africa.

The consent aspect of article 4(2) has not been litigated. The Women's Protocol has not been in effect for long,[514] and it is exceptional to use a human rights instrument to litigate what is widely considered an ethical guideline. The fact that so few human rights treaties mention informed consent specifically is symptomatic of a world-view which regards informed consent as falling within the realm of bioethics, rather than in the realm of human rights. A violation of the requirement of informed consent for participation in clinical research is thus seen as a violation of ethical guidelines, instead of a violation of a human rights treaty.[515]

Despite numerous abuses of the rights of research participants in Africa,[516] no communication related to research participation, or the right not to be subjected to

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513 Adopted in Maputu in July 2003, and entered into force on 27 November 2005.
514 The Women's Protocol came into effect in November 2005.
515 See below.
516 Elaborated upon in chapter 3 above.

medical experimentation without informed consent, has reached the African Commission on Human and Peoples' Rights.[517]

Nevertheless, in three communications particularly, the jurisprudence of the African Commission establishes general principles potentially relevant to the protection of HIV vaccine trial participants (although none of the three cases deals with informed consent). These communications do not concern so-called first generation or civil and political rights, but rather second and even third generation rights.[518] They are *SERAC and Another v Nigeria,*[519] *Free Legal Assistance Group and Others v Zaire*[520] and *Purohit and Another v The Gambia.*[521]

The communication in *SERAC and Another v Nigeria* concerns the Nigerian state's concerted violation of numerous articles of the African Charter, including sections 2, 4, 14, 16, 18(1), 21 and 24. These rights were violated by the activities of a (government-controlled) oil company, the Nigerian National Petrolium Company (NNPC), the majority shareholder in a consortium with Shell Petrolium Development Corporation, in an oil-producing part of Nigeria known as Ogoniland. The oil company's activities caused wide-scale contamination, degradation and devastation of the area's air, water and soil resources. For example, numerous oil spills occurred in the proximity of Ogoni villages, with serious consequences for the short and long-term health of the inhabitants, such as respiratory ailments, increased risk of cancers, neurological and reproductive problems.[522]

In finding that violations had occurred, the African Commission argues the indivisibility of the different generations of rights, and emphasises that all three generations of rights entail positive and negative duties:[523]

> Internationally accepted ideas of the various obligations engendered by human rights indicate that all rights – both civil and political and social and economic – generate at least four levels of duties for a state that undertakes to adhere to a rights regime, namely the duty to *respect, protect, promote and fulfil* these rights. These obligations *universally* apply to all rights and entail a *combination of negative and positive duties*.

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517 Neither has such a communication reached any of the UN bodies.

518 As pointed out, this characterisation of rights into three generations is outdated. In this regard, see Viljoen (2007) (forthcoming).

519 *Social and Economic Rights Action Centre (SERAC) and Another v Nigeria* (2001) AHRLR 60 (ACHPR 2001).

520 *Free Legal Assistance Group and Others v Zaire* (2000) AHRLR 74 (ACHPR 1995).

521 *Purohit and Another v The Gambia* (2003) AHRLR 96 (ACHPR 2003).

522 *Social and Economic Rights Action Centre (SERAC) and Another v Nigeria* para 2.

523 As above, para 44. My emphasis.

The Commission quoted from various international human rights law precedents[524] and remarked:[525]

> Governments have a duty to protect their citizens, not only through appropriate legislation and effective enforcement, but also by protecting them from damaging acts that may be perpetrated by private parties ... This duty calls for positive action on the part of governments in fulfilling their obligation under human rights instruments.

These comments are relevant in respect of the position of participants in clinical trials in Africa undertaken by international pharmaceutical companies (so-called non-state actors). The Commission reiterates that the relevant articles of the African Charter *impose an obligation* on governments to take (positive) measures (in terms of article 24) to *prevent* pollution and ecological degradation, to promote conservation, and to ensure an ecologically sustainable development and use of natural resources.[526] By analogy, the other rights in the African Charter, such as in articles 4, 5 and 6, create obligations of this kind on African governments to *prevent* abuses of research subjects in clinical research, which they can do only if they take proactive measures to ensure these rights.[527]

As well, according to the theory of implied rights, the right to be free from medical experimentation without participants' informed consent may be considered to be *implied* in other rights in the African Charter. As was pointed out in chapter 4, article 4 of the African Charter which provides that 'human beings are inviolable', and that 'every human being shall be entitled to respect for his life and integrity of his person', and article 5, which ensures that every 'person shall have the right to liberty and to the security of his person', may be used to support the notion that HIV-related clinical research participants give free and informed consent to research participation. Research without such consent violates the integrity and security of the person.

The *SERAC* communication also concerned article 21 of the African Charter: article 21(1) reads, '[a]ll peoples shall freely dispose of their wealth and natural resources. This right shall be exercised in the exclusive interest of the people ...' Assuming a correspondence in the communication between the violation of this guarantee and the exploitation by colonial powers of Africa's material resources and

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524 The Commission eg referred to *Velasquez Rodriquez v Honduras* (before the Inter-American Court of Human Rights) and *X and Y v Netherlands* (European Court of Human Rights).

525 n 519 above, para 57. My emphasis.

526 n 519 above, paras 52. My emphasis.

its peoples, the African Commission found that Nigeria had violated that right by allowing the oil companies to undertake oil explorations in Ogoniland. The Commission claims: 'colonial exploitation has left Africa's precious resources and people still vulnerable to foreign misappropriation'.[528] In the same way, clinical research which exploits its human resources, could be regarded as a violation of article 21, as not being in 'exclusive' interest of Africa's peoples. The Commission adds:[529]

> The drafters of the Charter obviously wanted to remind African governments of the continent's painful legacy and restore co-operative economic development to its traditional place at the heart of African society.

In endeavouring to develop a vaccine for HIV/AIDS, the collaborative effort between international corporations and African researchers and corporations should be mutually beneficial. A collaborative partnership, for example, would be one which offers training and the development of research capacity in under-resourced African counties. A research endeavour to which participants do not give free and informed consent, by definition, is exploitative.

In *Free Legal Assistance Group and Others v Zaire*[530] the African Commission dealt with a communication resulting from severe violations during a civil war in Chad. The finding, which identifies a duty on the part of the state to 'protect' civilians against violations by non-state actors, is directly relevant to the position of vaccine trial participants. In cases in which a government's own forces are not responsible for the killings committed by other (non-state) actors, does not absolve it of responsibility if it *fails to prevent or takes no action to investigate* allegations about assassinations and other killings.

In principle, international human rights law binds states alone, as states are the parties to international agreements and, therefore, the conduct of other parties is not within the ambit of international human rights law. States have a responsibility to protect the rights of their populations against violations by others. On the finding in the case, Viljoen comments: 'Going beyond the duty to 'respect', the Commission also interpreted rights in the Charter to entail a 'positive obligation' to 'protect' and 'fulfil' ... [the Free Legal Assistance Group and Others communication] exemplifies

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527 See ch 6 below, paras 5.4 and 5.5
528 n 519 above, para 56.
529 As above.
530 n 520 above.

the duty (or 'positive obligation') of the state to 'protect' civilians against violations by non-state actors.[531]

In *Purohit and Another v The Gambia,*[532] the African Commission dealt with a communication submitted on behalf of patients detained at Campama, a psychiatric unit of the Royal Victoria Hospital, as well as existing and 'future' mental health patients detained under the Mental Health Acts of the Republic of The Gambia.

The complainants alleges violations of articles 2, 3, 5, 7(1)(a) and (c), 13(1), 16 and 18(4) of the African Charter on Human and Peoples' Rights, on the basis that legislation governing mental health in The Gambia is outdated; that in the Lunatics Detention Act (the principle instrument governing mental health) there is no definition of who is a lunatic; and that there are no provisions and requirements establishing safeguards during the diagnosis, certification and detention of the patient. Moreover, the complainants allege that there is overcrowding in the psychiatric unit, that there is no requirement of consent to treatment or subsequent review of continued treatment (in particular, this allegation is significant for the current study).

In the course of delivering a finding, the Commission refers to *Media Rights Agenda v Nigeria,*[533] in which the African Commission holds that the term 'cruel, inhuman or degrading punishment and treatment' is to be interpreted as extending to the widest possible protection against abuses, whether physical or mental; and to *Modise v Botswana,*[534] in which the African Commission states that exposing victims to 'personal suffering and indignity' violates the right to human dignity.[535] The Commission emphasises that 'personal suffering and indignity can take many forms, and will depend on the particular circumstances of each communication brought before the African Commission'.[536]

Finding the state in violation of the articles of the African Charter, the African Commission holds as follows:[537]

> Enjoyment of the human right to health as it is widely known is vital to all aspects of a person's life and well-being, and is crucial to the realisation of all the other fundamental human rights and freedoms. This right includes the right to health facilities, access to goods and services to be guaranteed to all without discrimination of any kind.

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531 Viljoen (n 518 above).
532 n 521 above.
533 (2000) AHRLR 262 (ACHPR 2000).
534 (2000) AHRLR 30 (ACHPR 2000).
535 Para 58.
536 *Purohit and Another v The Gambia*, para 58.
537 As above, para 80.

Within the obligations on a state which has ratified the African Charter, the Commission orders a positive duty by the state to '[r]epeal the Lunatics Detention Act and replace it with a new legislative regime for mental health in The Gambia compatible with the African Charter on Human and Peoples' Rights and international standards and norms for the protection of mentally ill or disabled persons as soon as possible';[538] to '*provide* adequate medical and material care for persons suffering from mental health problems in the territory of The Gambia';[539] and '[r]equests the government of The Gambia to report back to the African Commission when it submits its next periodic report in terms of article 62 of the African Charter on measures taken to comply with the recommendations and directions of the African Commission in this decision'.[540]

States ratifying the African Charter have an analogous duty to fulfil the rights guaranteed in the Charter which includes the right to freedom and security of the person, and can be read as prohibiting indignities committed during clinical trials in Africa.

4.4 National human rights law on informed consent

4.4.1 Introduction

Informed consent is well-established in South African law as a requirement for lawful medical intervention. South African law regulates consent to participation in research as part of the wider concept of consent to medical intervention. Section 12(2)(c) of the Constitution is but one of a number of sources (albeit an important one) of informed consent law in South Africa and it cannot be seen in isolation from the wider relevance of informed consent in South African common law, case law and statutes. Before the analysis of informed consent focuses on the Bill of Rights, the juridical foundation of informed consent in the South African common, case and statute law is established.

This section is structured as follows: the juridical basis of informed consent in South African law is outlined prior to presenting the requirements for lawful consent developed in South African common law and case law, as well as the forms in which informed consent are expressed. Possible exceptions to the researcher's duty to disclose information are indicated, and the legal consequences of a research

538 Para 87.
539 As above.
540 Para 88.

intervention without informed consent are described. Difficulties which relate to the requirement of causation in the context of research-related liability are deliberated upon and the provisions of the new National Health Act on informed consent to participation in research analysed.

This chapter has a very specific focus – informed consent to participation in preventive HIV vaccine efficacy trials. As a consequence the discussion on informed consent in South African common, case and statute law is limited to:

- a discussion of the law on informed consent as it pertains to **competent**[541] **adult**[542] persons;
- a discussion of the law on informed consent as it pertains to **preventive** HIV vaccine research or experimentation (and therefore not research to find a cure or treatment for HIV, or so-called pure 'therapeutic'[543] research); and
- a discussion of the law as it pertains to **controlled clinical trials** and not to standard medical interventions or treatment.

Common law and case law do not deal with informed consent in a research setting. Therefore the general principles of informed consent to medical interventions need to be extrapolated to a research setting.

4.4.2 Juridical foundations of informed consent

Under South African law, legal liability for wrongful (delictual) or unlawful (criminal) conduct during a medical intervention is based on one or a combination of the following: contractual liability; delictual liability; criminal liability or professional censure for unprofessional or unethical conduct.[544]

Any medical intervention, therapeutic or experimental, is considered lawful only in the presence of certain grounds of justification, which are: consent, necessity

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541 In the light of current ethical, legal and constitutional provisions preventive HIV vaccine trials are unlikely to be undertaken on incompetent or mentally incapacitated persons. Regarding research on mentally incompetent persons, see eg Van Staden 'Can involuntary admitted patients give informed consent to participation in research?' (2007) 13 *SA J Psychiatry* 10.

542 A discussion of the participation of children in HIV vaccine research falls outside the scope of this thesis, and is referred to merely in passing. For more on the participation of children in HIV vaccine research, see the sources referred to in n 26 above.

543 See para 5.2 below.

544 Carstens and Pearmain (n 13 above) 872. As pointed out above, the discussion in this chapter centres on delictual and criminal liability for medical research performed without informed consent.

and *negotiorum gestio*;[545] the list of justifications, however, is not closed.[546] The general criterion determining lawfulness is the *boni mores* or legal convictions of society.[547] The grounds of justification merely are a crystallisation of the *boni mores* test for circumstances that frequently occur in practice. Judge Thirion, in *Clarke v Hurst*, remarks that the 'stereotyped grounds of justification are specific grounds of justification of otherwise wrongful conduct which with the passage of time have become crystallised, with their own rules limiting the scope of their application'.[548]

Consent is a pre-requisite for lawful medical interventions based on the principle or defence of *volenti non fit iniuria*.[549] The defence of *volenti non fit iniuria*, in certain circumstances, may exclude the wrongfulness or unlawfulness of a crime or delict:[550] the literal meaning is 'no harm is done to someone who consents thereto':[551]

> No man can complain of an act which he has expressly or impliedly assented to. This principle, which was well known to the Roman and Roman-Dutch law, is commonly expressed by the maxim *volenti non fit injuria*. Literally interpreted, the maxim is applicable only to cases where a person has consented to suffer something which would otherwise be an intentional wrong, eg consent to undergo a surgical operation or consent to the publication of a defamatory statement. But the maxim is used in a wider sense, and is applied to cases where a person has consented to run the risk of unintentional harm, which would otherwise be actionable as attributable to the negligence of the person who caused it.

Consent therefore excludes unlawfulness: 'where a person legally capable of expressing his will gives consent to injury or harm, the causing of such harm will be lawful'.[552] As in the extract above, *volenti non fit iniuria* can be interpreted narrowly (the research subject consents to *specific* harm) or more widely (the research

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545 Strauss (1991) 31; other commentators mention additional grounds, such as therapeutic privilege, unauthorised administration and relative impossibility (see Carstens and Pearmain 873) and unauthorised agency and therapeutic privilege (see Claassen and Verschoor (1992) 75 – 78). For some, therapeutic privilege is a sub-species of *negotorium gestio* – see eg the discussion by Coetzee (2001) 'Medical therapeutic privilege' (unpublished LLM thesis, University of South Africa) 77.

546 Snyman (2006) 95; Neethling *et al* (2006) 71; Carstens and Pearmain 937.

547 See eg *Clarke v Hurst* 1992 (4) SA 630 (D) 653B. See also Neethling *et al* 70.

548 *Clarke v Hurst* 650.

549 The ground of justification of consent is based on the rule that when a legally competent person consents to an action which would otherwise be unlawful, that infringement of her rights is regarded as lawful (Carstens and Pearmain (n 13 above) 875; Neethling *et al* (n 546 above) 71). See also Van Oosten (n 11 above) 10. Similar grounds of justification exist in other countries; however, they are not always based on the doctrine of *volenti non fit iniuria*, but on the doctor's duty of care towards her patient (see *Rodgers v Whitaker* (1993) 67 ALJR 47).

550 As above; *Stoffberg v Elliott* 1923 CPD 148.

551 McKerron, cited in *Lampert v Hefer* 1955 2 SA 507 (AD) 512.

552 Neethling *et al* (n 546 above) 89.

subject consents to the assumption of the *risk* of harm).[553] Consent to harm is consent to a *specific* harm, but not harm which is not yet determined or which is not defined,[554] and constitutes a one-sided action. An example is a patient who consents to an operation for a certain medical condition.[555] At the time the consent is given it is certain that the operation (or harm) will take place. In consenting to the *risk* of harm there is a possibility or even the likelihood that the actions of the other party will cause harm, but no certainty.[556] The person who consents to the operation, consents to the *risk* of a certain side-effect materialising during the operation and, therefore, to the risk of harm.[557] In a research setting the second of the two forms, the assumption of the *risk of harm*, is more likely to be present. Though some of the risks of a researched drug or intervention are known at the beginning of a trial not all risks can be known, neither can the researcher predict the likelihood of known risks materialising. In the case of preventive HIV vaccine efficacy trials there are a number of unknown risks[558] that may materialise and, therefore, subjects can be said to assume the risk of possible harm.

Consent as a ground of justification has a number of characteristics. They are:[559]

- Consent to injury is a unilateral act and need not necessarily be made known to the actor or defendant. No contract or agreement needs exist between the parties. Because it is a unilateral act consent may be withdrawn at any time prior to the act of harm.
- Consent is a legal act which restricts the injured person's rights. In order to qualify as a legal act the consent must be apparent or manifest.
- Consent may be given expressly or tacitly. Mere acquiescence does not constitute consent.
- Consent must be given *before* the prejudicial conduct.[560]
- Generally, the prejudiced person herself must give consent but exceptions to the rule exist.[561]

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553 Van Oosten (n 11 above) 14; Neethling *et al* 92.
554 Neethling *et al* 93.
555 As above.
556 As above.
557 As above.
558 See para 4.5 of ch 2 above.
559 Neethling *et al* 92 - 93; Snyman (n 546 above) 122 - 127.
560 ' 'Approval' given after the fact is not consent but may amount to an undertaking not to institute an action against the defendant (*pactum de non petendo*)' (Neethling *et al* 99).

These are the general *characteristics* of consent as a ground of justification. For the defence of informed consent to an experimental or therapeutic intervention to succeed, certain *requirements* have to be met; these are discussed below.

4.4.3 Requirements for lawful informed consent

Van Oosten outlines the requirements for legally valid informed consent:[562]

- Informed consent must be recognised by law: it must not be against the *boni mores* or public policy.[563]
- The person who consents must have the legal capacity to consent, that is, the consenting person must be legally and factually capable of understanding information and deciding on a course of action.
- The consent must be *informed*, that is, information and comprehension should be present so that the consenting party knows what risks and benefits she is consenting to.[564]
- Consent should be free and voluntary.[565]
- Consent should be clear and unequivocal.
- Informed consent must be comprehensive.[566]
- It must be prior consent or consent given in advance.
- It must be revocable.[567]

Certain requirements are particularly problematic or significant in relation to research generally and to preventive HIV vaccine efficacy clinical trials specifically. They are discussed below.

a) Informed consent must be recognised by law.

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561 Such as proxy consent in the case of incompetent persons.

562 Van Oosten (n 11 above) 17 – 25.

563 See Strauss 'Bodily injury and the defence of consent' 1964 *SA L J* 179 183.

564 Carstens and Pearmain (n 13 above) 878; Strauss (n 545 above) 4; Claassen and Verschoor (n 545 above) 59.

565 See *R v McCoy* 1953 2 SA 4 (SR).

566 Also see *Christian Lawyers Association v Minister of Health* 1998 (4) SA 1102 (W) where the Court stated that the woman has to 'subjectively' consent and that her consent must be comprehensive in that it must cover the entire transaction and its consequences.

567 Because consent is a unilateral act, it may be unilaterally revoked by the consenting party at any stage before the defendant's conduct (Neethling *et al* 91).

This requirement, in other words, means that the consent should correspond to the *boni mores* of society.[568] In this regard, it is important that the concept of the legal convictions or *boni mores* of society, now, necessarily must incorporate the values and norms of the Constitution.[569] The courts have an obligation to develop the *boni mores* as part of the common law in accordance with the spirit, objects and purport of the Bill of Rights – 'in brief, to develop the *boni mores* of our constitutional community'.[570] Johann Neetling holds further that the element of wrongfulness should be defined more broadly to provide better protection of the values (such as physical integrity) underpinning the Bill of Rights.[571]

As pointed out,[572] any consent to physical harm or risk of such harm is *prima facie contra bonos mores* unless a ground of justification exists.[573] Consent to HIV research or experimentation which would be regarded against the *boni mores*, for example, is experimentation where there is a serious risk of injury to otherwise healthy HIV-negative individuals, or research which involves the publication of participants' HIV status. Research which allows for the peri-natal transmission of HIV without intervention in the form of ARVs, in order to study the epidemiology of the mode of transmission, similarly, would be *contra bonos mores*.

In the case of research conducted on healthy individuals, or research which risks serious harm to participants, the legal position as to what is *contra bonos mores*, is not clear. Van Oosten mentions that factual consent to wanton experimentation is *contra bonos mores*.[574] Strauss and Strydom argue that no valid consent can be given to research which involves a risk of serious harm.[575] Moreover, research on healthy individuals (so-called non-therapeutic research),[576] which may involve lasting, serious consequences, is almost certainly *contra bonos mores*. The MRC guidelines strictly prohibit non-therapeutic research involving more than 'minimal' risk.[577]

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568 Neethling *et al* 94.
569 Neethling (2005) 122 *SA L J* 580.
570 As above.
571 As above.
572 Para 4.4.2.
573 Neethling *et al* 94.
574 Van Oosten (n 15 above) 14.
575 Strauss and Strydom (1967) 246 – 250.
576 See para 5.2 below for a discussion of the distinction between therapeutic and non-therapeutic research.
577 See para 3.4.1 above.

It is submitted that whether preventive HIV vaccine efficacy trials are in keeping with the *bonos mores*, depends on whether such research is defined as therapeutic or non-therapeutic, and on whether the possible harm which attaches to the trials is considered to be serious. These aspects of the trials are taken into consideration below;[578] it is sufficient here that adult participation in non-therapeutic research which does not involve more than minimal risk would not be considered *contra bonos mores*, or that therapeutic HIV research (where the participants are HIV positive or have AIDS) would not be *contra bonos mores* if the risk is minimal.

b) The person who consents must have the legal capacity to consent.

Consent is given by someone who is legally and factually capable of consenting.[579] Alternatively, proxy consent is allowed if a person is incapable of consenting.[580] Adults who are competent may consent to medical interventions and research;[581] spouses consent independently of each other.[582]

Adults may lack legal capacity or competence to consent as a result of mental illness, or because they find themselves in a state of unconsciousness, or other factors.[583] Not all mentally ill persons, even all institutionalised mentally ill persons, are legally incapable of consenting to participation in research.[584] In the case of research on mentally ill persons, it must be assessed whether the mental disorder prevents the person from (i) understanding to what she is consenting; (ii) choosing decisively for or against participation in research; (iii) communicating her choice; or (iv) accepting the need for an intervention.[585] Werdie Van Staden argues, congruent with current South African laws, that a functional approach[586] to the question of whether a mentally ill and institutionalised person can give valid consent to participation in research requires that her capacity to give informed consent be

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578 See para 5.2 below.

579 Van Oosten (n 15 above) 10. See also the extensive discussion by Carstens and Pearmain (n 13 above) 897 – 905.

580 Van Oosten (n 15 above) 15.

581 Carstens and Pearmain (n 13 above) 898.

582 Claassen and Verschoor (n 545 above) 61; Carstens and Pearmain (n 13 above) 902. Also see para 5.4 below for views on culture, individualism and informed consent.

583 See the discussion in Carstens and Pearmain on the capacity of mentally ill persons to consent to medical interventions (899 – 902).

584 Burchell (1988) *Acta Juridica* 217 – 218; Van Oosten (n 15 above) 5 – 18.

585 Van Staden and Kruger (2003) 29 *J Med Ethics* 41; Van Staden (n 541 above) 10.

586 Rather than a categorical approach which predicates that people should be considered incapable by virtue of their belonging to a certain category, for example, being involuntarily admitted to a psychiatric hospital (Van Staden 10).

assessed clinically rather than assumed by virtue of her belonging to a certain category of legal admission status.[587]

It is also possible that the nature of the research to be undertaken has an influence on whether mentally ill persons would be considered suitable research participants. Van Oosten comments:[588]

> Although mentally ill or mentally defective persons may, in principle and in fact, be capable of consenting to participation in medical research, it is submitted that their capacity to consent be limited to *therapeutic research* on account of i) it's [*sic*] potential personal benefit; and ii) the undeniable potential of undue influence being exerted, wittingly or unwittingly, on such patients. A possible exception would be where the proposed form of non-therapeutic research involves no risk or danger at all as, for instance, in cases of an unlinked and anonymous (i) gathering of information from the patient by means of questionnaires or from medical records, or (ii) examination of a specimen taken from a patient.

Van Oosten's view should be supported, however, it is submitted that there is little likelihood that preventive HIV vaccine efficacy trials will be conducted amongst institutionalised mentally ill persons, should they be capable of giving legally valid consent to participation. Scientific and methodological imperatives[589] negate the value of such trials, but, almost certainly, they would be considered *contra bones mores* because of fears of exploiting a captive vulnerable group. Therapeutic research, which is aimed at alleviating the burden of disease of the specific research participants, will be acceptable if conducted in strict compliance with legal and constitutional imperatives.[590]

Legal capacity to consent to medical interventions, such as participation in research, is influenced also by a person's age. The capacity of minors to consent to participation in research is outlined elsewhere.[591]

*c) The consent must be **informed**.*[592]

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587 Van Staden 10.

588 Van Oosten (n 15 above) 16.

589 For example, in a closed environment, such as a hospital for the mentally ill, exposure to the virus against which the vaccine is supposed to protect is a minimal risk, consequently, it would be difficult to illustrate the efficacy of the vaccine.

590 This is the extent of the discussion of the capacity of mentally ill persons to consent to participation in research. For more on this topic, see the sources quoted in ns 15 and 584, as well as Carstens and Pearmain (n 13 above) 899 – 902.

591 See para 4.4.6. As pointed out at the beginning of the chapter, the thesis is concerned with *adult* HIV vaccine efficacy trial participation and the position of minors, therefore, is dealt with only in passing. For more on the capacity of minors to consent to medical interventions, see Carstens and Pearman 902 – 904.

592 *Castell v De Greef* (n 13 above) 420 – 421; Van Oosten (n 11 above) 54 – 60; Carstens and Pearmain (n 13 above) 882; Neethling *et al* (n 546 above) 93 – 94.

Consent cannot be judged informed unless the research participant knows what she is consenting to. Research participants usually are lay persons without scientific and medical knowledge; it is the responsibility of the researcher to provide the information which enables participants to make an informed decision. Van Oosten asserts, 'information furnished by the doctor as an expert to the layman as a patient serves the purpose of providing the patient with sufficient *knowledge* and *appreciation* of the harm or risks to enable him to reach a decision on whether to grant or withhold consent to a medical intervention'.[593] Both *information* and *comprehension* must be present so that the consenting party knows the risks and benefits to which she is consenting.

In order to decide if *informed* consent is present, the court examines the facts of the case.[594] The researcher or health care worker must not only show that she has provided the patient or research participant with information regarding the research or intervention, but that the information has been *understood* by the patient or research participant;[595] that she '*appreciates* and *understands* what the . . . purpose ... is'.[596] Of course, *appreciation* proposes more than mere *knowledge*. Knowing that vaccination with HIV during a clinical trial may cause 'immune tolerance' is different from appreciating the consequence of not being eligible to be inoculated with a vaccine for HIV should one subsequently become available.

The provision of information is not sufficient if the patient or research participant is unable to meaningfully *act* on that information. *C v Minister of Correctional Services* deals with an HIV test performed on a prisoner without his informed consent.[597] The Constitutional Court found that, despite having twice been informed that the test was for HIV and other sexually transmitted diseases and that

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593 Van Oosten (n 11 above) 20. My emphasis.

594 Neethling *et al* 92. The onus of establishing liability for an intervention without informed consent lies with the plaintiff (in a civil case) and the state (in a criminal case). Once a *prima facie* case of non-disclosure has been established, the doctor will have to refute the allegation of non-disclosure by providing evidence that the patient had indeed given informed consent (Carstens and Pearmain (n 13 above) 891).

595 Van Oosten (n 11 above) 24. See also *C v Minister of Correctional Services* 1996 (4) SA 292 (T). My emphasis.
Ngwena remarks: 'Pre and post [test] counselling are integral to informed consent requirements in view of the serious implications of an HIV positive result' (Ngwena 'Constitutional values and HIV/AIDS in the workplace: Reflections on *Hoffmann v South African Airways*' (2001) 1 *Developing World Bioethics* 55).

596 Van Oosten (n 11 above) 24. Of course, appreciation implies more than mere knowledge.

597 *C v Minister of Correctional Services* 301D.

he had the right to refuse, the prisoner's consent had not been *informed* as he was not given the information in private,[598] nor had the prisoner been given sufficient time to consider whether to refuse the test.[599]

In the context of this thesis, a person invited to participate in a HIV vaccine efficacy trial or a therapeutic HIV clinical trial, if that person is not provided with enough time to consider participation, or is not offered alternative means of accessing health care or HIV-treatment, cannot be regarded as having given informed consent, as they would be considered to have had no alternative course of action.

Castell v De Greef places emphasis on what a reasonable patient would want to know about a procedure rather than the information considered essential by the doctor. The 'reasonable patient or person' standard requires that the information disclosed conforms to that which a (hypothetical) reasonable patient would want to know about the potential risks and benefits of the proposed procedure or treatment, as well as alternative treatment:[600]

> For a patient's consent to constitute a justification that excludes the wrongfulness of medical treatment and its consequences, the doctor is obliged to warn a patient so consenting of a material risk inherent in the proposed treatment; a risk being material if, in the circumstances of a particular case:
>
> a) a reasonable person in the patient's position, if warned of the risk, would be likely to attach significance to it; or
>
> b) the medical practitioner is or should be aware that the particular patient, if warned of the risk, would be likely to attach significance to it.

The reasonable patient or person standard is viewed as being most likely to deliver respect for patient autonomy.[601] The authority to determine what information to

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598 304C-E.

599 As above. In *Christian Lawyers Association v Minister of Health* (n 566 above) the Court had to interpret the meaning of 'informed consent' as it is used in the Choice on Termination of Pregnancy Act 92 of 1996. Judge Mojapelo observed that in South African law informed consent rests on three legs: knowledge, appreciation and consent. He supports the definition given in *Waring and Gillow v Sherbourne* 1904 TS 340 where the Court remarked that:
'It must be clearly shown that the risk was known, that it was realised, that it was voluntarily undertaken. Knowledge, appreciation, consent – these are the essential elements; but knowledge does not invariably imply appreciation; and both together are not necessarily equivalent to consent' (344).
According to Judge Mojapelo, a woman who consents to the termination of her pregnancy must also 'comprehend and understand the nature and extent of the harm or risk'.

600 426F-G.

601 See eg Burchell (n 584 above) 216.

disclose to research participants, thus, has shifted from doctors or researchers to patients or participants.[602]

The extent of the information that needs to be understood and appreciated by the research participant needs to be assessed: should the researcher inform about all the significant risks of the proposed research? Those which occur most often in a particular research setting or all the risks, or that some risks even may be unknown at the point of consent?

In *Castell v De Greef* the Court determined that a patient in a doctor-patient relationship be informed of all 'material' risks.[603] However, the situation of a research participant is different from that of a patient; more so in cases of 'non-therapeutic' research. In a research situation the researcher initiates the relationship by approaching the participant to take part in research. Whatever risks the participant is exposed to are a direct result of the research situation. It is therefore submitted that a still greater duty lies with the researcher to be certain that informed consent is given to participation in research. Consequently, it is not sufficient to warn the participant of the risks of the research in line with the determination by the court in *Castell v De Greef*, it is submitted that the research participant should be informed of *all* the known risks attaching to the research endeavour, and, if there is a likelihood that the research intervention carries risks that are yet unknown, the participant should be told that these risks may materialise in the course of the research.[604] Van Oosten comments that full disclosure in a research context is necessary because:[605] i) research subjects who are not fully informed may be abused

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602 The approach in *Castell v De Greef* contrasts with that previously held in *Richter v Estate Hammann* 1976 (3) SA 226 (C), in which the court adopted a 'reasonable doctor' standard:
'in principle his conduct should be tested by the standard of the reasonable doctor faced with the particular problem. In reaching a conclusion a court should be guided by medical opinion as to what a reasonable doctor, having regard to all the circumstances of a particular case, should or should not do' (2323H).
This principle of testing conduct according to what a 'reasonable doctor' should do, is in accordance with the English law principle known as the 'Bolam principle or test'. The Bolam principle was endorsed by a majority of the House of Lords in the case of *Sidaway v Governors of Bethlehem Royal Hospital and Others* (1985) 2 WSR 480 (HL) (E), [1985] 1 All ER.

603 *Castell v De Greef* (n 13 above) (428 F-G). A departure from the position in an earlier case, *Lymbery v Jefferies* 1925 AD 236, in which the court held that a patient who had received X-ray treatment of the uterus, 'must have understood' that she will be infertile after the treatment. The question now is not what the patient ought to have understood, but what the patient did understand in fact. In this regard, see also Strauss and Strydom (n 575 above) 214.

604 Carstens and Pearmain (n 13 above) share this view – see 894 – 895.

605 Van Oosten (n 15 above) 27.

in the research setting; ii) standard (and tested) medicine, in most cases is available to the research participant; iii) research involves increased risks and dangers from those present in standard medicine; iv) often there is no personal benefit to research participants who take part in non-therapeutic research; v) a confict is likely to arise in research between the patient's autonomy and his health; and, therefore, vi) the principle that the scope of the information to be imparted to the patient increases in proportion to the measure in which the proposed research is new and untried, must in all cases be adhered to. This is also the approach adopted by the National Health Act 61 of 2003.[606]

It is unlikely to provide that the information provided the research participant will cause her to become expert in the field; to do so would be time-consuming and, even, improbable. In the case of HIV vaccine trials, the science underlying the trials is of such a complex nature that, certain intricacies may not be fully comprehensible to even an educated lay person. It is therefore submitted that a research participant be brought to a level of understanding of the information comparable with that of an educated lay person.

In respect of informed consent to preventive HIV vaccine efficacy research, the information and comprehension aspects are particularly problematic. These aspects are discussed in further detail below.[607]

d) Consent should be free and voluntary.

Under South African law, informed consent resists medical paternalism and supports patient autonomy. The court remarks as follows in this regard in *Castell v De Greef*:[608]

> It is clearly for the patient to decide whether he or she wishes to undergo the operation, in the exercise of the patient's fundamental right to self-determination ... It is, in principle, wholly irrelevant that her attitude is, in the eyes of the entire medical profession, grossly unreasonable, because her rights of bodily integrity and autonomous moral agency entitle her to refuse medical treatment.

Informed consent, according to the Court in *Castell v De Greef*, is the expression of a patient's fundamental right to self-determination. Even knowing that the patient is acting against her best interests, a doctor cannot make the decision for her. Judge

606 See para 4.4.6 below.
607 See para 5.3.2 below.
608 *Castell v De Greef* (n 13 above) 420G-421A.

Ackerman stresses that 'it is in accord with the fundamental right of individual autonomy and self-determination to which South African law is moving'.[609]

Informed consent should be freely given and not be induced by fraud, fear, or force.[610] Only informed consent which is freely and voluntarily given can be considered as adhering to the patient's right of self-determination. Factors which influence the freedom and voluntariness of informed consent in a research setting, for example, are the fraudulent or negligent misrepresentation of the research (such as, if a participant in research is under the impression that she is undergoing treatment instead of taking part in research, and if that misrepresentation can be ascribed to the researcher's intentional or negligent actions, the research may be held liable due to a lack of informed consent)[611] and disproportionate financial incentives (if payment is given for participation in research in a setting in which participants are destitute and the payment is more than compensation for costs incurred and inconvenience suffered). Because this requirement for informed consent is particularly problematic in a South African HIV vaccine efficacy trial context, it is discussed in greater detail below.[612]

e) Consent should be clear and unequivocal.[613]

In a situation in which there is no clear distinction between research and treatment, it is possible that a research participant is under the impression that she is consenting to treatment, whereas she is consenting to taking part in research. It is therefore necessary that the experimental nature of any research endeavour clearly is pointed out to the participant.

Section 71(1) of the National Health Act requires that informed consent to participation in research is in writing.[614] It is unclear whether the legislator intends that the actual agreement or consent alone to be in writing, or whether the invitation to take part in research (also known as the 'informed consent document' or PIL, which sets out all the risks and possible consequences of research participation) should be in writing as well. Regardless of the interpretation of section 71(1), it is submitted that an invitation to take part in research should be in writing and that

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609 As above.
610 Van Oosten (n 15 above) 29; Strauss (n 545 above) 134; Claassen and Verschoor (n 545 above) 59;
611 See Neethling *et al* (n 546 above) 302 – 306; see also Claassen and Verschoor 59.
612 See para 5.3.1 below.
613 See also Strauss 8 -12.
614 See para 4.4.6 below.

consent also should be in writing. Only in cases where the experimental nature of the planned intervention has been set out clearly can it be established that a research participant was not under a misapprehension as to the nature of the intervention.

f) Informed consent must be comprehensive.[615]

The research participant's consent should cover every aspect of the planned research endeavour. In the context of preventive HIV vaccine efficacy trials, it is submitted that participants' consent should cover every research intervention, including the participant's repeated subjection to HIV testing. Consent should be given for each HIV test that is performed, accompanied by pre- and post-test counselling, separate from the participant's consent to take part in the vaccine trial.

Van Oosten argues that a health care provider is not allowed to deviate 'materially' from or extend the intervention initially agreed upon, unless pressing circumstances necessitate such a deviation.[616] This proposal has implications for informed consent in research: genetic testing sometimes is carried out as part of a larger, different research project. For example, a clinical trial for a new diabetes drug may involve genetic tests as a smaller, sub-investigation. It is submitted that if genetic testing is performed as part of a larger preventive HIV vaccine efficacy trial, participants should expressly be told that such tests will be done and should provide separate, documented informed consent to such testing. Consent to take part in genetic screening cannot be assumed as part and parcel of a drug trial.

Participants in research should consent not only to the research endeavour itself, but also to its consequences.[617] For example, if a necessary consequence of HIV vaccine trial participation is that a participant will test positive on standard HIV ELISA tests, the participant should be made aware of the fact and should consent thereto.

4.4.4 Forms of consent

Generally, informed consent may be expressed or implied.[618] Express consent may be given orally or in writing; the law generally does not require consent to be in

615 See also Strauss (n 545 above) 8 – 12.
616 Van Oosten (1998) 31 *De Jure* 197.
617 Van Oosten (n 11 above) 18.
618 Carstens and Pearmain (n 13 above) 898.

writing.[619] Implied consent is consent which is communicated by actions, such as taking prescribed medication, or visiting a health care provider.[620]

In the case of minor therapeutic interventions, oral or implied consent is regarded as sufficient. In the case of more serious interventions and in the case of participation in research, written consent is required.[621]

It is important that the researcher documents the scope of the proposed intervention in precise detail. Strauss argues that consent to submit to an unspecified operation or any treatment within the health care provider's discretion could be invalid on account of its vagueness.[622]

4.4.5 Exceptions to the consent requirement

Under certain circumstances a health care provider may justifiably proceed with a medical intervention without first obtaining the patient's informed consent.[623] In these circumstances either the information requirement or the consent requirement is lacking: the health care provider may either not inform the patient fully of the intended procedure or she may proceed without the patient's consent. Exceptions to the informed consent requirement are statutory authority; authorisation by a court; necessity and therapeutic privilege.[624] Each is defined and discussed below.[625]

a) Statutory authority[626]

Statutory authority, like consent, eliminates the element of wrongfulness in an act and is based upon the principle that a person 'does not act wrongfully if he performs an act (which would otherwise have been wrongful) while exercising statutory authority'.[627] Conduct authorised by a statute is reasonable or justified and, consequently, lawful.[628] Statutory provisions authorising medical interventions without informed consent usually have a pressing public interest or good as their

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619 Strauss 12; Claassen and Verschoor 59. There are exceptions to this general rule, such as when written consent is required in terms of a statute.

620 Strauss 4; 12 – 13; Carstens and Pearmain 898.

621 See sec 71(1) Act 61 of 2003; also see paras 4.4.3(e) above and 4.4.6 below.

622 Strauss 13.

623 Strauss 3; Claassen and Verschoor 69; Carstens and Pearmain 887 - 890.

624 Commentators list different grounds of justification for a medical intervention. Strauss lists consent, *negotorium gestio* and necessity; Claassen and Verschoor, necessity (emergency), unauthorised agency and therapeutic privilege.

625 As the focus of the thesis is informed consent to *research*, where prior written consent of the participant is mandatory, the discussion is a brief outline of these grounds of justification.

626 See Carstens and Pearmain (n 13 above) 917 – 918.

627 Neethling *et al* 95.

aim, such a provisions ensuring compulsory immunisation against communicable disease.[629]

Various statutes allow medical interventions without the informed consent of the patient, such as section 7(1)(c) the National Health Act 61 of 2003 and chapter 5, section 32 of the Mental Health Care Act 17 of 2002.[630]

It is submitted that, even though medical research to find a vaccine against HIV is a pressing public interest or good, it remains unlikely that a statute will prescribe research participation without informed consent to participation. Should such a statute be promulgated, it would be liable to constitutional challenge under section 12(2)(c).[631]

b) Authorisation by a court

The authorisation of a medical intervention by a court can take two forms: first, a court may authorise an intervention which is not against the patient's wishes but for which the necessary authorisation is lacking, such as in the case of a minor needing an operation and the court authorising the procedure in the absence of parental consent; second, a court may authorise a procedure that is against the patient's wishes, such as when it orders the removal of a piece of evidence lodged in a suspected criminal's body or the taking of a blood or tissue sample.[632]

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628 As above.

629 See eg sec 21(2)(k) National Health Act 61 of 2003.

630 Sec 32 reads:
'A mental health care user must be provided with care, treatment and rehabilitation services without his or her consent at a health establishment on an outpatient or inpatient basis if-
(a) an application in writing is made to the head of the health establishment concerned to obtain the necessary care, treatment and rehabilitation services and the application is granted; -
(b) at the time of making the application, there is reasonable belief that the mental health care user has a mental illness of such a nature that
(i) the user is likely to inflict serious harm to himself or herself or others; or
(ii) care, treatment and rehabilitation of the user is necessary for the protection of the financial interests or reputation of the user; and
(c) at the time of the application the mental health care user is incapable of making an informed decision on the need for the care, treatment and rehabilitation services and is unwilling to receive the care, treatment and rehabilitation required'.

631 See para 4.4.3 below.

632 At present, two provincial decisions provide conflicting authority in this regard: *Minister of Safety and Security v Gaqa* 2002 (1) SACR 654 (C) (where the removal of a bullet from a suspected robber was ordered by the court); and *Minister of Safety and Security v Xaba* 2003 (7) BCLR 754 (D) (where the court refused the state's request in a similar situation).
Also see Carstens and Pearmain (n 13 above) 918 – 920.

Court authorisation compelling a patient to undergo treatment or an intervention is controversial. Such an authorisation against the wishes of the patient, in the absence of a pressing social interest, is in violation of the patient's constitutional right to physical integrity. Strauss comments:[633]

> In the absence of an overriding social interest, or in the interest such as that of a minor child who is dependant upon the person concerned, the mentally competent individual's right to control his own destiny in accordance with his own value system, his *selfbeskikkingsreg*, must be rated even higher than his health and life.

As is the case with statutory authority, it is unlikely that court authorisation compelling participation in HIV vaccine efficacy trials, or any other research, against the would-be participants' wishes and consent, will pass constitutional scrutiny.[634]

c) Necessity

A state of necessity exists when a person is placed in such a position by superior force (*vis maior*) that she is able to protect her interests (or those of someone else) only by reasonably violating the interests of an innocent third party.[635] Like statutory authority and authorisation by a court, necessity excludes wrongfulness.[636]

Necessity allows a health care provider to inflict harm (by acting without prior informed consent) in order to prevent another, greater harm.[637] Necessity may apply to a great number of situations: for example, a health care provider who renders assistance at the scene of an accident; or if competent individuals are inoculated against their wishes to prevent the rapid spread of a dangerous viral infection.[638]

If necessity is used as a justification it must be proven that the harm that is being prevented is either present or imminent.[639] In other words, an emergency situation should be present, which the intervention must be aimed at avoiding. Strauss explains:[640]

> The law would not protect the health fanatic who forcibly attempts to prevent me from using a lot of sugar in my coffee - because he maintains – quite correctly so –

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633 Strauss (n 545 above) 31.
634 See above and para 4.4.3 below.
635 Carstens and Pearmain (n 13 above) 909; Neethling *et al* (n 546 above) 80 - 85.
636 As above.
637 Strauss (n 545 above) 91 - 92; Claassen and Verschoor (n 545 above) 75; Carstens and Pearmain 909.
638 Strauss 91 – 92; Strauss argues that an intervention to protect the health and life of an individual against that individual's expressed will is not justifiable on the basis of necessity, unless the intervention is directed at the protection of pressing societal interests (92).
639 Neethling *et al* 82. The harm must not have terminated, or be expected only in the future.
640 Strauss 93.

> that in the long run it may harm my health or even shorten my life. On the other hand, the doctrine of necessity will clearly avail the policeman who forcibly restrains me from committing suicide by jumping off a window ledge of a high building. A doctor would also clearly have the right to save the life of a would-be suicide, who has taken an overdose of pills, by pumping out the contents of the stomach, or by administering a neutralising agent.

Research without the informed consent of the research participant cannot be justified by the defence of necessity: it is difficult to imagine a situation in which subjecting persons to a research intervention (which would be yet unproven or untested) without their informed consent is justified on the ground of the protection of their own or other persons' interests (which must be in immediate danger).

d) Therapeutic privilege

Therapeutic privilege as an exception to the requirement of informed consent applies to a situation where the full disclosure of information to the patient would not serve her best interests.[641] Coetzee states, although an exact definition of the concept remains elusive, therapeutic privilege may be described as a doctor's 'professional privilege ... to withhold certain information from a patient, or it can signify a legal defence in terms of which a doctor can justifiably withhold certain information from a patient'.[642]

A doctor justifiably can withhold information if disclosure would be harmful and would 'cause anxiety and distress';[643] if such information would 'endanger a patient's life or would detrimentally affect his physical or mental health';[644] if disclosure is detrimental to a patient's best (medical) interests';[645] if the information would 'cause the patient to react in a way which would call into question the success of the intervention';[646] or 'have a detrimental effect on the physical and psychological well-being of the patient or would endanger the patient's life'[647] and in instances in which 'the risks attached to disclosure are as serious or more serious than those attached to the disease or the proposed intervention'.[648]

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641 Carstens and Pearmain 910.
642 Coetzee (n 545 above) 5.
643 As above, 102.
644 Coetzee 112.
645 Coetzee 122.
646 Coetzee 124.
647 Coetzee 112.
648 Coetzee 121.

VRM v The Health Professions Council of South Africa[649] highlights the issue of the requirements for informed consent to HIV testing as set down in South African law and the ethical guidelines of the Health Professions Council of South Africa (HPCSA), and illustrates the dangers of a reliance by a health care provider on the notion of therapeutic privilege rather than obtaining the patient's informed consent.[650]

In January 1999 VRM consulted Dr Labuschagne in respect of the delivery of her baby; at the time she was six months pregnant with her first child. Dr Labuschagne drew blood for 'routine tests' (which included a HIV test) and set the date for the delivery of her baby for 23 March 1999. VRM was not given pre- and post-test counselling as stipulated in the HPCSA's 1992 guidelines on the Management of Patients with HIV Infection or AIDS.[651]

Later VRM was billed for R160 from Drs Buisson and Partners (pathologists). At her next visit to Dr Labuschagne, VRM's husband asked for an explanation of the items in the account, in particular, of 'HIV ELISA' and if it had anything to do with HIV/AIDS. The details of Dr Labuschagne's response were in dispute, but indicate he avoided informing VRM that her test results revealed that she is HIV positive. In April 1999 VRM gave birth by caesarean section to a stillborn baby. Dr Labuschagne informed her the next day that she was HIV positive. He issued a death certificate for the baby which states that the cause of death is 'stillborn/HIV positive'.

VRM requested that Dr Labuschagne's conduct be investigated by the Health Professions Council of South Africa (HPCSA), alleging that Dr Labuschagne contravened the HPCSA's guidelines to which he was bound by conducting a HIV test without her consent and, in particular, without any pre- or post-test counselling. Further, Dr Labuschagne had not disclosed her HIV status at the consultation in

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649 TPD 1679/2002, 10 October 2003 (unreported).

650 Also see the discussion in 'Ought the notion of "informed consent" be cast in stone? *VRM v The Health Professions Council of South Africa*' <http://www.law.wits.ac.za/sajhr/2004/veriava.pdf> (accessed 3 May 2007).

651 HPCSA (1992) Management of Patients with HIV Infection or AIDS:
2.4.2 ... Routine testing of patients in the healthcare setting is unjustifiable and undesirable.
2.4.5 The patient should clearly understand what the purpose of the laboratory test is; what advantages or disadvantages testing may hold for him as patient; why the surgeon or physician wants this information; what influence the results of such a test will have on his treatment; and how his medical protocol will be altered by this information. The psychosocial impact of a positive test result should also be addressed. The principle of informed consent entails that the health care worker accepts that if the patient were HIV positive, appropriate counselling would follow. The health care worker must therefore ensure that the patient is directed to appropriate facilities that will oversee his further care and, if possible, counsel his family or sexual partners.

March when VRM and her husband raised the issue of the account received from Drs Buisson and Partners and specifically asked if an 'HIV ELISA test' had anything to do with HIV. He had not advised VRM on measures she should take to reduce the risk of MTCT transmission of HIV during birth although he was aware of her HIV status, neither had he performed the caesarean section immediately after VRM's waters broke to alleviate the risk of HIV transmission.

The Committee of Preliminary Inquiry of the HPCSA accepted Dr Labuschagne's explanation of what happened (he alleged that he had told VRM that he would test her blood for HIV and that there were no HIV pre- and post-test facilities at the hospital). Specifically, Dr Labuschagne claimed that '[VRM was] one month away from delivery and as stated above I thought it in her best interest, from a psychological point of view not to inform her of her status at this point in time'. The HPCSA, acting on the recommendation of the Committee, resolved that Dr Labuschagne's conduct had not been 'improper or disgraceful'.[652]

In October 2001 an application was launched in the High Court to review and set aside the decision of HPCSA. The application was dismissed, the Court finding (per Jacobs J) that consent was indeed obtained from VRM to have a HIV test.[653] The Court comments that 'this would probably not have constituted informed consent in the strict sense of the expression and was not entirely in line with the guideline issued by the first respondent' [HPCSA], but that 'the difference between consent and informed consent was marginal'.[654] The Court did not consider the HPCSA's ethical guidelines on informed consent to HIV testing to be 'cast in stone'.[655]

A further appeal was instituted to a full bench of the High Court. This Court found that the existence of a dispute over the facts required that the Committee of Preliminary Inquiry refer the complaint for further inquiry to the HPCSA. The Court held further that it was improper conduct for Dr Labuschagne to test VRM for HIV without informing her of the purpose of the test.

The case is not about therapeutic privilege per se, but rather examines the exercise of powers of a quasi-judicial tribunal. However, it demonstrates the pitfalls facing a health care provider who resorts to the defence of therapeutic privilege and to doing what 'doctor thinks best'.

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652 *VRM v The Health Professions Council of South Africa* 58 – 60.

653 Jacobs J's judgement to be found in *VRM v The Health Professions Council of South Africa* TPD 1679/2002, 7 August 2002 (unreported).

654 *VRM v The Health Professions Council of South Africa* 12.

655 As above.

Undoubtedly, Dr Labuschagne believed that he was sparing the expectant mother emotional shock and trauma. Nevertheless, had he, in the first place, sought her informed consent for the HIV test, he could have prepared her for the possibility of testing HIV positive and VRM would have been in a better state to cope with the information. Second, had he sought her informed consent, better treatment of mother and baby could have been instituted, such as treating the infection that likely caused the baby to be stillborn, and providing anti-retrovirals to prevent MTCT of HIV. The trial court's view that that 'the difference between consent and informed consent was marginal', is regrettable and displays an anachronistic and paternalistic view of the relationship between health care provider and patient.

Although the defence of therapeutic privilege is considered a part of South African law,[656] it is doubtful that the defence will be utilised in a research situation. Burchell states:[657]

> where a person is to be a subject in a non-therapeutic research procedure he should be informed off all the known possible risks, whether they are likely or remote, because it is only on this basis that he can consent so as to justify a procedure that is not for his direct, or possibly even indirect, benefit.

In support of this view, Van Oosten insists there is 'no room at all for the therapeutic necessity defence; and, in principle, no room at all for the waiver defence in cases of non-therapeutic research'.[658]

Even in the case of therapeutic research, which, by its nature, potentially may be of benefit to a participant, the intervention remains unproven and experimental and, as such, potentially carries risk or even danger. It is submitted a researcher cannot rely upon therapeutic privilege in cases of therapeutic research as well. Van Oosten declares that a reliance on therapeutic privilege in such a situation would be misplaced and that there is 'precious little room for therapeutic necessity and waiver as defences to non-disclosure in cases of therapeutic research'.[659]

Preventive HIV vaccine efficacy trials, whether they are described as 'therapeutic' or 'non-therapeutic' research,[660] carry risks, some of which may be

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656 See *Castell v De Greef* (n 13 above) 426(H): 'This obligation is subject to the therapeutic privilege, whatever the ambit of the privilege may today still be'.

657 Burchell (n 584 above) 225.

658 Van Oosten (n 15 above) 28.

659 As above.

660 See para 5.2 below.

potentially very serious and others which are unknown.[661] Whether and to what extent these risks will materialise is unsure. It is submitted that therapeutic privilege cannot be used as a defence for not disclosing the potentially serious nature of the risks to participants in clinical trials. There is the possibility that prospective HIV vaccine efficacy trial participants, if given a clear picture of the extent of the possible risk, will choose not to participate. Alexander Politis insists that researchers should never withhold information out of fear that research subjects, once informed of the risks, consequences and dangers of the proposed intervention, will refuse to participate or withdraw from the research altogether.[662] He supports the view that 'the interests of the patient and the patient's right to information supersedes any professional, academic or financial interest that the researcher or medical practitioner may have in involving the patient in the research or experiment'.[663] The notion that preventive HIV vaccine trial participants are fully informed of all the risks and consequences of the trials is in line with the increased emphasis that is placed upon patient autonomy in South African law.[664]

The very nature of vaccine research requires the use of 'deception' by the researcher in the form of the use of a placebo group. It is submitted that participants in preventive HIV vaccine efficacy trails must be informed that a placebo group will be used and exactly what the use of a placebo entails. They should be informed of the chance of their not receiving the active experimental vaccine. Without such information it cannot be said that participants have given their informed consent to participation.[665]

This concludes the discussion of exceptions to the informed consent requirement in research. The legal consequences of a research intervention without the participant's informed consent are indicated below.

4.4.6 Legal consequences of research interventions without informed consent

Van Oosten[666] presents the legal consequences that a researcher or health care worker may incur in the case of medical research undertaken without the

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661 See ch 2 para 4.5 above and para 2.3.1 above.
662 Politis (2003) 105.
663 As above.
664 See para 1 above.
665 See also, generally, Politis (n 662 above) 105 – 106 and Burchell (n 584 above) on the use of placebos in research.
666 Van Oosten (n 11 above) 12.

participant's effective consent:[667] they may be liable for breach of contract;[668] civil or criminal[669] assault (a violation of physical integrity);[670] civil or criminal *iniuria* (a violation of the *dignitas* - dignity or privacy);[671] or negligence.[672] The doctor or researcher is liable regardless of whether the medical intervention or research eventually eventuates as having been in the best interest of the patient, or whether it was performed with the necessary care and skill.[673] Although the duty to inform rests primarily upon the doctor or researcher, it may be delegated to qualified health care personnel.[674]

The next section outlines aspects of a researcher's liability in subjecting participants to research without valid informed consent.[675] First civil liability, based upon the commission by the researcher of a delict, is outlined, followed by criminal liability, based upon the commission of a crime. A researcher who proceeds with research without obtaining the participant's prior informed consent may be liable on both these grounds simultaneously.

Throughout, specific reference is made to preventive HIV vaccine efficacy research.

a) Civil or delictual liability

A delictual cause of action will succeed only if the plaintiff is able to prove that all the requirements for the delict have been met.[676] Two 'types' of delict may be distinguished: delicts leading to patrimonial damages (*damnum iniuria datum*) and those leading to compensation for the infringement of aspects of the personality (*iniuria*).[677] The *actio legis Aquiliae* is instituted for wrongful and culpable (intentional

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667 As above, 12. See also Strauss (n 545 above) 178 – 179; Carstens and Pearmain (n 13 above) 890.

668 eg *Behrmann v Klugman* 1988 (W) (unreported) but discussed by Strauss (n 545 above) 41, 176 – 177.

669 Van Oosten (n 11 above) 51; *S v Kikunyana* 1961 (3) SA 549 (E).

670 eg *Stoffberg v Elliott* (n 550 above); *Esterhuizen v Administrator, Transvaal* 1957 SR 48 55; *S v D* 1998 1 SACR 33 (T).

671 eg *Stoffberg v Elliott* (where the patient's right to self-determination was recognised); *C v Minister of Correctional Services* (n 595 above).

672 eg *Stoffberg v Elliott*; *Lymbery v Jefferies* (n 603 above); *Richter v Estate Hammann* (n 602 above). See also Carstens and Pearmain (n 13 above) 676.

673 Van Oosten (1995) 28 *De Jure* 167. See below.

674 Slabbert (2006) 69 *J Contemporary Roman Dutch L* 37.

675 An in-depth study of the topic falls outside the scope of the thesis. For an excellent and detailed discussion of the liability of the researcher, see Politis (n 662 above) 135 – 155.

676 Neethling *et al* 3 - 4.

677 As above, 5.

or negligent) causing of patrimonial loss or damage; the *actio iniuriarum* is instituted for satisfaction (*solatium* or sentimental damages) in instances in which personality rights are infringed.[678] An action for pain and suffering may also be instated.[679]

i) The right to the *corpus* or body (civil assault)

Civil assault is the physical infringement of a research participant's body without her consent: the 'corpus (bodily and psychological integrity) is protected against every factual infringement of a person's physique or psyche'.[680] Even infringements of the senses, whereby a physical feeling of disgust, discomfort or repugnance is caused, are included in the protection afforded to the corpus.[681] Physical infringements may occur with or without violence and with or without pain.[682] Neethling *et al* argue that, in order to establish liability under the *actio iniuriarium*, the bodily infringement need not be accompanied by *contumelia* in the form of an insult.[683] Certain requirements must be met before the *actio iniuriarium* may be relied upon: the infringement must not be trivial; it must be wrongful; and it must be committed *animo iniuriandi*.[684] For the *actio iniuriarum*, the plaintiff must prove intent on the part of the wrongdoer.[685] A justified violation of the body is 'naturally also lawful'.[686] Consent constitutes such a justified violation. In *Castell v De Greef*[687] the Court commented upon this issue as follows:[688]

> The issue is not treated as one of negligence, arising from the breach of the duty of care, but one of consent to the injury involved and the assumption of an unintended risk. In the South African context the doctor's duty to disclose a material risk must be seen in the contractual setting of an unimpeachable consent to the operation and its *sequelae*.

The application of the concept of assault is a result of the placement by South African courts of a medical practitioner's duty to disclose information to obtain informed consent within the framework of the wrongfulness element (with *volenti non fit iniuria*) rather than with the fault element of the delict (intention or

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678 Neethling *et al* 5.
679 As above.
680 Neethling *et al* 301.
681 As above.
682 As above.
683 As above, 302.
684 As above.
685 See para (a)(ii) below.
686 Neethling *et al et al* 302.
687 n 13 above. In *Castell*, the plaintiff's action based upon a lack of informed consent did not succeed, but her claim based upon negligence succeeded.
688 425F-G.

negligence).[689] Assault is a suitable cause of action if the medical intervention was carried out with the necessary care and skill and was to the benefit of the patient – that is, no negligence was present and, therefore, it can not be used as a ground of action.[690]

Boberg supports the view that liability for non-disclosure or defective disclosure of information to the patient should be based on assault rather than negligence:[691]

> The answer is that this liability is based, not upon negligence, but upon his intentional invasion of the patient's body without the patient's consent. Though the patient purported to consent, his consent was legally ineffective because he did not appreciate the attendant risks. In other words, the doctor is liable for assault, not negligence (for there was none), and it is the defence of consent, not assumption of risk, that fails.

The position is more complicated in cases where the intervention was *not* to the benefit of the patient because an undisclosed risk materialised.[692] Van Oosten maintains that it would be wrong to argue that an action based upon negligence is impossible in cases where the medical intervention 'was performed with due care and skill, but the undisclosed risk or danger materialised and it has been established that the patient, had he been properly informed of the undisclosed risk or danger, would not have suffered an impairment of his health'.[693]

This is what happened in the case of *Richter v Estate Hammann*:[694] the plaintiff alleged that it was negligent of the neuro-surgeon not to have warned her that there were certain serious risks attached to the administration of a phenol block, and that she may have elected not to have the procedure had she been aware of these risks. The Court found that, as the there was only a remote possibility of the risk materialising, the neuro-surgeon had not been negligent in not warning her of the risks. The Court observes:[695]

> It may well be that, in certain circumstances, a doctor is negligent if he fails to warn a patient, and, if that is so, in principle his conduct should be tested by the standard of the reasonable doctor faced with the particular problem.

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689 Van Oosten (n 673 above) 178; *Castell v De Greef* (n 13 above) 425.
690 As above.
691 Boberg (1989) 751.
692 See eg *Lymbery v Jefferies* (n 603 above); *Prowse v Kaplan* 1933 EDL 257; *Dube v Adminstarator, Transvaal* 1963 (4) SA 260 (W), where the court found that the defendants were liable based upon negligence.
693 Van Oosten (n 673 above) 178.
694 n 602 above.
695 232H, per Watermeyer J.

Strauss disagrees. In commenting upon the decision in *Richter v Estate Hammann*, he remarks:[696]

> It is to be noted that the court did not conclusively decide that failure of the doctor to adequately inform the patient would in fact constitute negligence. If this was decided, a new principle would be introduced into our law ... It is submitted that to consider failure to inform as negligence would not be in accordance with the Roman-Dutch concept of *culpa* which until now has been defined as the failure to foresee the damaging consequences and to take reasonable measures to avoid it. The essence of negligence in the medical context is unskilful treatment.

However, in the case of *Broude v McIntosh and Others*[697] the Court questioned the notion that a lack of consent should be characterised as assault and expressed the hope that this basis will be re-evaluated in due course. The Court remarks: [698]

> Pleading a cause of action such as this as an assault to which the patient did not give informed consent is of course a familiar and time-honoured method of doing so. However, I venture to suggest with respect that its conceptual soundness is open to serious question and merits reconsideration by this Court when an appropriate case arises ... It seems to me to be inherent in the notion that, even if the risk does not eventuate and the surgical intervention is successful, the practitioner's conduct would nonetheless have constituted an assault. That strikes me as a bizarre result which suggests that there is something about the approach which is unsound.

It is submitted that a medical intervention without informed consent does not constitute negligence, but rather that it constitutes an assault. The relevant element of the delict and/or crime is that of wrongfulness or unlawfulness and not that of fault. A medical intervention without proper informed consent amounts to assault as it is a violation of the individual's physical integrity. This is not a 'bizarre result' as the Court in *Broude v McIintosh* remarks, but in fact the conceptually most sound approach. The Court in Broude criticises the fact that the 'conduct would still have resulted in an assault'.[699] This is of course true, but it seems that the Court is here disregarding the fact that it is not the consequences, but the initial act of violating the patient's physical integrity that is blameworthy. Assault can therefore be the only logical basis of liability.[700]

It is therefore submitted that preventive HIV vaccine efficacy trails in which participants have not given fully informed consent to participation result in liability based upon the delictual ground of assault. An action based upon assault exists

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696 Strauss (n 545 above) 268.
697 *Broude v McIntosh and Others* 1998 3 SA 60 (SCA).
698 67 – 68; these remarks are made *obiter*.
699 See above.
700 See also Carstens and Pearmain (n 13 above) 687.

regardless of whether harm is suffered by the participant, as the action is based upon the physical infringement without the justification of consent.

ii) Rights related to the *dignitas*: dignity and privacy (civil *iniuria*)

Under South African law, the rights to dignity and privacy are recognised as independent personality rights.[701] Dignity includes a person's subjective feelings of dignity or self-respect.[702] An infringement of a person's dignity arises from an insult to the person by word or belittling or contemptuous behaviour.[703] Publication of the insult to third persons is unnecessary; publication to the person herself is sufficient.[704] The plaintiff must allege *animus iniuriandi*.[705]

Privacy is 'an individual condition of life characterised by seclusion from the public and publicity, the extent of which is determined by the individual himself'.[706] Privacy is infringed by unauthorised acquaintance by outsiders with the individual and her personal affairs in two ways: first, when an outsider herself becomes acquainted with the individual or her personal affairs (instances of acquaintance or intrusion); or, second, where the outsider acquaints third parties with the individual or her personal affairs which, although known to the outsider, remains private (instances of disclosure or revelation).[707]

The wrongfulness of a factual infringement of dignity and privacy is determined by means of the *boni mores* or reasonableness criterion and the presence of a ground of justification excludes the wrongfulness of the action.[708]

In the context of preventive HIV vaccine efficacy trials, it is unlikely that participants' dignity is infringed by their participation in the trial, unless a situation arises in which a participant's sense of herself is demeaned by the researcher's conduct.[709] It is, however, conceivable that a participant's privacy may be infringed by events during a trial.

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701 Neethling *et al* (n 546 above) 321 - 322.
702 Neethling 321.
703 As above.
704 As above.
705 Carsten and Pearmain (n 13 above) 962; *Jansen Van Vuuren NO v Kruger* 1993 (4) SA 842 (A).
706 Neethling *et al* 322.
707 As above.
708 Neethling *et al* 322 – 323.
709 For example, where the participant is 'talked down to' or patently regarded as someone of no or little intelligence.

Blood tests taken without the informed consent of the participant may be regarded as a wrongful invasion of privacy by intrusion, and the disclosure of private facts, such as a participant's HIV status,[710] is an example of a violation of a participant's privacy by disclosure.[711]

An illustration of a violation of privacy rights constituting the delict of *iniuria* is found in the case of *C v Minister of Correctional Services*[712] which deals with a HIV test on a prisoner without his informed consent. While C (the plaintiff) was a prisoner in the custody at the Johannesburg Prison, a blood sample was taken from him which was later subjected to a HIV test. On the day in question C was a member of a group of prisoners standing in a row in a passage in a hospital when he had been informed, together with the other prisoners, by a sergeant in the Department of Correctional Services employed as a medical health aid and as a nurse, that the blood test was for HIV and other transmissible sexual illnesses and that he had the right to refuse to undergo the test.

This information was repeated to C in the closed consulting room in which the blood was taken, and in the presence of W, a prisoner assisting the sergeant with the drawing of blood. The plaintiff, accordingly, was fully aware that the test was, *inter alia*, for the HIV virus and that he had the right to refuse to be tested when he consented to undergo the test. However, he was given no pre- and post-test counselling[713] in conformity with the Department of Correctional Services' policy and national guidelines.

C, who was subsequently advised that he had tested positive for HIV, instituted an action for damages against the Department of Correctional Services on the grounds of alleged wrongful invasion of his right to privacy.

Judge Kirk-Cohen held that there could be informed consent only if the person appreciated and understood what the object and purpose of the HIV test are, what an HIV-positive result entails and what the probability of AIDS occurring

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710 See *Jansen Van Vuuren v Kruger* (n 705 above).

711 See above.

712 n 595 above.

713 Pre-test counselling entails informing the prisoner of the meaning of HIV infection; the manner of transmission of the disease; the nature of the test and that consent is required; the social, psychological and legal implications of the test; what was expected if the result of the test proves positive; and the prisoner has to be granted time to consider the information before consenting to the test being administered. In the event of a positive blood test, post-test counselling requires that psychologists, social workers and nursing staff be at hand to support the prisoner and to provide advice so that the result can be accepted.

thereafter is.[714] Further, he held that the principles with regard to the definition of *animus iniuriandi* applied in C's case, that is, that it is sufficient that the injury suffered by C had been inflicted by the sergeant with deliberate intention and that it is not necessary to prove ill-will or spite on his part or his motive.[715]

Therefore, even though C knew what the test was for, he did not give true informed consent, and the taking of blood not only constituted an assault on C's *corpus*, it constituted an *iniuria* as it is an invasion of his privacy.

As a consequence of the light it sheds upon the issue of the unauthorised publication of the HIV status of a participant in HIV-related clinical research, the case of *NM, SM and LH v Smith and Others*[716] is discussed at length below.

The case is an appeal in the Constitutional Court against an order handed down in the Johannesburg High Court in an action for damages based upon the *actio iniuriarum* against the respondents jointly and severally for a violation by the respondents of the applicants' rights to privacy, dignity and psychological integrity arising from the unauthorised disclosure by the respondents of the applicants' HIV status.

In the action in the Johannesburg High Court it was alleged that the three applicants' names and HIV status had been published without their prior consent, thus, violating their rights to privacy, dignity and psychological integrity. The High Court dismissed in part the application with costs, handing down the following order:[717]

> 1. The Plaintiffs claims against the First and Second Defendant are dismissed with costs;
> 2. The Third Defendant is ordered to pay each of the Plaintiffs an amount of R15 000;
> 3.1 The Third Defendant is, at its cost, directed to delete, from all copies of the book "Patricia de Lille" in its possession, the reference at page 170 and 171 to the Plaintiffs names;
> 3.2 Until such deletion is made, the Third Defendant shall not sell any further copies of the book;
> 3.3 To ensure that this part of the court's order has been carried out, the Plaintiffs attorney shall, at any time after 30 June 2005, have the right on 72 hours notice to inspect all copies of the book in the Third Defendant's possession;
> 4. The Third Defendant is to pay the Plaintiffs costs;

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714 *C v Minister of Correctional Services* 301B.

715 As above.

716 *NM, SM and LH v Smith and Others* CCT 69/05, judgment 4 April 2007 (yet unreported).

717 In *NM and Others v Smith and Others* [2005] 3 All SA 457 (W), quoted by the Constitutional Court in para 2 of its judgment.

> 5. The court file is to be handed to the Registrar of this court, who shall keep it in a safe place and who shall not, without an order from a Judge in Chambers, disclose any part of its content that discloses the name, identity or HIV status of the Plaintiffs.

The High Court action arose from the publication in March 2002 by New Africa Books of the names and HIV status of the three applicants, in a biography entitled *Patricia de Lille*, written by Charlene Smith. NM, SM and LH are three unemployed women living in Atteridgeville, Pretoria, who had taken part in a clinical trial that was to determine the efficacy and safety of a combination of HIV antiretrovirals.[718] De Lille had investigated complaints surrounding the high number of serious adverse events (including deaths) experienced during the trail, as well as whether trial participants, in fact, had given informed consent to participation in the trial.

De Lille's enquiries prompted two investigations by the University of Pretoria into the trial, which had been conducted by its Faculty of Health Sciences. Dr Freislich conducted the first investigation and his report was submitted to the Faculty of Health Sciences Ethics Committee and to Professor Grové (the Registrar of the University) in July 2000. This report, according to the applicants, was sent to the second respondent (de Lille) on 12 October 2000. She read the report and filed it with other AIDS-related documents in her 'AIDS file'.[719]

The second investigation was conducted by Professor S A Strauss for the University in August 2000. The second respondent was not invited to attend the enquiry, but the applicants and a number of other trialists were present. At the enquiry the three applicants repudiated their earlier statements and Professor Strauss in his report (Strauss Report) exonerated the University and the Faculty of Health Sciences, stipulating there was no substance in the statements and no evidence of any improper conduct on the part of researcher in the trial, Dr Botes.

Professor Grové sent the Strauss Report to the second respondent, but without the annexures attached.[720] The second respondent read the report and filed it with other AIDS-related documents, and proceeded no further in the matter. A copy of the report was sent to Ms Vermaak, the journalist present at Professor

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718 The three women participated in the FTC-302 trial, which is discussed in detail below in para 5.3.2.

719 *NM, SM and LH v Smith and Others*, para 13.

720 The annexures contained the informed consent forms signed by the three applicants and which revealed their identity.

Strauss' enquiry. Martin Welz, a journalist and editor of *Noseweek*, obtained a copy as well.[721]

September to November 2001 Smith (the first respondent) was commissioned by New Africa Books to write a biography of de Lille. A chapter in the book was to report on Ms de Lille's work in campaigning for the rights of those living with HIV/AIDS. During the trial, Smith stated that although she had seen the Strauss Report, she did not have access to the annexures to it which contained the terms of the consent forms signed by the applicants. The consent forms did not permit public disclosure of the identity of the three applicants and of the fact that they are living with HIV/AIDS, but only limited disclosure for the purposes of the University's investigation.

Smith further stated that there was nothing in the Strauss Report, nor in the covering letter sent by the University of Pretoria to de Lille that suggested the report was to be treated as confidential and indicated in support that the report had also been circulated to two journalists. She confirmed in evidence that she knew that the annexures contained the terms of the consent of the applicants. She acknowledged that she knew that, ordinarily, media ethics would require her not to disclose a person's HIV/AIDS status without their consent. She declared that initially she had attempted to meet with the three women, but had not succeeded.[722]

New Africa Books published the biography in March 2002. Some 5 000 copies of the biography were printed and were distributed to various bookshops during March 2002. Dr Botes (the researcher in the clinical trial) bought a copy and, after having read the relevant chapter, informed the applicants that their names and HIV status had been disclosed. The applicants denied consenting to the publication of their names and HIV status in the book.[723]

After initially attempting to obtain an interdict to prevent publication of the biography with the help of the University of Pretoria Law Clinic,[724] on 26 July 2002 the applicants sent a letter to the respondents' attorneys requesting the removal of their names from the biography. Smith's and de Lille's attorneys replied to the letter stipulating that their clients did not regard themselves accountable to the applicants

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721 *NM, SM and LH v Smith and Others*, para 14.
722 *NM, SM and LH v Smith and Others*, para 15.
723 As above, para 16.
724 The application for the interdict was withdrawn.

and that if action was to be taken against them, it would be defended. New Africa Books did not reply to the applicants' request.[725]

The applicants proceeded to sue the respondents for damages. They claimed: (a) a private apology from the respondents; (b) the removal or excision of their names from all unsold copies of the book; (c) payment by the respondents of the sum of R200 000 to each of the applicants, and (d) costs of suit. The case went to trial in the Johannesburg High Court and judgment was given on 13 May 2005. The applicants appealed to the High Court for leave to appeal to the Supreme Court of Appeal, which was refused. On 29 November 2005, the Supreme Court of Appeal dismissed with costs an application for leave to appeal without giving reasons.[726]

The case before the Constitutional Court concerns (a) whether the issues raised in the application are constitutional matters and, if so, whether it is in the interests of justice to hear them; (b) whether the disclosure or publication was of private facts; (c) whether the disclosure was wrongful; (d) whether the publication was done with knowledge of the wrongfulness of the conduct and with the intention to harm the applicants; (e) whether the common law of privacy should be developed so as to impose liability on those who negligently publish confidential information; (f) if liability is established, what would be the appropriate quantum of damages?; and (g) what effect an offer of settlement which was made by the respondents in terms of Rule 34(1) should have on the costs order.[727]

In the High Court the respondents admitted the publication of the names and HIV status of the applicants but denied that the publication was intentional or negligent. Moreover, the respondents pleaded that the HIV status of the applicants was not a private fact at the time of the publication of the book. Furthermore, the respondents pleaded that the publication of the HIV status of the applicants was not unlawful because earlier the applicants had given their consent to their names being included in the Strauss Report which was undertaken at the instance of the University.[728] In the alternative, the respondents pleaded that it was reasonable for any reader of the Strauss Report to assume that the necessary consent had been obtained since nothing in the report indicated that it was confidential. There was accordingly no malice on the part of the respondents in publishing the names of the

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725 Para 18.
726 Para 20.
727 Para 21.
728 Para 23.

applicants and their HIV status. The publication of the names was intended to lend authenticity to the biography.[729]

Before the Constitutional Court the applicants complained that the High Court had failed to protect their rights to privacy, dignity and psychological integrity. While these rights were claimed by the applicants under the *actio iniuriarum*, they are also protected under the Constitution. They contended that as a result of the disclosure of their names and HIV status to the public the respondents had wrongfully and intentionally or negligently violated their rights of personality, more particularly their right to privacy, dignity and psychological integrity. They therefore averred that they had suffered damages.[730] The respondents, denying any liability to the applicants, relied on the fact that the applicants' names had previously been disclosed in the Strauss Report and that the report was not marked 'confidential'.

In finding that the publication by the respondents of the HIV status of the applicants' constituted a wrongful publication of a private fact and that the applicants' right to privacy was therefore breached by the respondents, the majority of the Constitutional Court, remarks (per Judge Madala):[731]

> The disclosure of an individual's HIV status, particularly within the South African context, deserves protection against indiscriminate disclosure due to the nature and negative social context the disease has as well as the potential intolerance and discrimination that result from its disclosure. The affirmation of secure privacy rights within our Constitution may encourage individuals to seek treatment and divulge information encouraging disclosure of HIV which has previously been hindered by fear of ostracism and stigmatisation. The need for recognised autonomy and respect for private medical information may also result in the improvement of public health policies on HIV/AIDS.

The Court based its decision on the fact that the first respondent did not 'sufficiently pursue her efforts to establish if the necessary consents had been obtained, despite having ample time to do so'.[732] The Court is of the opinion that the respondent could have used pseudonyms instead of the real names of the applicants, without rendering the biography less authentic.

The Court further finds that, although there is 'nothing shameful about suffering from HIV/AIDS',[733] the 'social construction and stigma associated with the disease make fear, ignorance and discrimination the key pillars that continue to

729 Para 24.
730 Paras 28 – 29.
731 Para 42. Moseneke DCJ, Mokgoro J, Nkabinde J, Skweyiya J, Yacoob J and Van der Westhuizen J concur in the judgment of Madala J.
732 Para 46.
733 Para 47.

hinder progress in its prevention and treatment',[734] and it is an 'affront to the infected person's dignity for another person to disclose details about that other person's HIV status or any other private medical information without his or her consent'.[735] In the light of this, the Court remarks that the[736]

> indignity experienced by the applicants as a result of the disclosure of their names, seems to have been treated lightly by the court *a quo*. The case of the applicants was reduced to a malady that had befallen 'lesser men or women'. They were regarded as poor, uneducated, coming from an insignificant informal settlement and their plight disclosed in the book was not likely to spread far beyond the community where they resided. There was, in my view, a total disregard for the circumstances of the applicants and the fact that because of their disadvantaged circumstances their case should have been treated with more than ordinary sensitivity.

In order for a court to award damages based upon the *actio iniuriarum*, it must be shown that the injury to the dignity and privacy of the applicants was done *intentionally*. The applicants, however, alleged that the invasion of their privacy by the respondents was not intentional but negligent. As a result they enquired whether or not the common law of privacy should be developed so as to impose liability on those who negligently (instead of intentionally) publish confidential medical information (in particular a person's HIV status) through not first obtaining the express informed consent of that person, unless the public interest clearly demands otherwise.[737]

The Court responded to this enquiry by stating that the present case was not appropriate for departing from the age-old approach to the *actio iniuriarum*. The majority of the Court finds that, on examination of the conduct of the respondents and despite their denial of having acted *animo iniuriandi* and their further contention that they acted reasonably, that it is satisfied that the 'respondents were certainly aware that the applicants had not given their consent or at least foresaw the possibility that the consent had not been given to the disclosure'.[738] The Court states that as seasoned campaigners in the field of HIV/AIDS the respondents well knew of the wrongfulness of their conduct and that the disclosure of private facts was likely to invade the privacy rights of the applicants,[739] and, therefore, finds that the respondents have not rebutted the presumption that the disclosure of private facts

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734 As above.
735 Para 48.
736 Para 53.
737 Para 56.
738 Para 6. The Court is here arguing that intention in the form of *dolus eventualis* is present.
739 As above.

was done with the intention to harm the applicants and, thus, that the had the requisite intention or *animus iniuriandi*.[740]

Judges Langa, Sachs and O'Regan delivered dissenting judgments. Judge Langa found, on the facts, that there had been no intention on the part of the respondents as they did not actually foresee that the publication could cause the women harm, but that they had acted negligently.[741] The reasonable media defendant would not have relied on the Strauss Report as a document that removed their duty to ensure informed consent had been obtained and would have foreseen the possibility that there was no consent. Because the possible harm was great, the effort necessary to avoid that harm minimal and the benefit of publishing the names negligible, a reasonable journalist or publisher would have taken steps to avoid that harm.[742]

Judge O'Regan's dissenting judgment is similar to Judge Langa's in that it finds, on the facts, that there had been no intention present on the part of the respondents. She argues that the applicants' HIV status was not a matter of public record and that the respondents published private medical information of the applicants without their consent.[743]

Judge O'Regan observes, although the Strauss Report included the names of the applicants without any express indication that their names were to be kept confidential, either in the text of the report or in the covering letter under which it was sent to Ms de Lille, that when Professor Strauss interviewed the three applicants he obtained a consent form in limited terms, authorising disclosure of their HIV status to only a *limited number of people*, including Ms de Lille.[744] Moreover, according to Judge O'Regan, throughout Smith's evidence the persistent theme is, given her understanding of HIV/AIDS, that it was impossible to believe that Professor Strauss would have published his report without full consent from the applicants or without clearly setting out the limited nature of the consent. Ms Smith emphasised that she had little to gain and much to lose if she had purposefully revealed the names of the women, recklessly disregarding whether they had consented or not.[745] On the evidence Judge O'Regan finds that De Lille, too, had not acted intentionally: she writes, 'neither the first nor the second respondent had formed *animus*

740 As above.
741 Paras 92 – 93.
742 Para 111.
743 Para 143.
744 Para 158.

injuriandi. It is also consistent with the fact that neither of them ever contemplated that the applicants had not given full consent to disclose to Professor Strauss. In my view, this is the inescapable conclusion of fact to be drawn from the record'.[746] She remarks further that an appellate court should be slow to interfere with the conclusion of a trial court on the facts unless the record clearly suggests that the trial court erred and that nothing on this record is suggestive of such error.[747] She finds it relevant that, by and large, the applicants did not argue that *animus iniuriandi* had been established on the record, either directly or in the form of *dolus eventualis*, and they did not argue on the basis that the respondents had unsuccessfully rebutted a presumption that they had acted *animo iniuriandi*.[748]

Judge O'Regan then turns her attention the applicants' plea that the common law should be developed so that the fault requirement of the *actio iniuriarum* includes, not only actual intention but also negligence, making a person who *negligently* discloses a private fact about another liable in delict.[749]

Judge O'Regan proceeds to examine the existing law of delict for defamation by the press. She quotes *National Media Ltd and Others v Bogoshi*,[750] in which the Supreme Court of Appeal held that a defence by the press of reasonable publication of false defamatory allegations exists in our law, and that that the press could not rebut the presumption of intention that arises upon proof of publication of defamatory material by simply showing the absence of knowledge of unlawfulness.[751] The press would in addition have to establish the absence of negligence: establishing that a media defendant could not avoid liability for defamation unless it could show that it had not acted negligently.[752] This was a development of the traditional rules of the *actio iniuriarum*. She refers to Hefer JA who held in this case that there are important reasons for distinguishing the media from ordinary citizens in relation to intention in the context of defamation.[753]

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745 Para 165.
746 Para 168.
747 Para 169.
748 As above.
749 Para 170. In the alternative, they argued that a defendant who wishes to rebut a presumption of intention may not simply show that he or she made a mistake, but must also show that the mistake was reasonable on the facts of the case.
750 1998 (4) SA 1196 (SCA); 1999 (1) BCLR 1 (SCA).
751 Para 170.
752 Para 172.
753 n 750, 1202E-F and 1204D-E.

However, O'Regan remarks that the law as developed in the case of *Bogoshi* is not automatically applicable, as the case deals with an infringement of the right to privacy and not to damage to the reputation of the applicants. Therefore, she argues that the *actio iniuriarum* in respect of privacy should be developed in the same way as has been done for the law of defamation, so as to include the infringement of privacy rights by the media.[754] She states: 'I conclude that it is appropriate to require the media when publishing private facts without consent to establish either that the publication is reasonable in the circumstances, in which case they will rebut wrongfulness, or that they have not acted negligently in the circumstances in which instance they will need to rebut the requirement of intention'.[755]

On the question of whether the respondents can be considered the 'media', O'Regan finds that the first and third respondents were not acting as 'ordinary private citizens'[756] but, as an author and a publisher who are fully aware of the ordinary constraints upon the publication of private information, therefore, were acting in the role as 'media'.[757]

On the question as to whether the respondents had acted negligently, O'Regan holds, on the evidence, that the respondents simply did not entertain the possibility that either the University of Pretoria or Professor Strauss would have sent a report to a Member of Parliament in circumstances in which the consent given was of a limited variety only in a publication that did not draw attention to that fact[758] and that the first and third defendant, therefore, had not acted negligently, as '[t]o hold that in the circumstances as outlined above they were under a further duty to contact either the University or the applicants to ensure that they had in fact consented to publication of their names would impose a significant burden on freedom of expression'.[759] Judge O'Regan writes further that if there is a reasonable basis for suspecting that the publication of private information is without consent, a journalist, of course, bears an obligation to check the fact. If there are no grounds for such suspicion, it cannot be said that a journalist acts negligently by not checking.[760]

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754 Para 177. The argument is set out in paras 177 and 178 of the judgment.
755 Para 179.
756 Para 182.
757 Paras 181 – 182.
758 Para 184.
759 Para 185.
760 Para 187.

Judge O'Regan concludes, even on the assumption that it is appropriate that the *actio iniuriarum* be developed to found liability against defendants such as the first and third respondents in circumstances in which they publish private facts negligently, that the applicants have not established that the respondents should be liable for the disclosure of their names and HIV status.[761]

It is submitted that Judge O'Regan's argument is correct that, in certain circumstances, the common law should be developed to allow for a liability of the press for negligent delicts committed against the privacy and dignity of another person. Unless there exists an overwhelming public interest, journalists and publishers should not publish information identifying the HIV status of individuals unless they have taken the *utmost care* to ensure that individuals have given informed consent to the publication or that the information is already in the public domain.

Yet, whereas Judge O'Regan finds on the facts that no negligence was present, it is submitted, at least in the case of Smith and the publisher, that they indeed had acted negligently in not making sure that the applicants had consented to the publication of their HIV status. Neither Smith nor New Africa Books, it would appear, made sufficient effort to verify that consent had been given by the three women to the publication of their status: after all, it had been admitted that first publication was in a report intended for limited publication. Their action does not pass the test of reasonableness: understanding that information about a person's HIV status is regarded as particularly sensitive, the reasonable author and publisher would take steps to verify that permission had been given for its publication and would not have acted on presumptions.

In concluding the discussion, Judge Sachs' view is endorsed:[762]

> In the present matter the publishing of the actual names of the applicants could have added only minimally to the vibrancy and texture of the story, if at all. At the same time it was devastating to the applicants. When the expressive interests are balanced against the privacy interests, the scales come down with a clang on the side of privacy. In the result, the steps taken by Ms Smith, Ms de Lille and the publishers to avoid unwitting damage through unauthorised disclosure of private medical facts, did not meet the standard of reasonableness.

iii) Negligence[763]

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761 Para 189.
762 Para 207.

Generally, fault refers to the 'blameworthy attitude or conduct of someone who has acted wrongfully'.[764] Negligence, as a from of fault, is an attitude or conduct of 'carelessness, thoughtlessness or imprudence because, by giving insufficient attention to his actions he failed to adhere to the standard of care legally required of him'.[765] The standard referred to is that of the 'reasonable person' or '*bonus paterfamilias*'.[766]

The test for negligence in South African law was laid down by Judge Holmes in *Kruger v Coetzee*:[767]

> For the purposes of liability *culpa* arises if –
> a) a *diligens paterfamilias* in the position of the defendant –
> i) would foresee the reasonable possibility of his conduct injuring another in his person or property and causing him patrimonial loss; and
> ii) would take reasonable steps to guard against such occurrence; and
> b) the defendant failed to take such steps.

Even if the consent of the patient or research participant has been obtained, the doctor or researcher remains civilly (and, perhaps, criminally) liable for negligently performed actions during the therapeutic or research endeavour.

The criterion of the fictitious reasonable person is central to the determination of negligence.[768] In the case of an expert the criterion of the reasonable *expert* is used – a reasonable doctor or researcher with the same level of knowledge and skill as the defendant.[769] The highest level of care is not expected – only that of the *reasonably* careful, knowledgeable, able, experienced, skilful researcher.[770] No exceptional ability is called upon – a reasonable amount of expertise and care is sufficient.[771]

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763 See Carstens (1996) 'Die strafregtelike en deliktuele aanspreeklikheid van die geneesheer op grond van nalatigheid' (unpublished LLD thesis, University of Pretoria).

764 Neethling *et al* (n 546 above) 116.

765 As above, 116.

766 As above, 117.

767 *Kruger v Coetzee* 1966 (2) SA 428 (A) 430. The Court states:
'This has been constantly stated by this Court for some 50 years. Requirement (a)(ii) is sometimes overlooked. Whether a *diligens paterfamilias* in the position of the person concerned would take any guarding steps at all and, if so, what steps would be reasonable, must always depend on the particular circumstances of each case. No hard and fast basis can be laid down.'

768 Neethling *et al* 117; 120 - 122.

769 Neethling *et al* 120 – 122; 124 - 126; see eg *Esterhuizen v Administrator Transvaal* (n 670 above) 723; *Richter v Estate Hammann* (n 602 above) 231 – 235.

770 Neethling *et al* 124 - 126.

771 As above, 125.

A research participant claiming delictual damages based upon injuries sustained during negligently conducted HIV vaccine research, relies on the duty of reasonable care owed to her by the researcher. The facts that could or should have been foreseen by the researcher and which lead to the delict must be declared. The onus is on the research participant to establish that a *bonus paterfamilias* in the position of the researcher:[772]

> (a) would have foreseen the possibility of his or her conduct injuring him or her and causing him or her patrimonial loss; and
>
> (b) would have taken reasonable steps to guard against such injury; and
>
> (c) that the researcher had been negligent in failing to take those steps.

The criterion of the fictitious reasonable person if applied to a researcher in preventive HIV vaccine efficacy trails, demands that the researcher carefully and diligently will conduct the procedures involved in the trial and, furthermore, carefully will consider the potential adverse effects of participation upon those involved in the trial. For example, she will carry out the physical examination of research participants with skill and competence; adhere carefully to the inclusion and exclusion criteria of the trial; conduct the informed consent process with competence and diligence; and perform the actual vaccination of participants in the trial with due care and skill.

However, the reasonable researcher in the position of the defendant, if she would have undertaken the research without extensive and sufficient examination of the attendant risks or complications and the researcher has not done so before embarking upon the trial, she will have acted negligently.[773]

As noted above, a diligent researcher obtains informed consent based upon the known or foreseen risks of participation in HIV vaccine research. Politis argues, if a medical intervention has been performed with due care and skill, but the undisclosed risk or danger materialises and it is established that the patient, had he or she been properly informed of the undisclosed risk or danger, would not have undergone the intervention or procedure, a medical practitioner faces liability in

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772 *Kruger v Coetzee* (see above).

773 Politis (n 662 above) 143 – 144. It is sometimes argued that if standard or accepted treatment is ineffective, a researcher will be justified in taking greater risks in an attempt to provide effective treatment, provided that the *utmost level of care* and caution is observed and steps are taken to prevent any harm to the patient (see Politis 144).

negligence.[774] It is submitted that this view cannot be correct. The liability of a researcher in HIV vaccine research who fails to disclose known or foreseen risks to participants is based upon assault, as she has infringed their physical integrity without their consent.[775] The conduct amounts to assault regardless of whether or not those risks later materialise.

The situation in which *unforeseen* risks materialise during the research needs to be examined as well. Is the researcher negligent in the case of unforeseen (and consequently undisclosed) risks? In respect of preventive HIV vaccine efficacy research it is conceivable that a hitherto unknown risk may materialise during the research process because of the precarious state of HIV vaccine science. It is submitted that in this instance the researcher cannot be held liable based upon negligence. The risks are unknown at the start of the trial, and the researcher cannot take steps to avoid the risks materialising. In other words, the risks are unknown even to the researcher, thus, the first part of the test for negligence fails – the researcher could not have foreseen the possibility of her conduct injuring the research participant as the risk which materialised is unknown to her. Consequently, in preventive HIV vaccine efficacy trails the researcher is obliged diligently to disclose known and foreseen risks – she cannot be considered negligent it she fails to disclose unforeseen or unknown risks.

The following section examines possible criminal liability for actions committed during preventive HIV vaccine efficacy trails.

b) Criminal liability

i) Assault

In criminal law assault is the unlawful and intentional (i) application of force, directly or indirectly, to the person of another, or (ii) inspiring a belief in another person that force is immediately to be applied to him.[776] The sanctity of a person's physical being flows out of society's belief in the sanctity of human life.[777] The criminal law punishes the unlawful application of force to a person's physical being.

Criminal assault is excluded by the consent of the individual. A surgeon operating upon the person of someone who has given legally valid consent is not

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774 Politis 145.
775 See para (a)(i) above.
776 Snyman (n 546 above) 432 (definition translated from the Afrikaans).

committing a crime.[778] The situation of a researcher conducting preventive HIV vaccine efficacy trails is the same – the prospective participant's informed consent excludes the possibility of the researcher being held liable for criminal assault.

There is no possibility of negligent assault in South African criminal law, therefore, in order for assault to be proven the defendant needs to have acted with intent.[779]

ii) *Crimen iniuria*

Crimen iniuria is the unlawful and intentional impairment of the dignity or privacy *(dignitas)* of another person.[780] A person's *dignitas* is described as a person's right to dignity, self-respect, privacy, and mental tranquillity.[781]

To determine in which circumstances an invasion of someone's privacy amounts to the crime of *crimen iniuria*, one has to look at the *boni mores* of society at that time and place.[782] Unlike an infringement of someone's dignity, of which the victim needs to be aware, it is not necessary that a person whose privacy has been infringed should be aware of the infringement.[783] Not all infringements of the dignity or privacy of others amount to *crimen iniuria* – the infringement needs to be reasonably serious: the Court remarked in *S v Walton*[784] that '[i]n the ordinary hurly-burly of everyday life a man must be expected to endure minor and trivial insults to his dignity'.[785]

Conduct during a research endeavour which involves not only an infringement of the research participant's physical security, but also her *dignitas*, amounts to the crime of *crimen iniuria.* The *boni mores* of society is likely to support the view that information about one's HIV status should remain private.[786] It is open to speculation that a violation of the consent requirement for research constitutes

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777 As above.
778 Snyman 437 - 438.
779 Snyman 438; *R v Steenkamp* 1960 (3) SA 680 (N).
780 Snyman 457 (definition translated from the Afrikaans).
781 Snyman 458. Before, *dignitas* was understood to refer only to dignity, but it is now understood to include privacy rights as well (458).
782 Snyman 462.
783 Snyman 462; *Holliday* 1927 CPD 395 401 – 402.
784 *S v Walton* 1958 (3) SA 693 (R).
785 696.
786 See *NM, SM and LH v Smith and Others* (n 717 above) and *C v Minister of Correctional Services* (n 595 above).

not only the crime of assault but that of *crimen iniuria* as well. This was discussed in detail elsewhere.[787]

iii) Culpable homicide

Culpable homicide is the unlawful negligent killing, or causing the death of another human being.[788] For culpable homicide to be proven it must be shown that the accused acted negligently and that the action was the factual and legal cause of the deceased's death.[789] The test for negligence is virtually the same for culpable homicide as under delictual liability outlined above:[790] it must be shown that a reasonable medical practitioner (or researcher) in similar circumstances, would have foreseen death as a result of the proposed course of conduct and that she would have taken steps to prevent it.[791]

In respect of preventive HIV vaccine research, if the researcher did not foresee the risk of death as a consequence of a research-related activity, in an instance in which the reasonable researcher would have foreseen such a risk and the research participant subsequently dies, the researcher will have acted negligently and may be charged with culpable homicide. However, as argued above,[792] if a risk is not foreseeable, negligence is not present and the researcher cannot be charged with culpable homicide. Similarly, if the reasonable researcher would have foreseen the risk, and have taken steps to prevent the risk materialising, yet the accused did not take such steps, she is guilty of acting negligently and may be charged with culpable homicide in the circumstances of the research participant subsequently dying.

Due to the many unknown factors related to vaccine science, it may be impossible to foresee the risk of death occurring as a result of the HIV vaccination. In this instance a researcher is not liable, if the reasonable researcher in her position could not have foreseen the risk of death materialising. However, participants in preventive HIV vaccine research are healthy volunteers, therefore, there is a compelling duty placed on the researcher to take extra care to avoid any risk of

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787 Also see the discussion in paragraph (a)(ii) above.

788 Snyman (n 546 above) 427 (definition translated from the Afrikaans).

789 Snyman 427; *S v Ntuli* 1975 (1) SA 429 (A); *S v Kramer* 1987 (1) SA 887 (W). In *S v Berman* 1996 (T) unreported, a doctor was convicted of culpable homicide for negligently performing a blood transfusion upon the wrong patient. An intentional act is considered murder.

790 See para (a) (ii) above.

791 Snyman 428.

death. It is submitted that research such as preventive HIV vaccine trials, which is carried out on healthy volunteers, should not be undertaken if a risk, however remote, of death exists.

Slabbert[793] raises a further important aspect to the negligence requirement: non-compliance and non-observance of statutory regulation may amount to evidence of negligent conduct.[794] It is submitted, preventive HIV vaccine trials carried out in contravention of the various statutes and the MRC guidelines, of itself, may constitute negligence.

iv) Murder

Murder is the intentional unlawful killing or causing the death of another human being.[795] Consent is not a ground of justification for murder.[796] Intention needs to be proven for an accused to be guilty of murder; either direct intention or indirect intention or *dolus eventualis*.[797]

It is unlikely that direct intention will be present in the case of a researcher conducting clinical research. The researcher is conducting the trials with the hope of eventually saving lives and not to intentionally murder participants in the trial. However, *dolus eventualis*, as a form of intention, requires that the researcher merely must foresee the possibility of the death of a research participant and must have reconciled herself to that possibility.[798] Although not directly willing a participant's death she will have *reconciled* herself to the possibility that her research may bring about the participant's death.

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792 See para (a)(ii) above.

793 n 674 above, 42.

794 However, in this context the only ethical guidelines that qualify as 'statutory regulation' are the MRC guidelines and the MRC vaccine trial guidelines (as the MRC guidelines were promulgated in terms of a statute – see n 42 above). See Slabbert 42: she quotes *Sand & Co v SAHR&H 1948* (1) SA 230 (W) 243 where Ettlinger AJ remarks:
'It is clear that a breach of a statutory regulation may sometimes in itself be taken for negligence. Where a statute prescribes that certain precautions are to be taken for the safety of others, then a failure to take such precautions resulting in injury will, *per se*, found an action for damages provided that if the statute was enacted for the benefit or protection of a particular class of person, the injured person was of that class'.

795 Snyman 423 (definition translated from the Afrikaans).

796 Snyman 425; *S v Robinson* 1986 (1) A 666 (A). However, other grounds of justification exist – self-defence and necessity.

797 Snyman 425.

798 Snyman 425.

It is on occasion difficult to distinguish between a negligent action which causes another person's death and the intentional killing (in the form of *dolus eventualis*) of another person. In respect of negligence the researcher does not foresee the eventuality of death, where she should reasonably have foreseen it, and, therefore, does not take the steps reasonably required of her to prevent the death of a participant. In the case of *dolus eventualis*, the researcher foresees the risk but reconciles herself to that risk. Research conducted in such a manner shows a wanton disregard for human life and may be likened to the criminal actions that have occurred in the history of medical research.

These remarks conclude the discussion of a researcher's liability for research undertaken without the participant's informed consent. The discussion, in certain instances, is general, and does not focus only on the lack of consent but upon negligently performed actions during research as well. Before turning the discussion to the examination of statutory provisions on informed consent, consideration is given to causation as a requirement for delictual and criminal liability for preventive HIV vaccine research conducted without the participant's informed consent.[799]

4.4.7 The element of causation: An impossible hurdle in establishing preventive HIV vaccine research-related liability?

The section deliberates upon difficulties arising from the requirement of causation in the context of preventive HIV vaccine research-related liability. The discussion is not exhaustive but aims to hint at the anticipated difficulties.[800]

To be found guilty of the commission of a crime or to establish liability for the commission of a delict, a causal relationship is required between the act and the eventual damage that ensues.[801] Applied to the research context the act (the research intervention without or with deficient consent) should be causally connected to damage suffered by the research participant.

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799 Actual damage will have to be established - in the present context damage resulting from an assault will usually consist of patrimonial damage (such as medical costs and loss of income) and non-patrimonial damage (for example, pain and suffering, loss of amenities in life, etc) (Neethling (n 569 above) 589).

800 For a more comprehensive discussion on the topic, see Politis (n 662 above) 155 – 165 and Carstens and Pearmain (n 13 above) 509 - 515.

801 Neethling *et al* (n 546 above) 159; Snyman (n 546 above) 76 – 92; Carstens and Pearmain 509.

Causation has two components: factual and legal.[802] The former component relates to the factual causal link between the researcher's action (the research intervention without informed consent) and the damage suffered by the research participant. This factual causal link has to be established on a balance of probabilities;[803] the test to be applied in this regard is the *conditio sine qua non* or 'but for' test.[804]

In accordance with the *conditio sine qua non* test, in order to determine if the conduct of the researcher caused the damage, that conduct has to be mentally eliminated in considering whether the damage still exists.[805] If the damage is still present it has not been caused by the actions or conduct of the researcher.[806] An examination of this sort requires a retrospective analysis of what probably would have occurred, based upon the evidence and on what can be expected in the ordinary course of events during a research-related intervention of this kind.[807] It should be borne in mind that for factual causation to be established it is sufficient that the researcher's conduct contributed in any way to the eventual damage.[808] It is not necessary, therefore, to establish that the conduct in question was the only, primary or sole cause of the damage that ensued.[809]

The latter component, legal causation, relates to the question for which harmful consequences of her wrongful and culpable actions (research intervention without the informed consent of the participant) the researcher should be held liable; in other words, which consequences *legally* should be imputed to the researcher.[810] In the ordinary course of events, a single act on the part of the researcher may set in motion a chain of events – it needs to be established which of these events legally may be imputed to be the consequences of the researcher's act. Generally, the researcher cannot be held liable for consequences or damage that are too remote.[811]

In this regard South African courts adopt a flexible approach since none of the existing criteria for legal causation (such as adequate causation and

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802 Neethling *et al* 150 – 160; Neethling (n 569 above) 588; Carstens and Pearmain 509.
803 As above.
804 As above; Neethling *et al* 161 – 171.
805 Neethling *et al* 162 - 163.
806 As above.
807 As above; Neethling (n 569 above) 588; *Minister of Safety and Security v Carmichele* 2004 (3) SA 305 (SCA) 328.
808 Neethling *et al* 171; Snyman 87; Neethling 588.
809 As above.
810 Neethling (n 569 above) 588.
811 Neethling *et al* 178 - 179; Snyman 82 - 83.

foreseeability) is suitable in all instances.[812] In *S v Mokgethi and Others*, Judge of Appeal Van Heerden remarks:[813]

> Wat die onderskeie kriteria betref, kom dit vir my ook nie voor dat hulle veel meer eksak is as 'n maatstaf (die soepele maatstaf) waarvolgens aan die hand van beleidsoorwegings beoordeel word of 'n genoegsame noue verband tussen handeling en gevolg bestaan nie. Daarmee gee ek nie te kenne nie dat een van die kriteria nie by die toepassing van die soepele maatstaf op 'n bepaalde sort feitekompleks subsidiêr nuttig aangewend kan word nie; maar slegs dat geen van die kriteria by alle soorte feitekomplekse, en vir die doeleindes van die koppeling van enige vorm van regsaanspreeklikheid, as 'n meer konkrete afgrensingsmaatstaf gebruik kan word nie.

In accordance with a flexible approach, the question that needs to be answered is whether there is a sufficiently close link between the researcher's act and the harmful consequences that may be imputed to her in view of policy considerations based upon aspects such as reasonableness, fairness and justice.[814]

In the area of clinical research it is peculiarly difficult to establish a sufficiently close link between an act and the damage suffered. This is especially the case in a field such as preventive HIV vaccine science and experimentation, as the science is in its infancy and many side-effects of the candidate vaccines are unknown,[815] or side-effects may become apparent only many years after the actual research intervention.[816] It may be difficult, if not impossible, to attribute a certain consequence to participation in a preventive HIV vaccine trial. Unlike other medical interventions, in which a lack of informed consent prior to an operation or test, may have immediate and direct consequences (such as unexpected risks materialising), in the case of preventive HIV vaccine clinical research the harm or injury suffered may take years to become manifest. Even then it may appear unrelated to participation in the clinical trial.

It is submitted, in the case of damage suffered because of participation in a HIV vaccine trial, the flexible approach to causation needs to be adapted in order to take into account the unique situation of trial participants and in line with policy considerations based upon aspects such as reasonableness, fairness and justice.[817]

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812 Neethling (n 569 above) 588; *S v Mokgethi* 1990 (1) SA 32 (A).

813 *S v Mokgethi* 40I – 41B.

814 Neethling (n 569 above) 588 – 589 above.

815 See ch 2 para 4.5 and para 2.3.1 above.

816 Such as, eg, the possibility of immune tolerance, which will become apparent only when the research participant is given a subsequent vaccine (see para 2.3.1 above).

817 Of course these terms are rather vague and empty – and will have to be given content through interpretation by the courts – the true essence of the flexible approach.

Below, statutory requirements on informed consent are discussed.

4.4.8 The National Health Act and other legislation[818]

With the enactment of the National Health Act 61 of 2003, informed consent in research or experimentation became a statutory imperative. Section 71(1) of Act 61 of 2003 determines that[819]

> ... research or experimentation on a living person may only be conducted in the prescribed manner; and with the *written* consent of the person after he or she has been informed of the object of the research or experimentation and *any possible* positive or negative consequences to his or her health.

It is important to note that this section represents a radical departure from the precedent created by the case of *Castell v De Greef* in so far as it alters the *extent* of the information that is required before consent may be considered informed. The prospective research participant needs to be informed of 'any possible' positive or negative consequences, not just those that a reasonable research participant would want to know about, or those that a reasonable doctor would share with the participant. This expectation places a heavier burden on the researcher than was insisted upon in *Castell v De Greef* – the participant should be informed of *all* positive and negative consequences of participation, no matter how remote.

Section 71(1) of the National Health Act has important consequences for informed consent to HIV vaccine efficacy trial participation in South Africa. Because the vaccine is experimental, some of the potential side-effects of the vaccine remain unknown. Is a research sponsor expected to inform the prospective participant of side-effects that yet are not known? It is submitted that this is not what is intended by the legislature. Only side-effects of the vaccine which are known at the time that consent is given need to be included in the information provided to research participants. However, a prospective research participant will have to be informed of *all* known side-effects, and not only the most likely ones.

Whereas before there were no formalities for informed consent, according to section 71(1) such consent must now be in writing.

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818 Also see the discussion by Carstens and Pearmain (n 13 above) 897 – 905.

819 My emphasis. The National Health Act has entered into force in 2006, but chapter 9, which deals with issues related to health research, has not yet come into effect as of 31 May 2007.

The informational or knowledge aspect of informed consent is discussed in detail in sections 6(1) and 7(1) of the National Health Act. According to section 6(1), informed consent encompasses knowledge about:[820]

(a) the user's health status except in circumstances where there is substantial evidence that the disclosure of the user's health status would be contrary to her best interests;
(b) the range of diagnostic procedures and treatment options generally available;
(c) the benefits, risks, costs and consequences generally associated with each option; and
(d) the user's right to refuse health services and the implications, risks, obligations of such refusal.

Section 71(2) governs the participation of minors in research. It reads: '[w]here research or experimentation is to be conducted on a minor for a therapeutic purpose, the research or experimentation may only be conducted – i) if it is in the best interests of the minor; ii) in such a manner and on such conditions as may be prescribed; iii) the consent of the parent or guardian of the minor; and iv) if the minor is capable of understanding, with the consent of the minor'.

A minor is taken to be anyone under the age of 18.[821] It is important to note that the National Health Act reintroduces the distinction between therapeutic and non-therapeutic research.[822] A minor may participate in therapeutic research only with the consent of the minor's parent or guardian, as well as that of the minor. The requirement that only a 'parent' or 'guardian' may consent to the minor's participation in research, and not another person that has the care of the minor,[823] is a radical departure from the previous position. Whereas in the past a minor over the age of 14 was able to consent to medical treatment,[824] that minor now needs the consent of a parent or guardian.

Section 71(3) governs the position of minors participating in non-therapeutic research. It reads that 'where research or experimentation is to be conducted on a minor for a non-therapeutic purpose, the research or experimentation may only be conducted i) in such a manner and on such conditions as may be prescribed; ii) with

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820 Sec 6(1)(a) - (d).
821 As determined by the Constitution 1996 and the Children's Act 38 of 2005.
822 See para 4.4.1 above.
823 Such as a carer; in the Child Care Act the 'custodian' was also permitted to give consent. This may present problems, especially in situations where children are in homes or other places of safety, and where their parents cannot be found or are dead.
824 Sec 39(4) of the Child Care Act 74 of 1983 determined that a minor over the age of 14 could consent independently to medical treatment; and one over the age of 18 could consent independently to a surgical operation.

the consent of the Minister; iii) with the consent of the parent or guardian of the minor; and iv) if the minor is capable of understanding, the consent of the minor'. The intention of this subsection is clearly the protection of the minor against unscrupulous practices. The subsection sets a higher threshold that needs to be met when minors are participating in non-therapeutic research: the Minister (of Health) is to consent to participation in research, additional to the consent of the parent or guardian of the minor.

Moreover, the Minister may not consent to the minor's participation in non-therapeutic research if the objects of the research may be attained if that research were carried out on adults; and if the research poses a 'significant risk' to the health of the minor; or 'some risk', though there is a likelihood of 'potential benefit', if it does not significantly outweigh that benefit.[825]

The new legislative position introduced by the Health Act presents a problem as it appears to be inconsistent with existing legislation. First, the Health Act does not set an age for independent consent to medical research; in the past minors over the age of 14 were independently able to consent to research.[826] Second, section 71(2) of the Health Act may be interpreted to mean that the consent of the minor is needed, and only the assent of parents in cases of therapeutic research.[827] Third, section 71(2) directs that minors can consent only if they are 'capable of understanding'. This is contrary to the Children's Act, which determines that the minor's wishes are important and should be taken into consideration, even if she cannot understand.

Finally, the different Acts, as well as South African ethical guidelines, present varying risk standards for different types of research: in the case of non-therapeutic research, the risk should not be 'significant'; whereas the MRC Guidelines require risk that is 'negligible'.

Section 9 of the Children's Act 38 of 2005, reads: 'In all matters concerning the care, protection and well-being of a child the standard that the child's best interest is of paramount importance, must be applied'. Note the use of 'child' instead of children, indicating that the specific child's interest should be of utmost

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Also note that, according to the Choice on Termination of Pregnancy Act 92 of 1996, a minor female of any age may consent to the termination of her pregnancy.

825 sec 71(3)(b).

826 Also see the Child Care Act and the Children's Act. The Children's Act entered into force in 2006, but the provisions related to children's informed consent are not yet in force.

827 See eg Strode *et al* (n 4 above) 224 – 228.

importance. Therefore, it is not enough to show that the research is in the interest of children generally; it must potentially benefit the specific child in question.

Section 129(2) and (3) of the Children's Act determines that a child may consent to her own medical treatment or to the medical treatment of her child, if

(a) the child is over the age of 12 years; and

(b) the child is of sufficient maturity and has the mental capacity to understand the benefits, risks, social and other implications of the treatment.

According to subsection 3, a child may consent to the performance of a surgical operation on him or her or his or her child, if

(a) the child is over the age of 12 years; and

(b) the child is of sufficient maturity and has the mental capacity to understand the benefits, risks, social and other implications of the surgical operation; and

(c) the child is duly assisted by his or her parent or guardian.

According to subsection 4, the parent, guardian or care-giver of a child may, subject to section 3(1), consent to the medical treatment of the child, if the child is:

(a) under the age of 12 years; or

(b) over that age but is of insufficient maturity or is unable to understand the benefits, risks and social implications of the treatment.

Melodie Slabbert remarks that the requirement of parental assistance for surgical operations is 'difficult to grasp'.[828] She poses the question whether it refers to parental advice, supplementary support, parental approval or legal assistance.[829] She also, rightly, questions the position of a child whose parent or care-giver refuses to assist them – would such a child's consent be invalid in the absence of the required assistance?[830]

In order to point to the inconsistencies that occur within the different Acts and the ethical guidelines, the relevant Acts and ethical guidelines are represented in tabular form:

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828 Slabbert (n 674 above) 38.

829 As above, 38 – 39.

830 As above, 39.

	Age of independent consent	**Formalities**	**Who may give surrogate consent**	**Risk standards mentioned – determine independent consent**
Health Act	> 18	In writing	Parent or guardian	Therapeutic and non-therapeutic; not defined
Children's Act	'treatment': >12 & of sufficient maturity; 'surgical operation': >12 & is assisted by parents or guardian	None mentioned	parent, guardian or care-giver of a child	None mentioned
Termination of Pregnancy Act	Any age	None mentioned	N/A	N/A
MRC Ethics Book 1 & 5	> 18 & of sound mind; 'in certain circumstances persons below the age of 18 years are considered able to give their own consent'	'record of their explicit consent should be obtained, through the signing of the informed consent form'	proxy consent by a parent or legal guardian	Distinguish therapeutic and non-therapeutic research Terms defined
Good Practice Guidelines	None mentioned	Both written & verbal IC; if participant is illiterate, verbal consent 'in the presence of and countersigned by a literate witness'.	None mentioned	None mentioned

The position regarding the informed consent of children who are participating in research appears unclear at the moment, as South African law and ethical guidelines are contradictory and inconsistent.

4.4.9 Draft health research regulations

In terms of section 90 of the National Health Act, various draft regulations have been published for comment in the Government Gazette.[831] One, entitled 'Regulations

831 Such as Regulations on the 'Use of DNA, RNA, cultured cells, stem cells, blastomeres, polar bodies, embryos, embryonic tissue and small tissue biopsies for diagnostic testing, health research and therapeutics: Draft' (Gazette 29526); 'Artificial fertilisation and related matters: Draft' (Gazette 29527).

relating to research on human subjects' (Draft health research regulations),[832] published on 23 February 2007, is of particular relevance to the present discussion.

Chapter 1 of the Draft health research regulations delineates 'principles on health research', in terms of which any health research 'conducted in South Africa involving the participation of human subjects'[833] must ensure that research participants are 'well informed to make informed choices'.[834]

Setting aside the circularity of 'well informed to make informed choices', the description does not add to the current debate on informed consent as provided for in the National Health Act. The Draft health research regulations give no indication of what is meant by 'well informed' or the extent of the information which determines that a prospective participant is 'well informed'. In linking 'well informed' with the requirement to make an 'informed choice', clause 2 limits the scope of the information that is provided to research participants: information that is relevant to the *choice* as to whether or not to participate, alone, is required. It could be argued that it is always the aim in the consent process to produce a well-informed participant; however, information of a different type, such as details with regard to the procedure of withdrawing from the research intervention, which do not have bearing on the decision to participate, nevertheless is essential. Clause 2 appears to be in contradiction with a later clause in the Draft health research regulations, that specifically gives an account of the nature of the information that the participant has a 'right to be informed of'.[835]

Although its purpose is to supplement the requirements for the participation of minors in research in terms of section 71(2)(ii) of the National Health Act, clause 4 of the Draft health research regulations neither elucidates, nor elaborates on the position set out in section 71. It stipulates that children can only participate in health research in instances where 'the parent or legal guardian of the child gives consent for such a child to participate' and that 'refusal to participate by the child should precede the consent of the parent/legal guardian'.[836] As seen above, section 71(2) of the National Health Act requires the consent of the parent or guardian in the case of therapeutic research,[837] and the case of non-therapeutic research, the

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832 R 135 (Gazette 29637) published 23 February 2007.
833 Cl 2 Draft health research regulations.
834 Cl 2(d) Draft health research regulations.
835 See below.
836 Cl 4(c) Draft health research regulations.
837 Sec 71(2)(c) Act 61 of 2003.

consent of the Minister.[838] The Draft health research regulations are problematic on various grounds. First, in terms of clause 4, is the Minister's consent for non-therapeutic research on minors no longer necessary? Second, clause 4 has not clarified the uncertainty surrounding who is permitted to consent in cases of minors who are without parents or guardians and who are looked after by 'care-givers'. The addition of the word 'legal' in the clause does not offer a solution because a 'care-giver' is not a 'legal' guardian in terms of South African law.

The second part of clause 4 further needs clarification. Although 'refusal to participate by the child should *precede* the consent of the parent/legal guardian',[839] it appears that refusal may be overridden by the parent or guardian's consent, creating the situation in which a minor may be forced be her parents to participate in research against her will. This possibility is not only out of step with current legislation,[840] but is also likely to be considered *contra bonos mores*. The sense of the clause would be more transparent if it were to read '**consent** to participate by the child should precede the consent of the parent/legal guardian'.

Clause 6 of the Draft health research regulations exclusively focus on informed consent in health research participation. Participants 'have the right to be informed of', amongst others, the purpose of the research;[841] treatments and the possibility of random assignment of each treatment, if the research involves treatment;[842] methods and procedures to be followed or used during the research;[843] alternatives apart from participating in the research;[844] potential or real harm and risks involved in participation;[845] expected benefits for the participant and other persons in the research;[846] extent to which confidentiality and privacy will be maintained;[847] incentives given for participation as well as differences in incentives, if any;[848] and, in cases of clinical trials, the availability of treatment beyond the duration of the trial.[849]

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838 Sec 71(3)(ii).
839 My emphasis.
840 See eg sec 29(2) and 29(3) of Act 38 of 2005.
841 Cl 6(a) Draft health research regulations.
842 Cl 6(b) Draft health research regulations.
843 Cl 6(c) Draft health research regulations.
844 Cl 6(d) Draft health research regulations.
845 Cl 6(e) Draft health research regulations.
846 Cl 6(f) Draft health research regulations.
847 Cl 6(g) Draft health research regulations.
848 Cl 6(j) Draft health research regulations.
849 Cl 6(k) Draft health research regulations.

Clause 6 attempts to regulate the extent of the information provided to participants in health-related research so as to ensure informed consent. The clause is modelled on the requirements pertaining to information governing many ethics committees in the country and is not a departure from common practice.[850] However, it sets a minimum standard of information that needs to be provided to the research participant, even if 'have a right to be informed of' at the beginning of the clause is phrased tentatively and would have more impact as an imperative.

4.4.10 Section 12(2)(c) of the Constitution

The Constitution of the Republic of South Africa 1996 is the supreme law[851] of the Republic. The human rights entrenched in Chapter 2 bind the legislature, the judiciary, the executive and all organs of state and apply to all law (statutes, common law, and customary law).[852] Any law or conduct that is in conflict with the Constitution may be struck down as unconstitutional and void.[853]

Various rights guaranteed in the Constitution find application to the position of research participants in HIV vaccine research, namely, the right to life;[854] the right to human dignity;[855] the right to equality;[856] the right to privacy;[857] the right of access to health care;[858] and the right to bodily and psychological integrity.[859] In *Ex Parte Minister of Safety and Security and Others: In Re S v Walters and Another,*[860] Judge Kriegler remarked on the interrelationship between section 12 and other rights, as well as the importance of these rights:[861]

> What looms large in both the threshold and the limitations phases of the exercise in the present case is that the right to life, to human dignity and to bodily integrity are individually essential and collectively foundational to the value system prescribed by the Constitution. Compromise them and the society to which we aspire becomes

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850 eg the University of Pretoria Health Research Ethics Committee, and that of the University of the Witwatersrand, already requires informed consent documents to includes the information in cl 6.

851 Sec 2 Constitution of the Republic of South Africa 1996.

852 Sec 8(1) Constitution of the Republic of South Africa 1996.

853 Sec 2; *Executive Council of the Western Cape Legislature v President of the Republic of South Africa* 1995 (4) SA 877 (CC) para 62; *Fose v Minister of Safety and Security* 1997 (3) SA 786 para 87.

854 Sec 11 Constitution of the Republic of South Africa 1996.

855 Sec 10 Constitution of the Republic of South Africa 1996.

856 Sec 9 Constitution of the Republic of South Africa 1996.

857 Sec 14 Constitution of the Republic of South Africa 1996.

858 Sec 27(1)(a).

859 Sec 12(2)(c).

860 *Ex Parte Minister of Safety and Security and Others: In Re S v Walters and Another* 2002 (4) SA 613 (CC).

861 As above, para 28.

> illusionary. It therefore follows that any significant limitation of any of these rights would for its justification demand a very compelling countervailing public interest.

At the risk of defining the problem too narrowly, the thesis limits the investigation to the protection of informed consent in section 12(2)(c), which reads: '[e]veryone has the right to bodily and psychological integrity, which includes the right ... not to be subjected to medical or scientific experiments without their informed consent'. This subsection is part of the wider guarantee in section 12 to freedom and security of the person. Section 12 consists of two distinct parts: subsection 1, which deals with freedom and security of the person; and subsection 2, which deals with the right to bodily and psychological integrity, of which subsection 12(2)(c) is part. Van Wyk remarks that section 12 'deals with freedom from *direct* physical abuse in three of its most fundamental senses (freedom from violence, torture, cruel and degrading treatment and medical and scientific experimentation)'.[862]

The right to bodily and psychological integrity in section 12 is stated in general terms – '[e]veryone has the right to bodily and psychological integrity'. After this general statement, the subsection mentions three specific instances of bodily and psychological integrity, namely, the right to make decisions concerning reproduction;[863] the right to security in and control over their body;[864] and the right not to be subjected to medical or scientific experiments without their informed consent.[865] The three specific instances of the general right to bodily and physical integrity are introduced by the phrase ' ... which includes the right ...'. The word 'includes' indicates that these are only some of the many possible manifestations of the right to physical and psychological integrity.

The inclusion of subsection 12(2)(b) - 'the right to security in and control over their body' is puzzling: at first glance it seems to be a mere restatement of the more general guarantee of 'bodily and psychological integrity'. Stu Woolman and Michel Bishop assert that section 12(2)(b) tests 'our ability to give distinct meaning to "bodily and psychological integrity", on the one hand, and "security in and control over the body", on the other ... we must interpret "bodily and psychological integrity"

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862 Van Wyk (2001) 64 *J Contemporary Roman Dutch L* 18. Original emphasis.
863 Sec 12(2)(a).
864 Sec 12(2)(b).
865 Sec 12(2)(c).

to mean something over and above "security in and control over" the body'.[866] According to Woolman and Bishop, section 12(2)(b):[867]

> creates a sphere of individual inviolability. Section 12(2)(b) tells us that this inviolability has two components. 'Security in' and 'control over' one's body are not synonymous. The former denotes the protection of bodily integrity against physical invasions by the state and others. The latter guarantees the freedom to exercise autonomy or the right to self-determination with respect to the use of one's body.

It is precisely the right to autonomy, implicit in the second component of the section 12(2)(b) right, that underpins the right to make informed decisions about whether to participate in research – the right to self-determination to decide whether to participate in research. Research without informed consent would amount to a violation of the first component of the right as it amounts to an invasion of one's body.

Are the 'right to bodily integrity' in 12(2), as well as the right to security in and control over their body' not broad enough to embrace protection against research without informed consent. Why does section 12 make explicit mention of 'the right not to be subjected to medical or scientific experiments without their informed consent'?

Various answers to these questions are suggested: the right to informed consent is mentioned explicitly in the ICCPR; the inclusion of the right might be a reaction to abuses during the previous constitutional dispensation during which research subjects were perhaps subjected to medical experimentation without informed consent; and the inclusion of informed consent as a constitutional imperative highlights the importance ascribed to autonomy - section 12(2)(c) 'alerts us to the threats to personal integrity that flow from everyday medical research and treatment'.[868]

The use of 'everyone' in the section indicates that the rights conferred in section 12 are not limited to South African citizens. Section 12 is not a political right (which normally indicates that the right applies to citizens only); the right applies to citizens and non-citizens. Everyone in South Africa taking part in HIV vaccine efficacy trials may rely on section 12(2)(c) to protect their interests.[869]

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866 Woolman and Bishop in Woolman *et al* (eds) (2005) 40-57 – 40-58.

867 Woolman and Bishop in Woolman *et al* 40-63.

868 Woolman and Bishop in Woolman *et al* (n 866 above) 40-69.

869 This statement oversimplifies the situation, and does not account for the position of temporary and permanent residents, nor does it account for the position of persons who are illegally in the country. In this regard, see Klaaren 'Non-citizens and equality' (1998) 14 *South African J of Human Rights* 286.

Van Wyk is of the opinion that 'experimentation' as used in section 12(2)(c) probably means medical or scientific 'research'.[870] The view is correct, given the fact that the two terms are used interchangeably in various international ethical documents and the National Health Act.[871] After an exhaustive analysis of the matter, Van Wyk remarks regarding the interpretation to be given to the term 'experiment' in section 12(2)(c):[872]

> The question now is which interpretation can be given to the term 'experiment'. The first option equates 'experiment' with research, whether it is of a therapeutic or non-therapeutic nature. This seems to be the straightforward, literal meaning, which is also compatible with most of the sources dealing with research ethics quoted above. It is also in keeping with a purposive, generous interpretation of the right not to be subjected to research without one's own consent, in that it gives effect to the right to personal dignity, integrity and autonomy in its widest sense. When section 12(2)(c) is read in context with the whole of section 12 – which deals with the freedom and security of the person – the conclusion is the same.

Another important aspect of section 12(2)(c) is the mention of medical *or scientific* experiments. The drafting history of the subsection shows that the words *or scientific*, are a later addition to the drafting of the subsection – added to the March 1995 draft of the Bill of Rights.[873] The inclusion of the word 'or' indicates that scientific is something different from 'medical'. 'Scientific' is certainly a term wider in meaning than medical; most medical experimentation may be termed 'scientific', not all scientific experiments are 'medical'. Not only experimentation in the medical sciences, but also other 'scientific' experiments which are conducted using human subjects fall under the ambit of section 12(2)(c). In this regard, is experimentation in, for example, the human sciences, included in the term 'scientific' as human subjects are often used in such experiments? It is submitted that the answer to this question is positive: all experimentation on human subjects, whether in the human or natural sciences, requires the informed consent of research subjects.

In addition, section 12(2)(c) makes no distinction between therapeutic and non-therapeutic experimentation, unlike the National Health Act.[874] All experimentation is prohibited, regardless of the category to which it belongs.[875] It is

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870 Van Wyk (n 28 above) 8.

871 See eg the Nuremberg Code, which refers to 'experimentation'; the CIOMS Guidelines which refer to 'research' and the Declaration of Helsinki, which refers to both 'experimentation' and 'research'. Also, the National Health Act refers to 'experimentation' and 'research' as alternatives for the same concept.

872 Van Wyk (n 862 above) 18.

873 See Woolman and Bishop in Woolman *et al* (n 866 above) 40-5, fn 3.

874 See above.

875 See above, para 5.4.1.

unlikely that the distinction between 'medical *or scientific* experiments' is meant to separate therapeutic (medical) from non-therapeutic (scientific) research.

The use of the word 'their' in section 12(2)(c) has elicited comment from scholars. Van Oosten remarks: 'The use of the word "their" in section 12(2)(c) makes it patently clear that the only person who is capable of giving consent to medical research is the research subject and that surrogate consent to medical research is out of the question'.[876] No research may be allowed on persons incapable of giving their own consent. Van Oosten argues that surrogate consent to medical research on incompetent minors and mentally ill persons is impossible - an overly strict interpretation of the word 'their'. Van Wyk's view is preferable to that of Van Oosten. She argues convincingly that:[877]

> [Van Oosten's strict interpretation] would preclude research in South Africa on legally incompetent people, such as young children, who are not capable of providing voluntary informed consent. This would also preclude research where proxy consent from their parents or care-givers is obtained. This would render South Africa out of step with the rest of the world in this respect, and would undeniably hinder medical progress.

Van Wyk would allow 'therapeutic' research on other than competent individuals, as long as the necessary surrogate consent has been obtained.[878] It is submitted that non-therapeutic or 'scientific' research on incompetent people, which carries more than minimal risk, is not allowed under the South African Constitution.[879] HIV vaccine efficacy trials, as they carry significantly more than minimal risk, thus, cannot be carried out on incompetent minors or mentally ill persons.

Few reported cases on informed consent as embodied in section 12(2)(c) subsequent to the enactment of the 1996 Constitution have reached the South African courts. The 2004 Cape High Court case of *Oldwage v Louwrens*,[880] and its 2006 reversal on appeal, *Louwrens v Oldwage*,[881] therefore, merit attention.

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876 Van Oosten (n 11 above) 9.

877 Van Wyk (2005) 68 *J Contemporary Roman Dutch L* 38.

878 See Van Wyk 8.

879 Art 7 of ICCPR, however, allows for such research in certain circumstances, if certain requirements are met. See para 5.1.3 (b) above.

880 *Oldwage v Louwrens* 2004 (1) SA 532 (C). However, this is not the only case on section 12 to reach the courts. For example, in *Minister of Safety and Security and Another v Xaba* (2002 (2) SA 703 (D)), the court refused to grant an order that would allow a bullet to be removed from a prisoner's leg without his consent on the basis that the prisoner's sec 12 rights would be infringed by such an operation. Also relevant to the protection offered by sec 12 are *Christian Lawyers Association of South Africa v Minister of Health* (see n 566 above).

881 *Louwrens v Oldwage* 2006 (2) SA 161 (SCA).

In *Oldwage v Louwrens* the Cape High Court had to decide whether the medical practitioner misrepresented a particular procedure to relieve pain. The Cape High Court affirmed that informed consent should be based on a 'substantial knowledge of *all the material risks*' of the procedure. It held that the principles laid down by the Court in *Casstell v De Greef*[882] set the standard for determining whether a patient gave informed consent to a procedure.

On appeal, the Supreme Court of Appeal quoted and approved of the requirements for informed consent to operate as a defence laid down by Judge Ackermann in *Castell v De Greef*. They are, *inter alia*:[883]

(a) the consenting party 'must have had knowledge and been aware of the nature and extent of the harm or risk;
(b) the consenting party 'must have appreciated and understood the nature and extent of the harm or risk;
(c) the consenting party 'must have consented to the harm or assumed the risk;
(d) the consent 'must be comprehensive, that is extend to the entire transaction, inclusive of all its consequences.

Overturning the Cape High Court's judgment on the facts, the Supreme Court of Appeal held that it was not expected of a surgeon to warn a patient of the likelihood of a complication in a procedure if there was a mere 2 per cent chance of this risk materialising; that is, the Supreme Court of Appeal affirmed the requirement that informed consent should be based on knowledge of the 'material risks' of a procedure.

Carstens and Pearmain argue that, in view of previous legal opinion and case law, the judgment of the Supreme Court of Appeal in *Louwrens v Oldwage* is 'ambivalent, confusing and contentious'.[884] They criticise the Court on a number of grounds, but most relevant to the current discussion, for simultaneously applying *Castell v De Greef* and *Richter v Estate Hammann*, and thereby invoking the discarded standard of the reasonable doctor in the context of informed consent.[885]

Moreover, Carstens and Pearmain criticise the Supreme Court of Appeal for following a one-dimensional approach which ignores the impact of the Constitution on the existing law on informed consent. They observe that:[886]

> in addition the court follows, in context of the issue of informed consent, a one-dimensional approach, by only referring to some common law principles relating to informed consent. There is a total absence of the multi-layered approach which

882 n 881 above.
883 n 881 above, para 22B-C.
884 Carstens and Pearmain (n 13 above) 683.
885 As above, 685.
886 As above, 686.

> is now indicated in terms of the transcendental nature of medical law in the context of the constitutional paradigm – ie in addition to the common law, the applicable provisions of the Constitution (particularly section 12(2)(b) dealing with bodily integrity) and applicable legislation governing informed consent (sections 6 and 7 of the National Health Act). In the absence of an assessment of these considerations impacting on informed consent, one has to state, that the judgment, in this regard is with respect, not well-considered (as opposite to the principled judgment of by Yekiso J in the court *a quo*).

It is submitted that Carstens' and Pearmain's criticism of the case is well-founded. *Louwrens v Oldwage* is the first case to reach the Supreme Court of Appeal after the enactment of the 1996 Constitution; however, the Court missed an ideal opportunity to provide a well-nuanced and principled approach to informed consent in South African law in the light of the Constitution, and to clear up uncertainty surrounding the question of whether a lack of informed consent constitutes assault or negligence.

One more case needs mention. In *McDonald v Wroe*,[887] in dealing with a dentist's the failure to warn his patient about the risk of permanent nerve damage during the extraction of her wisdom teeth, the Cape Provincial Division found that the plaintiff's right to bodily integrity entrenched in section 12(2) of the Constitution was infringed. The Court remarks:[888]

> In obtaining plaintiff's consent to the procedure, defendant failed to fully inform her of the nature and extent of the risk of permanent nerve damage, with the result that plaintiff consented thereto without appreciating the risk of permanent nerve damage. Defendant's omission is accordingly linked to the harm suffered by plaintiff. To this I should add that plaintiff's right to bodily integrity is entrenched in section 12(2) of our Constitution of the Republic of South Africa, 1996, which right the defendant has violated by subjecting her to surgery without obtaining her informed consent.

4.5 Conclusion

This section explores the views of international and national human rights law on informed consent applicable to South African preventive HIV vaccine efficacy trials. The examination of the provisions in the South African Constitution on international law suggests that, on the whole, international law has to be 'domesticated' before it can apply[889] to the situation of preventive HIV vaccine trial participants. In the

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887 *McDonald v Wroe* [2006] 3 All SA 565; also discussed in Carstens and Pearmain (n 13 above) 634.

888 *McDonald v Wroe* 575, para 39.

889 Customary international law is lower in status than specific national law and the Constitution, but subordinate legislation, common law and case law are lower in status than international customary law; international agreements or treaties are not law in the Republic unless they have been approved by resolution in the National Assembly and the National Council of Provinces; s 39 of the Constitution compels the use of international law in the interpretation of the Bill of Rights – but does not bind

situation of international treaties signed but not ratified by South Africa, nothing may be done that is interpreted as violating the purport and objects of the treaty.[890] Further, in interpreting the rights in the Bill of Rights, a court must consider international law.[891]

International human rights law protects the right to free and informed consent to medical research or experimentation. International human rights conventions, such as the ICCPR (of which South Africa is a state party) and the Protocol to the African Charter on Human and Peoples' Rights on the Rights of Women in Africa, make explicit provision for this right; and other international law instruments, as well as customary international law (such as some provisions in the Universal Declaration of Human Rights), establish a broad range of obligations on governments with respect to the informed consent of participants in clinical research through guarantees to equality, dignity, access to health care and physical integrity. Human rights law requires that protection is provided against government intrusion upon individual freedom and autonomy, and requires positive action to ensure that informed consent is obtained from research participants.

Furthermore, according to section 233 of the South African Constitution, domestic legislation should ensure both *de jure* and *de facto* compliance with international human rights law obligations. In addition to the development of legislation that meets the requirements of international human rights law, legislation can be used to reform policies and practices to bring informed consent into compliance with international standards, should such compliance be lacking.[892]

The South African constitutional system recognises constitutional supremacy. This means that domestic human rights law offers supreme protection in terms of informed consent in South Africa – it is a vital constitutional imperative. Research protocols which violate participants' section 12(2)(c) right not to be subjected to medical experimentation without their informed consent are prohibited by the

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the judiciary in their interpretation to international law: it should merely consider such law.

890 See para 5.3 of ch 4 above.

891 See para 5.2.1 of ch 4 above.

892 South African national law on informed consent, on the whole, is in compliance with international standards, especially after the enactment of the National Health Act 61 of 2003.

constitution. Whether such a violation occurs in a specific situation is a factual question to be determined by a court.[893]

A statutory body (such as a university or the MRC), or a private pharmaceutical company doing HIV vaccine efficacy trials is bound to respect the research participant's constitutional right to informed consent. In terms of section 8(2), '[a] provision in the bill of rights binds a natural or a juristic person if, and to the extent that, it is applicable, taking into account the nature of the right and the nature of the any duty imposed by the right'. The duty imposed by section 12(2)(c) - to respect an individual's right not to be subjected to experimentation without informed consent - is not an onerous one,[894] and therefore binds a statutory body, such as a university, as well as a private pharmaceutical company.

Although it is guaranteed by international human rights law, the requirement that informed consent be given before a person is subjected to medical treatment or scientific experimentation is explicitly mentioned only in two of the international human rights instruments under investigation in the thesis - most notably, in the ICCPR and the Protocol to the African Charter on Human and Peoples' Rights on the Rights of Women in Africa.[895]

That the right is not explicitly guaranteed elsewhere may be due to two possible reasons. First, the right not to be subjected to experimentation without free and informed consent is seen as implicitly included in other rights which are guaranteed, such as the right to human dignity, to physical and psychological integrity, to health and so on. Second, drafters of international human rights instruments regard the right as falling within the ambit of ethical guidelines and not human rights, and therefore not 'worthy' of inclusion in a human rights instrument. If this is the case, it is extremely regrettable, as a unique opportunity for the protection of research participants has been missed.

Moreover, even in instances in which the right not to be subjected to medical experimentation without informed consent is mentioned in international (and national) human rights instruments, it is not given specific content. For example, it is not indicated either by national or international human rights law who may

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893 A Court will have to determine whether the conduct in question constitutes 'medical experimentation', and whether informed consent was give.

894 Such as would probably be duties imposed by socio-economic rights such as the right to health care (sec 27).

895 Of course, the Council of Europe's Convention on Human Rights and Biomedicine explicitly guarantees the right to free and informed consent. This instrument does not, however, fall within the scope of this chapter of the thesis.

consent, the formalities needed for valid consent, and so on. Compared to ethical guidelines on informed consent, human rights law is far less specific; international human rights law sets a standard that must be adhered to and does not lay down any procedural requirements that must be met for the realisation of the right.

It is the task of national law to give substance to the international law norm, and to lend specificity to the standard. In South Africa, national law in the form of the National Health Act for the first time makes informed consent a legislative imperative, as does the Constitution. The Constitution is 'vague' and non-specific in its phrasing of the consent requirement; the Health Act, however, is much more specific in what is meant by 'informed consent'.

However, South African national statute law contains conflicting requirements for informed consent. The table reprinted above[896] shows that, especially regarding the position of children, the requirements for informed consent are unclear. The National Health Act has reintroduced confusing and discredited terms, such as the distinction between 'therapeutic' and 'non-therapeutic research', and is not in line with ethical guidelines on informed consent. As well, the Draft health research regulations recently published for comment in terms of section 90 of the National Health Act, instead of clearing up the uncertainties and inconsistencies, create more confusion.

South African common law and case law on informed consent do not deal specifically with informed consent in a research setting, and it is therefore necessary to extrapolate principles to the preventive HIV vaccine efficacy trial setting. The analysis of South African common law and case law on informed consent argues that a researcher or health care worker who fails to obtain vaccine trial participants' informed consent may be liable for civil or criminal assault; civil or criminal *iniuria*; or negligence. It is concluded that a conceptually sound approach dictates that research without informed consent constitutes not negligence, but an assault, as the relevant element of the delict and/or crime is that of wrongfulness or unlawfulness and not that of fault.

Moreover, a researcher in the HIV vaccine trial context who does not perform trial-related procedures with the necessary degree of care and skill, will be held liable for negligence.

In the case of damage suffered because of participation in a HIV vaccine trial the flexible approach to causation needs to be adapted in order to take into account

the unique situation of trial participants, where trial-related damage may not be immediately apparent. Such an approach is in line with policy considerations based upon aspects such as reasonableness, fairness and justice.

Significantly, informed consent in a research context has not been litigated under international human rights law;[897] it has been mentioned within the context of the torture of prisoners. Informed consent as an international human right rarely has been used as way of protecting the interests and rights of research participants. This aspect is discussed in chapter 6 below.

5 INFORMED CONSENT APPLIED TO THE SOUTH AFRICAN PREVENTIVE HIV VACCINE EFFICACY TRIAL CONTEXT

5.1 Introduction

In South Africa, the ethical and legal imperative of obtaining the participant's informed consent should be seen against a background of an epidemic that is both caused by, and which causes, severe inequity. As was shown in a previous section,[898] HIV has its roots deeply embedded in social, economic and political contexts, which have important implications for participants' vulnerability to exploitation and their ability to give free and informed consent. Zion demands to know, 'how can you speak of informed consent' in such a context?[899]

The table in paragraph 2.3.1 above shows that, in South Africa, there are currently four preventive HIV vaccines being tested in humans, namely:

PROT #	START DATE	SPONSOR, FUNDER, DEVELOPER	TRIAL SITE(S)	VACCINE	# PRTCP	CLADE
HVTN 059 (Phase I)	Oct 2004	HVTN, SAAVI, Alphavax	US, South Africa, Botswana	VEE (Venezuelan equine encephalitis) vector with *gag*	96	C
HVTN	Jan 2004	NIAID, HVTN,	Thailand, Brazil,	Adenovirus vector	435	B

896 See para 5.4.1 above.

897 In has however, been litigated in *domestic* courts during private law actions arising out of the breach of domestic statutes. Art 7 of ICCPR has been invoked in a series of cases heard by courts in the United States of America. Eg, in *Abdullahi v Pfizer Inc* 2002 WL 31082956 (SDNY, 17 September 2002) (NO 01 CIV 8118), the New York District Court held that while the claimants need not rely on the ICCR to provide a private right of action, they may look to it to allege that Pfizer's conduct violated 'well-established, universally recognised norms of established international law'(*Abdullahi v Pfizer Inc* II.4). See Plomer (2005) 5 - 7 for a discussion of this and similar cases arising out of Pfizer's Trovan experiments in Nigeria. Also see ch 3, para 4.2.2 above.

898 Paras 2.3.1 – 2.3.3 above.

899 Zion (n 245 above) 174.

050/ MERC 018 (Phase I)		Merck	Haiti, Puerto Rico, South Africa, US, Malawi, Peru	with *gag*		
IAVI A002 (Phase II)	Nov 2005	Children's Hospital of Pennsylvania, Columbus Children's Research Center, Indian Council of Medical Research, National AIDS Control Org, Targeted Genetics Corporation	South Africa, Uganda, Zambia	AAV2 (adeno-associated virus type 2) vector with gag, pol, ÆRT	91	C
HVTN 204 (Phase II)	Sept 2005	DAIDS, HVTN, VRC, Vical, GenVec	US, Brazil, South Africa, Haiti, Jamaica	Prime: DNA vaccine with *gag, pol, nef + env* Boost: Adenovirus vector with *gag, pol + env*	480	B A, B, C

No Phase III preventive HIV efficacy trials are presently taking place in South Africa, but the two candidate vaccines in Phase II, protocols IAVA A002 and HVTN 204, are likely to enter Phase III trials in the near future, should the results of their Phase II trials be satisfactory. Pre-clinical testing is also ongoing.[900]

The product by AlphaVax, protocol HVTN 059, was the first candidate vaccine to be approved by the MRC for testing in humans.[901] The vaccine utilises virus-like particles, containing parts of an attenuated strain of Venezuelan equine encephalitis (VEE) virus and a gene from a South African strain of the HIV virus (*gag*), to deliver the vaccine to the immune system.[902]

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900 See SAAVI Annual Report 2004/2005 (2006) 1, 7 – 9 for a list of vaccine products by SAAVI currently in preclinical testing in South Africa; eg, the University of Cape Town has a number of DNA vaccines and a recombinant modified vaccinia Ankara vaccine that are almost ready for clinical testing. See also Williamson (2002) 53 *Life* 207-208.

901 'Medicines Control Council approves first HIV vaccine trial in South Africa' SAAVI press release, 18 June 2003.

902 As above. As the vaccine consists of only a small section of genetic material from HIV, and does not include all the genetic elements needed to reconstitute live HIV, scientists believe that there is no possibility of the vaccine itself causing HIV infection. However, compare concerns about the safety of using a VEE vector (see Veljkovic *et al* in para 2.3.1 above).

Clinical trials of the AlphaVax vaccine are taking place at two clinical trial sites in South Africa – the Perinatal HIV Research Unit at the Chris Hani Baragwanath Hospital in Soweto and the SAAVI Vaccine Research Unit at the Medical Research Council in Durban.[903] In the USA, trial sites are Johns Hopkins University, Columbia University, the University of Rochester and Vanderbilt University.[904]

All four vaccines being tested are live vector vaccines; in other words, they are using live bacteria or viruses, (supposedly)[905] harmless to humans, to transport specific HIV genes that introduce HIV proteins into the body. These genes are the *gag, pol, env, ÆRT* and *nef* genes indicated in the fifth columns of the tables above. Also, the South African HIV-1 epidemic is predominantly of clade C, and therefore this clade is used in the vaccines that are tested in South Africa (with the exception of the HVTN 204 trial, which is an interclade vaccine trial).[906]

One vaccine, the one being tested in protocol HVTN 024, is a prime-boost vaccine, where a DNA vaccine (DNA vaccines are direct injections of genes coding for specific HIV proteins – in this case *gag, pol, nef + env*)[907] plus a boost is given; in this case an Adenovirus vector with *gag, pol + env* proteins.

The table also shows that all four the South African preventive HIV vaccine trials represent internationally collaborative research[908] and that they are multi-centre trials.[909]

Furthermore, each of the four vaccines in the clinical trials in South Africa is the product of a partnership between the public and private sectors.[910] This is due to the fact that vaccines tend to be less commercially viable or successful than other treatments, and, for this reason, are a greater financial risk to pharmaceutical companies – 'vaccine research and development requires expenditures that are substantial, long term and relatively high-risk'.[911] It is estimated that the average

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903 As above.

904 As above. There are 48 trial participants in the US, and 48 in South Africa.

905 See above, para 2.3.1.

906 The trial product contains viral material from clades A, B and C.

907 When the DNA is injected, the encoded viral proteins are produced, just as with live vectors (NIAID, NIH (2003) 'Challenges in designing vaccines' 5, available at <http://www.niaid.nih.gov/factsheets/challenges/challvacc.htm> (17 November 2003).

908 See para 2.5 above.

909 See para 2.4.3 above.

910 See 3rd column under 'sponsor', 'developer', 'funder'.

911 Ruff (2002) 32 *Internal Med J* 127.

cost of developing a new human vaccine is around $US250 million.[912] A HIV vaccine is estimated to cost much more.[913]

It is at this point perhaps necessary to remember the vitally important distinction between *preventive* HIV vaccine efficacy trials and other (therapeutic) HIV drug research, or even *therapeutic* HIV vaccine efficacy trials. In the case of HIV-drug or therapeutic research, or even research aimed at finding a therapeutic vaccine,[914] clinical trial participants are necessarily HIV positive. As the clinical trial is aimed at studying the effect of the therapy on the individual, and on the progression of the disease, only those who are suffering from the disease may be enrolled in clinical trials. However, in the search for an effective *preventive* HIV vaccine, HIV negative trial participants are used to test the candidate vaccine.

This makes preventive HIV vaccine trials such a special case: otherwise healthy volunteers are inoculated with (attenuated) HIV. While this necessarily is done in all preventive vaccine research, on the whole other vaccine research deals with diseases less deadly.[915] In the case of preventive HIV vaccine trials, the infection (should it materialise) has no cure.

At present it is not foreseen that HIV researchers will soon[916] undertake clinical trials in humans using live virus material (see chapter 2, paragraph 4.2.1 and 4.2.2 on the distinction between inactivated or 'killed' HIV and live, attenuated HIV) but, as relatively little is known about the virus and the body's immune reaction to it and considering that candidate vaccines will be tested in healthy volunteers, the legal and ethical implications of such trials are far-reaching.

In the light of the conditions prevailing at the point of potential South African Phase III preventive HIV vaccine trial sites, obtaining informed consent from participants in

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912 WHO (1998) 'The world Heath Report - 1998', quoted in Ruff (n 912 above) 127. Vaccines are expensive to develop; the Global HIV Vaccine Enterprise estimates that US$1.1-US$1.2 billion is needed annually to speed the search for a safe, effective HIV vaccine (see AVAC (2006) *Report 2006*, 'AIDS Vaccines: The Next Frontiers' 19.

913 As above.

914 This is given to HIV-positive persons, so that the vaccine will 'teach' the body's own immune system to fight the disease, prolonging (perhaps indefinitely) the asymptomatic phase of the disease.

915 Measles, rubella, mumps.

916 See McCarthy (1997) 350 *The Lancet* 1083, who draws attention to the fact that some scientists hope to pursue 'live' virus vaccines as they have little faith that inactivated virus material will stimulate sufficient immune response to confer immunity. It is believed, however, that live virus material poses too great a risk to participant safety.

the trials may present difficulties. In the light of the analysis in paragraphs 4 and 5 above, this section outlines the problems related to obtaining informed consent in the South African HIV vaccine efficacy trial context.

It must be remembered that, as no large-scale Phase III trials have yet been undertaken in South Africa, only an estimate of the problems that are likely to be encountered can be presented, based on experience gained from Phase I and II trials, here and abroad.

5.2 HIV vaccine efficacy trials as 'therapeutic' or 'non-therapeutic' research

The classification of clinical research into 'therapeutic' or 'non-therapeutic' has important implications, not only for consent issues but also for the evaluation of risk and benefit as different kinds of research justify different levels of risk. It is, therefore, important to ascertain whether HIV vaccine efficacy trials are therapeutic or non-therapeutic research.

The Declaration of Helsinki states: [917]

> Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others.

Similarly, the World Medical Association's Operational guidelines for ethics committees that review biomedical research require that the 'risks to the research participants should be weighed against the benefits to both the participants and to the "concerned community" '. [918]

In the case of individuals who are suffering from a disease, it is acceptable that they be placed at risk to a degree to find an effective therapy or a cure for the disease, if not for their benefit, then for others suffering from the same disease.[919]

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917 Basic principle I.16, Declaration of Helsinki (2000 rev).

918 WHO (2000) 'Operational guidelines for ethics committees that review biomedical research', available at <who.int/tdr/publications/publications/pdf/ethics.pdf> (31 August 2006).

919 This is the motivation for the distinction in research ethics between therapeutic and non-therapeutic research.
See eg the definitions of therapeutic and non-therapeutic research in the Declaration of Helsinki (1996 revision):
Introduction:
'In the field of biomedical research a fundamental distinction must be recognised between medical research in which the aim is essentially diagnostic or therapeutic for a patient, and medical research, the essential object of which is purely scientific and without implying direct diagnostic or therapeutic value to the person subjected to the research.'

Where healthy volunteers are involved, no such justification exists. Guideline 9.12.4.4 of the MRC guidelines determines as follows:[920]

> In *therapeutic* research, the benefits likely to accrue to a participant should outweigh the risk of harm. As a general rule, research involving patients should not incur risk greater than minimal. An exception to this rule is where there is great potential benefit to the individual.
>
> In *non-therapeutic* research, the healthy volunteer may be subjected to no more than minimal risk as a result of participation. The *possibility or probability* that a particular investigation will be of benefit to humanity or to posterity, *affords no defence in the*

II Medical research combined with professional care:
'The physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that clinical research is justified by its potential diagnostic or therapeutic value for the patient' (guideline II.6); and
III Non-therapeutic biomedical research involving human subjects:
2. The subjects should be volunteers – either healthy persons or patients for whom the experimental design is not related to the patient's illness.

See also Van Oosten (n 15 above) 10 and Burchell (n 584 above) 217. For example, many writers have criticised this distinction as 'illogical', such as the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1975 – 1978). Levine argues that all clinical research includes elements that are therapeutic and elements that are non-therapeutic (see eg Levine (n 2 above) 8; Levine (1999) 341 *N Engl J Med* 531-534).

The argument is summarised by Spriggs (2004) 30 *J Med Ethics* 178:
Treatment is the utilization of knowledge whereas research creates knowledge. Although therapeutic research may have a therapeutic intention, it also has a research intention. And because it is research, the therapeutic intention is modified by the aim of advancing knowledge. Sometimes it is thought that research described as therapeutic confers benefit, and research termed non-therapeutic confers none.

.... The risk of harm in some therapeutic research can be considerable—for example, unexpected side effects of new treatments, whereas the risk in non-therapeutic research can be negligible. Examples of beneficial non-therapeutic research in children include Phase II vaccine trials when there is evidence in adults of the vaccine "preventing or slowing the progression of an infectious disease", and also vaccine trials for diseases that do not occur in adults or which manifest differently in children. An example of non-therapeutic research involving no additional risk or discomfort for individual children is the taking of extra blood during diagnostic or treatment procedures for 'legitimate research purposes'. Such research may benefit children as a whole.
As we can see, research is not meaningfully divided into 'therapeutic' and 'non-therapeutic' because it is not clear whether these labels should apply to a project as a whole, or to the individual subjects only. Some studies benefit some subjects but not others - example, studies which include placebo controls might not benefit half of the participants – those receiving the placebo - but the other half of the participants might benefit.

920 Original emphasis. Compare similar guidelines by the Royal College of Physicians:
'Second, society rather than the individual may benefit. In such situations, *however large the benefit*, to expose a participant to anything more than minimal risk needs very careful consideration and would *rarely be ethical*' (guideline 7.3 Royal College of Physicians (1996) Guidelines on the practice of ethics committees in medical research involving human subjects (3rd ed). Again original emphasis.

event of legal proceedings. *Incompetent* participants in research should not be subjected to more than negligible risk.

The distinction between therapeutic and non-therapeutic research is often made in South African ethical discourse, as well as in legislation.[921] But which category should be descriptive of preventive HIV vaccine efficacy trials - are such trials to be considered therapeutic or non-therapeutic? This issue has led to much uncertainty among members of South African research ethics committees and scholars.[922]

Preventive HIV vaccine efficacy trials fall squarely under the heading of non-therapeutic research (unlike therapeutic HIV vaccine efficacy trials which are by definition *therapeutic* research).[923] Volunteers in preventive HIV vaccine efficacy trials are HIV-negative at the start of the trial; they are healthy volunteers, and, nominally, have nothing to gain from their participation.

The MRC guidelines require that healthy volunteers be subjected to no more than 'minimal risk'. Furthermore, the MRC guidelines expressly reflect the 'possibility or probability that a particular investigation will be of benefit to humanity or to posterity' as a justification for exposing healthy volunteers to 'more than minimal' risk.[924]

Thus, if we understand HIV vaccine efficacy trials to be an example of 'non-therapeutic research', then these trials are not justified according to the above risk-benefit ratio. Contrary to the MRC guidelines, they pose 'more than minimal risk' to participants (be it physical, psychological or social) and are thus to be considered unethical.[925]

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921 See eg secs 71(2) and 71(3) of Act 61 of 2003 which also distinguishes between therapeutic and non-therapeutic research.

922 One of the questions asked during a recent IRENSA seminar in Cape Town (20 – 21 August 2006), was whether preventive HIV vaccine efficacy trials qualify as therapeutic or non-therapeutic research. It was clear that no certainty exists on this matter.

923 Healthy volunteers are not used in these trials – only HIV positive persons are used.

924 'Minimal risk' is defined in the MRC guidelines as indicating that 1) There is a small chance of a recognised reaction which is in itself trivial, such as a mild headache or a feeling of lethargy. 2). There is a very remote chance of serious injury or death, comparable, for example, to the risk of flying as a passenger on a scheduled aircraft (guideline 9.12.3.2).
The MRC guidelines provide an example of minimal risk: 'An example of minimal risk includes obtaining a single peripheral venous blood sample, say up to 10 ml at a limb site, from a younger child by a competent venesector, provided that the amount of blood collected is not excessive for the size of the child, and that the risks to which a child is exposed before entry into a research project are considered'.

925 See para 2.3.2 above for an outline of the risks and rewards of participation.

Is it, however, possible to argue that HIV vaccine efficacy trials are 'therapeutic' research and, therefore, justify greater risk of harm to the individual?[926]

In South Africa, as elsewhere, preventive HIV vaccine efficacy trial participants need to be at high risk of HIV infection to ensure that the effectiveness or not of the vaccine may be proven statistically. They are at increased risk of infection because of their lifestyle, or because of their social, cultural and economic circumstances.[927] Some scholars argue that for this reason they benefit from the object of the research - finding an effective preventive HIV vaccine - and that such research should therefore be considered 'therapeutic'.[928] Even if participants at high risk for HIV infection do not personally benefit, the class of subjects to which they belong – be it injection IDUs, MSM or the particular community in which they live – potentially, may benefit from the research as they will be given counselling on high-risk behaviour, and thus (it is hoped) reduce their chances of infection.

On the whole, it is difficult to fit preventive HIV vaccine efficacy trials into the category of either 'therapeutic' or 'non-therapeutic' research. In accordance with the guidelines laid down by the Declaration of Helsinki concerning therapeutic and non-therapeutic research,[929] preventive HIV vaccine efficacy trials fit neither category, by[930]

> combin[ing] medical research with professional care, the objective being the acquisition of new medical knowledge, *only to the extent that* clinical research is justified by its *potential diagnostic or therapeutic value for the patient.*

Because participants need to be at high risk for HIV infection, the trials are not conducted on real 'volunteers – either healthy persons or patients for whom the experimental design is not related to the patient's illness'[931].

The MRC, in its Guidelines for ethics in medical research: HIV vaccine trials (MRC vaccine trial guidelines),[932] considers preventive HIV vaccine trials as non-therapeutic research:[933]

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926 As was pointed out above, *therapeutic* HIV vaccine efficacy trials will, by definition, be considered therapeutic research, as they are conducted on participants who are HIV-positive.

927 See paras 2.3.1 and 2.3.2 above.

928 See eg Ladimer (1977) 55 *Bulletin of the World Health Organisation* 111 – 115.

929 See n 11 above.

930 Guideline II.6 (1999 rev).

931 Guideline III.2 (1999 rev). Some writers have advocated the need for a third category of research, that which is likely to benefit a class of individuals with which the subject identifies. See eg Engelhart in Spicker *et al* (1988) 123 – 140.

932 Book V.

933 Guideline 9.12.4.4.2 (Book V). My emphasis.

> In non-therapeutic research, *such as trials of HIV preventive vaccines*, healthy volunteers should be subject to no more than minimal risk as a result of participation, even if the particular research will be of great benefit to humanity.

Arguments over the distinction between 'therapeutic' and 'non-therapeutic' research may seem trivial;[934] the distinction, however, has a definite bearing on an ethical and legal analysis of informed consent, as different categories of research demand different legal and ethical safeguards.[935]

5.3 Problems in obtaining informed consent in the context of South African HIV vaccine efficacy trials

5.3.1 Voluntariness

Voluntariness describes an action that is free of the controlling or coercive influence of others.[936] Certain conditions, such as psychiatric illness and drug addiction, may reduce or eliminate the element of voluntariness.[937] In the context of this discussion, however, voluntariness is used in a sense to include 'acts of love, threats, education, lies, manipulative suggestions, and emotional appeals'.[938] Beauchamp and Childress outline three categories of influence which reduce or eliminate voluntariness: coercion, persuasion, and manipulation.

Coercion indicates a person's intentional and successful use of a 'credible and severe threat of harm or force to control another'.[939] Coercion is incompatible with informed consent because it eliminates the possibility of autonomous choice. Coercion renders even intentional and well-informed conduct non-autonomous.[940]

Persuasion is a form of influence that relies on an appeal to reason. In other words, 'a person must come to believe in something through the merit of reasons another person advances'.[941] Persuasion does not exclude voluntariness; autonomous action is still possible if sufficient reasons are put forward for a certain course of action and if those reasons are valid and adequately understood.

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934 Eg Spriggs (n 919 above) 178.
935 See paras 4 and 5 below.
936 McLean in Doyal and Thobias (eds) (2001) 166 – 167; Burchell (n 584 above) 218; Beauchamp and Childress (n 5 above) 93. This is a rather narrow view of voluntariness that is intended to differentiate it from a broader concept that would make it synonymous with autonomy.
937 Burchell (n 584 above) 216 - 218; Beauchamp and Childress 94.
938 Beauchamp and Childress 94.
939 As above.
940 Beauchamp and Childress 94.
941 As above, 94.

Manipulation is a 'generic term for several forms of influence that are neither persuasive nor coercive'.[942] The most common form of manipulation in research is the use of informational manipulation.[943] Informational manipulation refers to the manner in which a health care provider presents information (tone of voice, a forceful gesture, and so on) to change the listener's understanding of a particular situation, influencing her to act in a certain manner.[944] An example of informational manipulation is the positive statement 'we have a 35 per cent success rate', rather than the negative 'we have a 65 per cent failure rate'.[945] Another example of informational manipulation, this time from the South African context, is the use in translation of the word '*spaza*' for the term placebo during the vertical transmission trials in 1997.[946] Placebo means of no curative value; *spaza* means something that is 'half the real thing'. *Spaza* shops are shops in the townships that sell the same goods as supermarkets in the city. Thus, participants in the HIV transmission trials who were informed that they will be given a *spaza* drug, would have believed that they were being given 'half the real thing', instead of a placebo. It is thus likely that theirs was not informed consent to participation in these trials, as the presentation of information altered the research participants' 'perception and response, and thereby affect[ed] understanding and voluntariness'.[947]

Beauchamp and Childress argue that manipulation in research should not be overstressed as research participants often make decisions in a context of rival influences, such as 'personal desires, familial constraints, legal obligations, and institutional pressures'.[948] Such influences do not necessarily exclude autonomy; nevertheless, to ensure that research participants make autonomous choices, it is important to establish a point at which autonomous choice is put at risk. In many situations, it is difficult furthermore to distinguish between controlling and non-controlling influences.[949]

Beauchamp and Childress's account of voluntariness lacks an understanding of the form of manipulation that is likely to be most prevalent in a South African research setting, especially in HIV vaccine efficacy trials. They ignore the

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942 As above, 95.
943 As above.
944 As above.
945 As above.
946 See 'Mothers give support to placebo trials' *Mail & Guardian* 3 - 9 October 1997 5.
947 Beauchamp and Childress 95.
948 As above.
949 As above.

complexities of power relations in a South African setting, where a participant's autonomous choice is influenced by the context of the research. Participants in HIV vaccine trials are likely to be poor, uneducated and scientifically naïve, believing that 'doctor knows best' or that the trial may present their only chance of receiving medical care. Some may even be unable to distinguish research from care. In this context McNeill remarks that it 'it is the socially powerless that are most likely to be subjected to unethical research'.[950]

Various studies on informed consent in a South African setting have confirmed this lack of ability to distinguish between research and care.[951] For example, in an article entitled, ' "Even if they ask you to stand by a tree all day, you will have to do it (laughter) ...!": Community voices on the notion and practice of informed consent for biomedical research in developing countries', Molyneux *et al*[952] found that 'many community members had great difficulty in distinguishing between the clinical and research aims of the work ...'.[953] If the research subject is unable to understand that she is taking part in research, and that the drug or vaccine being tested is merely experimental and has no proven clinical value, it is self-evident that informed consent has not been obtained.

In an article entitled 'Informed consent for HIV testing in a South African hospital: Is it truly informed and truly voluntary?',[954] Abdool Karim *et al* report on their study that evaluates informed consent to HIV-testing and research at King Edward VII Hospital, a major referral state hospital largely serving black patients in Durban. Specifically, the study evaluates the informed consent obtained from women to participate in an antenatal transmission study; a separate study (from the one on informed consent) that is being undertaken by the hospital.

Women who attended the antenatal clinic for the first time were randomly selected to answer questions before and after HIV-testing and counselling on the research project. The women were divided into two groups, an evaluation study group who completed questionnaires before and after the HIV counselling and the information session regarding the research study (the antenatal-transmission study); and a sensitisation control group who completed only a post-counselling questionnaire.

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950 McNeill 'The ethics and politics of human experimentation', quoted in Barsdorf and Wassenaar (2005) 60 *Social Science & Med* 1087.

951 See eg the works quoted in n 954, n 962 and n 964 below.

952 Molyneux *et al* (n 375 above) 433.

953 As above, 451.

Karim *et al* conclude, firstly, that the women's knowledge of HIV-transmission and prevention was little improved by the pre-test counselling that they underwent (most women's knowledge at the outset was relatively high regarding the modes of transmission and prevention of HIV); and secondly, that, despite assurances that the HIV test was voluntary, 84 per cent of the women in the evaluation group and 93 per cent in the sensitisation group believed that it was compulsory to take the HIV test.[955] Moreover, 93 per cent of the women in the evaluation group and all of the women in the sensitisation group felt that the hospital would not allow them to quit the antenatal research study.[956] Almost a third of the evaluation group and quarter of the women in the sensitisation group felt that that the 'care they received at the hospital would change if they did not participate in the [antenatal] study'.[957] More significantly, 28 per cent of the women believed that the research was integral to service at the hospital and agreed to take the HIV test because they thought that refusal would compromise their care.[958] The authors of the article comment:[959]

> This subtle coercive element may stem from the social context of a hospital where the health professionals are held in high regard. This perception of potentially compromised quality of care is reinforced by the perception that the hospital would not allow them to quit the study even though they knew they had the freedom to do so.

Not only is the 'social context of a hospital' one in which 'health professionals are held in high regard', one should also remember that the hospital concerned is likely to be the only tertiary or state hospital that these participants have access to – it is their only chance to receive free medical care, and they are very unlikely to be able to pay for private medical care. Thus, they are convinced they have no choice but to subject themselves to whatever research the staff at the hospital demands of them – they *cannot* refuse to participate or quit the study.

The authors of the article conclude that in the medical care setting, even though informed consent can be said to be relatively informed, it cannot be truly voluntary:[960]

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954 Abdool Karim *et al* (1998) 88 *American J Public Health* 637 - 640.
955 As above, 638.
956 As above.
957 as above, 639.
958 As above, 640.
959 As above.
960 As above.

> These admittedly limited data provide empirical evidence that subtle and unexpected elements of coercion can reside in the perceptions (real or imagined) held by patients being recruited into a research project in a medical care setting.

If such perceptions exist, it is unlikely that informed consent has been achieved; research participants should be so situated that they are able to choose freely between the different alternatives offered. They should not feel compelled to choose to participate:[961]

> African subjects with relatively little understanding of medical aspects of research participation, indisposed towards resisting the suggestions of Western doctors, perhaps operating under the mistaken notion that they are being treated, and possibly receiving some ancillary benefits from participation in the research, are very susceptible to coercion.

During South African HIV vaccine efficacy trials, every effort will have to be made to avoid the misconceptions referred to above, and to ensure that trial participants do not in any way feel compelled to participate.

5.3.2 Comprehension

Many articles comment on research participants' inadequate comprehension of information given to them during the consent process.[962] In order to achieve consent that is informed research participants need to understand the information that has been provided. Moreover, they have to understand the impact of that information on all aspects of their lives, such as its impact on their physical, emotional and social well-being. In the context of HIV vaccine trials in South Africa, participants must, at least, understand the methodology of a vaccine trial, the nature of the risks posed by the trial, and the possible benefits of trial participation so that they may make an informed decision about participating in the trial. As researchers are responsible for obtaining and ensuring informed consent, they are also responsible for ascertaining that the research participant has understood the information that has been provided.

A research participant's ability to comprehend or understand information is a function of her intelligence, maturity and linguistic abilities. Information of a scientific

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961 The Hastings Center (1988) *The Hastings Center Report* 35.

962 See eg (most pertinent to the present thesis) Coletti *et al* 'Randomized, controlled evaluation of a prototype informed consent process for HIV efficacy trials' (2003) 32 *J Acquired Immune Deficiency Syndromes* 161; Lynöe *et al* 'Informed consent: Study of the quality of information given to participants in a clinical trial' (1991) 303 *British Med J* 610; Schultz *et al* 'Are research subjects really informed' (1975) 123 *West J Med* 76; Moodley *et al* 'Informed consent and participant perceptions of influenza vaccine trials in South Africa' (2005) 31 *J Med Ethics* 727. Moodley *et al* conclude

or technical nature is difficult to understand for lay people all over the world, no matter their level of education. In the context of the developing world, where poverty, low levels of education and illiteracy are the order of the day, the comprehension of scientific and technical information poses significant challenges to the research participant. In South Africa, due to their socio-economic background, HIV vaccine trial participants are likely to be illiterate,[963] to have little medical or scientific knowledge and to be second-language speakers of English. There are also likely to be cultural differences between the researcher and the research participants. Bayer comments that difficulties are often experienced in this context; and that explaining concepts such as placebo and randomisation to participants becomes very difficult.[964]

Gita Ramjee *et al* evaluated the comprehension of participants in a vaginal microbicide study conducted in KwaZulu-Natal.[965] According to the results of her study, almost 70 per cent of participants failed to understand vital scientific information regarding the study, as well as factual aspects related to the drug, such as the fact that the microbicide was experimental, that it could not protect against HIV and other sexually transmitted diseases, and that a placebo microbicide was used on some of the participants.[966]

In most cases, interpreters are used to translate the scientific and other trial-related information contained in the informed consent document from English into a local language. In a paper entitled 'Informed consent in a cross-cultural context',

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that participants' recall of informed consent in randomised controlled trials in South Africa and other developing countries may 'often be inadequate' (731).

963 The literacy rate in rural areas of South Africa, where some HIV vaccine efficacy trials are likely to take place, are lower than in urban areas. The following percentages summarise the literacy and basic education levels of adult South Africans aged 15 and over (2001 General Population Census):

Less than Grade 9 education: 48%
Less than Grade 7 education: 32%
No formal schooling: 16%

Therefore, 32% of the adult population in South Africa may be regarded as functionally illiterate, and the functional literacy rate amongst the adult population can be estimated at 68%.
(Statistics South Africa (2003) *Census 2001 Census in brief* (2nd ed), available at <http://www.statssa.gov.za/census01/html/default.asp> (31 January 2007)).

964 Bayer (2000) 14 *AIDS* 1051-1057. Also see Ives *et al* 'Does an HIV clinical trial information booklet improve patient knowledge and understanding of HIV clinical trials?' (2001) 2 *HIV Medicine* 241.

965 Ramjee *et al* (2000) 14 *AIDS* 2553-2557.

966 As above.

Molyneux observes that, although studies have indicated that interpreters who are culturally and linguistically matched to study participants generally improve participants' understanding and the transfer of content information, discrepancies in understanding of research procedures are still identified among South African research participants.[967] At the four South African vaccine testing sites in South Africa, every effort will have to be made to ensure that translations into local languages are accurate and that the translation does not impede comprehension. Differences in knowledge systems will have to be born in mind when translations are done and when certificates are issued which attest to the accuracy of the translated document.

Guideline 12 of the MRC Vaccine trial guidelines recommends that trial participants have an adequate understanding of the aims, procedures, duration, potential risks, expected benefits, and personal implications of trial participation.[968] They should also understand their rights as participants.[969] 'True' understanding requires that trial information is understood in terms of the participant's personal, or religious and cultural values.[970] Participants' short-term recall of technical information about trials is not an adequate indication of understanding.[971] The MRC Vaccine trial guidelines further recommend that a wide range of procedures should be used to assess both understanding of technical terms (such as placebo) and understanding of the personal implications of participation (such as possible stigma or discrimination).[972] Assessment procedures might include check-lists of understanding of technical information, as well as responses to narratives or vignettes related to participation. Procedures to assess understanding could be developed in consultation with community representatives.[973]

Note the emphasis on the assessment of comprehension in guideline 12.6.3. It is not enough for the researcher to make every effort to provide understandable information, but the participants' understanding of that information must be tested before that participant is able to be enrolled in the trial.

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967 Molyneux (2003) 'Informed consent in a cross-cultural context' Paper delivered at the First Annual IRENSA Conference, Cape Town.
968 Guideline 12.6 MRC Vaccine trial guidelines.
969 As above.
970 Guideline 12.6.1.
971 Guideline 12.6.2.
972 Guideline 12.6.3.
973 Guideline 12.6.4.

Information about a trial thus needs to be presented in a manner that is understandable to the prospective participant. Merz, amongst others, calls for the development of written material that is at a more 'simplistic' level, which does not use medical jargon and technical language.[974] He also recommends that, where the use of scientific information is unavoidable, definitions be provided in lay person's terms.[975] A user-friendly format, in which information is set out in a logical manner, which is easy to read because of its use of headings and emphasis on specific information, should be utilised.[976]

Research has been conducted on the comprehensibility of informed consent forms. For example, Cambell *et al* comment that, despite efforts being made to ensure a comprehensive informed consent process, research participants still make poorly informed decisions.[977] The quality of informed consent forms is generally poor: Burman *et al* remark that the majority of informed consent forms are poorly written and thus do not ensure effective informed consent.[978] They call for outside organisations to monitor the informed consent process to ensure that informed consent forms are of a sufficient quality.[979]

Drug trial FTC-302 investigated an antiretroviral drug known in the trial protocol as FTC-302. Trials for the drug were conducted at the HIV Clinic at Kalafong Hospital, Pretoria, during the period 1999 to 2000. The trial received ethical approval from the Faculty of Health Sciences Ethics Committee at the University of Pretoria and, as the trial related to an investigational drug, also from the Medicines Control Council's ethics committee.[980] The FDA had approved the drug for research purposes.[981]

An investigation into the trial was prompted by a letter from Patricia de Lille, MP, dated 3 May 2000.[982] De Lille's letter was accompanied by written complaints

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974 Merz (2002) 23 *Controlled clinical trials* 172-173.
975 As above, 173.
976 As above.
977 Campbell *et al* (2003) 56 *Social Science & Med* 671-684.
978 Burman *et al* (2003) 24 *Controlled Clinical Trials* 245-255
979 Burman *et al* 247.
980 Strauss (2001) 'The ethical and/or legal regularity or otherwise of drug trial FTC-302, performed on certain patients at Kalafong hospital, Pretoria in the period 1999-2000', report of inquiry conducted at the request of the University of Pretoria by Professor S A Strauss, (Strauss report) para 2.9.2.
981 As above.
982 Strauss report, para 1.1 – 1.3.

made by seven persons and on behalf of a deceased person, all of whom had been diagnosed with HIV and had participated in the FTC-302 drug trial.[983]

The complainants alleged they had not given informed consent to participation in the trial.[984] For example, AA[985] alleged, although she had signed the consent form on 7 September 1999 for participation in the FTC-302 trial, the form had never been explained to her.[986] The complainants further alleged that they were harmed by the investigational drug, FTC-302, and that the deceased person's death was the direct result of her participation in the trial.[987]

Regarding the lack of informed consent, AA testified that the consent form had not been explained to her, nor had the side-effects of the drugs been outlined. AA testified that Dr Botes (the study doctor or principal investigator)[988] had pressurised her to continue with the trial.[989]

During the course of his investigation, it became clear to Professor Strauss that, on the facts, not all the allegations made by the trial participants were correct.[990] For example, although she initially said that she had not given informed consent to participation in the trial, AA later stated that at the time when she agreed to participate in the trial she was told that she would vomit and have diarrhoea.[991] She was also told that 'all the side effects, which I experience, I should come to her [Dr Botes] and tell her about them'.[992] As to the purpose of the trial she replied, 'they said it will help my immune system'.[993]

Another participant, BB, had died by the time Professor Strauss was investigating the matter. According to her son, she had enjoyed good health until she was assigned to a 'drug trial' by Dr Botes at Kalafong Hospital.[994]

The third trial participant that was interviewed by Professor Strauss was CC. In his statement CC said that he had been diagnosed as HIV-positive in November 1998.[995] In October 1999 Dr Botes told him that she wanted to include him and his

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983 Strauss report, para 1.1.
984 Strauss report, para 2.1.1.
985 A pseudonym.
986 Strauss report, para 2.2.1.
987 As above.
988 See para 2.2.3 above.
989 As above.
990 Strauss report, para 2.1.
991 As above.
992 As above, para 2.1.2.
993 As above.
994 As above, para 2.2.2.
995 As above, para 2.2.4.

wife on 'the trials'.[996] Two weeks later when the results of the blood tests were available, Dr Botes called them to her office. CC remarks: 'She read through the consent form and told us to sign it. She did not have it translated for us into our own language or explain it to us. She told us that the drugs would make us better'.[997] A month after starting with the pills he became extremely sick: high fevers; vomiting; with a rash over his whole body 'which became open bleeding sores'.[998] He was hospitalised at Kalafong. When he told Dr Botes that the drugs were making him sick, she replied that it was not the drugs but HIV.[999] He stopped taking the drugs and within two weeks his health returned to normal.[1000] CC complained to Professor Strauss that he felt that Dr Botes had exposed him to danger and that she had never explained to him what the consequences could be.[1001]

CC further told Professor Strauss that he and his wife did not read the document (the patient information leaflet (PIL)), but that Dr Botes's assistant did so.[1002] As to his understanding of the content thereof, CC responded: 'While she was saying, I understood her □we understood what she was reading'.[1003] She told them, 'in case you become ill or meet some problems you can withdraw if you want from the trial'.[1004]

When Professor Strauss read out to CC the phrase under the heading 'What are the benefits and risks in this trial?' on page 5 of the PIL, referring to nausea, loose stools, skin rash, vomiting and so on, he replied that he understood it at the time, although he did not know what the degree of the rash would be.[1005]

This is the pattern of the testimony of the participants in the research conducted by Dr Botes, and subsequently investigated by Professor Strauss. All claimed that they did not give informed consent to participation in the trial, and that they were harmed by their participation in the trial.[1006] Specifically they claimed that had not been warned of the serious side-effects of the antiretroviral drugs.

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996 As above, 2.2.3.
997 As above.
998 As above.
999 As above.
1000 As above.
1001 As above.
1002 As above, para 2.3.5.
1003 As above.
1004 As above.
1005 As above, para 2.3.7.
1006 As above, paras 2.5 – 2.8.

It is difficult to evaluate, second hand, exactly what information had been shared with the trial participants regarding the risks of the trial during their interviews with Dr Botes's assistant, and whether, based on this information, they had indeed given informed consent to participation in the trial. It is clear that the participants and their relatives subsequently *felt* that they had not consented to participation.

A disquieting aspect of the clinical trial and the subsequent evidence given during the investigation, is the level of discourse used in the informed consent document. After a careful scrutiny of the evidence presented by the various actors in the trial, Professor Strauss came to the conclusion that all participants indeed had consented to participation. On the evidence presented in the confidential report it is clear that the risks and potential benefits of the FTC-302 trial were indeed explained to all the participants. Their recall of these risks, however, was less than optimal, and it may be that their understanding of the information presented to them was severely compromised by their poor understanding of the language used.

It is submitted that, because the consent document[1007] used in the FTC-302 clinical trial is written in language that is technical and obscure, participants must have found it difficult to gain information to give 'informed' consent to participation. The following offers two examples of the language that is used in the seven-page PIL in the study; from sections containing information that may be regarded as vital.

Under the heading 'What is the purpose of this trial', participants are told [t is unclear why 'Doctor' has an uppercase 'D']:

> Therefore, you have been asked by your Doctor to consider taking part in this research of a combination of 3 drugs as treatment for the HIV-1 infection. They are Emtricitabine (FTC) OR lamivudine (3TC), with stavudine, and Nevirapine or efavirenz. FTC is the drug that is being investigated in this study. The study will be conducted in a blinded fashion which means the study patients and the study Doctor/investigator do not know if you are on emtricitabine or lamivudine. The purpose of the study is to determine if emtricitabine is as safe and effective as compared to lamivudine when used in combination with two other effective antiretroviral drugs in HIV-1 infected patients. Emtricitabine is an investigational drug for the treatment of HIV-1 infection that has not yet been approved by the federal government for general use.

and under 'How will I receive my study medications?' they are told:

> Patients whose HIV-1 RNA (virus) level remains below a predetermined level (2000 copies/mL) through the end of the study will be offered the option to receive all study drugs (open-label) at the end of the study. If the level of HIV-1 RNA (virus) in

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1007 On file with author.

your blood is higher than the predetermined level you can not be offered these study drugs for open label use.

Although an effort has been made to increase the document's readability (such as putting the word 'virus' in brackets after 'HIV-1 RNA' and explaining a term such as 'blinded') these add little to the comprehensibility of the document, so that, despite the goal of making the PIL more accessible, the following remain as obstacles to comprehension:

- Although the participant is addressed as 'you', the PIL is written throughout in the passive. This is standard for official forms and enables the concealment of the agent from the process for which he or she is responsible. Consider the example 'The study will be conducted in a blinded fashion'. From the participant's point of view it is important to know who the agent is who will undertake the research, but, without prior knowledge, she will not gain the information from the PIL. Passives are notoriously difficult to read, and occur rarely in everyday speech.
- The extracts both contain unusually long sentences which is typical of technical writing. The first sentence of the first extract contains 40 words, the first sentence of the second extract 36. 27,6 words is the average for scientific topics.[1008] The participants in the FTC-302 trial almost exclusively are second or third-language speakers of English and are unlikely to have encountered scientific language of this nature before.
- Technical terms are in abundance; examples include 'predetermined level'; 'open label use' and 'federal'. The lay reader who does not have specialist medical or scientific knowledge is likely to be intimidated.
- Generally, the PIL uses difficult words where easier ones would do as well. Compare the following words used in the extracts (an easier alternative is provided in brackets): 'determine' (find out) and 'conducted' (done). Elsewhere 'inclusion / exclusion criteria'; 'blood plasma'; 'serology'; and 'verify that you are antiretroviral drug naïve' are used. With very little effort these words could have been 'translated' into colloquial language.

Excluding any information of the extent to which Dr Botes's assistant explained the trial and its procedures to the participants, but given the likelihood that the

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1008 Bhatia (1993) 106.

participants' level of understanding of English is not specialist, it is submitted that it is inconceivable that the document would have resulted in *informed* consent.

Professor Strauss commented with reference to the PIL used in the trial:[1009]

> I put it to Dr Botes that the document appeared to me to have been drafted in fairly technical terms, in somewhat 'learned' English, containing words, phrases and names of medicines which would probably have been incomprehensible to the patients involved. I quoted to her the phrase 'randomised double-blind equivalence trial, comparing Emtricitabine, Lamivudine within a triple combination of anti-retroviral drug naïve HIV-1 infected patients FTC 302'. That phrase, I suggested to Dr Botes, would ordinarily make no sense to a lay person with even a good degree of literacy.

In reaching his conclusion that Dr Botes is not guilty of any wrongdoing, and that BB died not from drug-related side-effects but from various AIDS-related illnesses, Professor Strauss adds:[1010]

> My recommendation, therefore, is that in addition to the official protocol consent document, a fairly brief information document should be compiled in each of the languages that patients best understand. That document should *explain in the simplest possible terms the essential aspects of the trial.* A *counsellor or interpreter who has a sound knowledge of the patient's language of choice should then sit with the patient and read out the document to the patient.* Once the counsellor / interpreter is satisfied that all of the patient's questions have been answered and that the patient understands what it is all about, the patient must sign the document. It goes without saying that in the document the name of the counsellor / interpreter should also appear, and the latter should be required himself/herself to sign a statement indicating that the content has been explained to the patient satisfactorily.

With this recommendation Professor Strauss expresses his unease regarding the language used in the consent form. The principal investigator in a clinical trial always is in a difficult position: she must comply with the legal requirements and adhere to the prescribed ('approved') consent document and PIL. At the same time, the consent form often uses highly technical language, designed not so much to inform but to protect the pharmaceutical company against future litigation.[1011] She must attempt to explain these technical terms in the language of a lay person. If that lay person is illiterate or a second-language speaker of English, the problem is compounded.

An assistant was present to help Dr Botes explain the difficult terms used in the PIL, but, as Professor Strauss indicates, an additional document phrased in

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1009 Para 2.9.16.
1010 Para 4.4. My emphasis.
1011 See chs 4 above and 6 below.

simpler terms is valuable in a situation in which trial participants are not primary speakers of the language and are not familiar with the terminology.[1012]

In 2004, a speech pathology student, Samantha Smith, conducted a pilot qualitative study aimed at exploring the process of obtaining informed consent within a Phase I HIV vaccine trial that was being initiated at the Perinatal HIV Research Unit at the Chris Hani Baragwanath Hospital in Soweto.[1013] She documented obstacles and facilitators to the informed consent process such as *ad hoc* interpreting and cultural, social and linguistic differences amongst participants, researchers and the individuals who originally devise informed consent protocols.

Smith audio and video-taped interviews between vaccine trial participants and health care workers who were in the process of obtaining informed consent from them. Because of its relevance to the thesis, Smith's study is commented upon in detail below.

Smith's case study included two HIV vaccine trial participants: ***participant A***, a Sotho-speaking female, 23 years of age and unemployed, who has a Grade 12 school-leaving certificate; and

participant B, a Zulu-speaking male, 29 years of age, who is a pastor in a local church and who also has a Grade 12 certificate.[1014]

The study co-ordinator and health care worker for the consent process was referred to as ***participant C***. She was a Sotho-speaking female, aged 35. C also functioned as an interpreter during the study.[1015]

Smith observed and video-taped the informed consent process, after which she interviewed the health care professional and the two prospective vaccine trial participants in order to establish whether participant knowledge was sufficient and whether the health care worker's belief regarding the participant's knowledge was accurate.[1016] She used conversational analysis techniques throughout to arrive at her conclusions.[1017]

1012 See paras 2.3.2 and 3.4.2 above.

1013 Smith (2004) 'Misinforming the uninformed? Issues of informed consent in the multicultural context of HIV vaccine trials', unpublished dissertation, University of the Witwatersrand.

1014 As above, 19.

1015 As above, 20.

1016 Smith 20 – 21.

1017 'Conversational analysis techniques look at recorded data at a microscopic level in particular looking at aspects such as stress, markers, inflections, topic management, and nonverbal conversational patterns to gain knowledge regarding specific themes

Smith describes the stages of the informed consent process in this HIV vaccine trial.[1018] First, patients from the HIV testing unit who were counselled and who tested HIV negative were given the opportunity to find out more about the study and trial. They were invited to a series of discussion groups where the concept of the trial and the relevant information were presented to the prospective participants in groups. This stage consists of a number of two to three-hour sessions. Those who were still interested in participating were invited to the pre-screening process where all the aspects of the informed consent protocol regarding the trial were addressed in a one-on-one situation with the trial co-co-ordinator or health care worker. Physical examinations were conducted at this stage, and participants signed the first part of a two-part consent document and information sheet. Prospective participants were then given a 56 day window period to decide whether they wished to participate. The final stage of the screening process involves the actual signing of the document, a process that takes approximately two minutes and which is done with the primary medical officer and study-co-ordinator who conducted the pre-screening session initially. Although Smith analyses various aspects of the consent process she observes, only some aspects will be dealt with here.

At the end of the informed consent process, Smith interviewed participant A to establish what information she understood. The following is a transcript of their interview:[1019]

S: What did you understand as being the procedure for this trial?

A: In this trial, neh, they take positive people and they must be healthy and they maybe don't have flu, maybe cancer, TB, or whatever ... ja

...

S: What did you understand as being the benefits and risks of the trial?

A: The risks – neh, you must use a condom even if you already used the vaccine, but – you must use a condom because maybe you are like HIV positive then you ...

S: And the benefits of the trial? Why did you come?

A: Why did I come? It was my partner, she was, he was sleeping with other, ja he was not straight for me. So I decided to come for the trial.

S: Did you get all the information you wanted? If not, what would you like to know?

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and occurrences within this process such as mitigation, defined as the modification of a speech act to reduce unwelcome effects of undesired information on the listener, speaker misunderstanding of content topic, speaker prejudices and assumptions, power relations, interest and fatigue which have been impeding on the successful transfer of information within the informed consent process' (Smith 23).

1018 Smith 27.

1019 Smith 68 – 69.

A: Yea, I understand everything.

It is clear that there is no likelihood that this participant has understood enough to be said to have given informed consent to participation in the trial. She has no idea of the risks or benefits of the trial; neither does she seem to understand the most basic prerequisite for participation in the trial – only HIV *negative* people are enrolled.

Participant B was interviewed next:[1020]

S: Did you understand everything the health professional told you? Tell me about the procedure for the trial.
B: Yes. On day one they inject you and they gonna take blood for certain research and then you'll be vaccinated on the second time that you visit and after vaccination you will visit every day for observation.
S: Are there risks to the trial?
B: ... it's just that they want to check, if this thing will work, so I see no risks there.

B also felt that he had understood the information regarding the trial.

Smith concludes that the results of the study 'identified significant faciliatory and inhibitory patterns which impacted on the successful achievement of informed consent in the study'.[1021] Mostly, the transfer of information was impeded during the process.[1022] Her observations are:[1023]

- 'notable issues of poorly obtained informed consent occurred during the sessions';[1024]
- linguistic barriers, especially due to the fact that English was used, hindered the transfer of information;
- C, the health care worker, did not present the information in a coherent manner;
- all aspects of the vaccine trail information were not included in the information sessions;[1025]

1020 As above, 70.
1021 As above, 83.
1022 As above, 75.
1023 As above, 76 – 85.
1024 Smith (n 1013 above) 78.
1025 As above.

- 'issues of cultural inappropriateness and over-complex language that was not sufficiently translated into the native language of participants also suggests that information transfer ... has been undermined';[1026]
- there were equal amounts of read and explained information;[1027]
- 'in particular it appears that numerous problems arising within the trial related directly to the inappropriate matching of western methodologies, language and cultural assumptions to a context that was vastly mismatched to the assumptions and beliefs that underlie these aspects'.[1028]

Smith concludes: 'Results from this research study have thus identified significant compromises within the current informed consent protocols in HIV vaccine trials within this particular reviewed context'.[1029] Although Smith's study, by her own admission, is limited due to its poor generalisability,[1030] it does have important implications for the informed consent process in South Africa. From the transcribed interviews with the two participants, it is clear that informed consent was not obtained from them. This result is especially alarming when one considers that both participants have a Grade 12 education.

Health care workers in Kenya, similarly, are uninformed. In a study entitled, 'Knowledge and attitudes about HIV vaccine research among health care providers (HCP) in two provinces in Kenya: a baseline survey conducted Feb-April 2005',[1031] Florence Manguyu sets out to discover the knowledge and attitudes of health care providers in relation to HIV/AIDS vaccine research and development. Of the respondents, 79.6 per cent had a college education; 11.5 per cent had a university education. The results of the questionnaire showed a definite lack of knowledge among health care providers regarding HIV vaccines. Upon being asked what vaccines are made of, only 9.8 per cent gave the correct answer. A total of 57.2 per cent believed that informed consent was a legal document; while 59.4 per cent

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1026 As above.
1027 As above.
1028 As above, 79.
1029 Smith 83. Also see Ives *et al* 'Does an HIV clinical trial information booklet improve patient knowledge and understanding of HIV clinical trials?' (n 964 above) 241, who conclude that while participants' general knowledge and understanding of clinical trials improved over time, this was not improved by the information booklet and their recollection of the details of the trial protocols remained poor.
1030 Because of the limited number of participants studied.
1031 Manguyu 'Knowledge and Attitudes about HIV vaccine research among Health Care Providers (HCP) in two provinces in Kenya: a baseline survey conducted February-April 2005' Paper presented at the AIDS 2006 conference Toronto, August 2006.

believed that someone could be infected by HIV because of her participation in a clinical vaccine trial.

A study by Newman *et al*, entitled 'HIV vaccine concerns and mistrust among vulnerable communities: Towards proactive, culturally-appropriate interventions',[1032] empirically explores the beliefs and concerns about HIV vaccines among low socio-economic, ethnically diverse adults at elevated risk for HIV infection.[1033] The researchers accessed 266 participants at community health clinics serving Latinos and African Americans, gay/lesbian community centres and needle exchange sites. They used semi-structured interviews which were taped and transcribed verbatim, narrative thematic analysis and ethnographic qualitative software to arrive at their results. They found that participants:[1034]

- displayed a mistrust of government and big pharmaceuticals;
- believed in AIDS conspiracy theories;
- held many misconceptions about HIV vaccines;
- feared breaches in confidentiality during HIV vaccine trials;
- feared discrimination in healthcare if they should participate; and
- also feared vaccine-related discrimination.

Commenting on a study which shows that, despite intensive counselling, research participants still understood little of the trial that they were participating in, Paul Farmer writes that the fact that so few volunteers could pass the simple test is a reminder that, increasingly, researcher and subject are living in two different worlds.[1035] He is of the opinion that counselling sessions that are conducted before signing a consent form do little to change the social conditions that 'structure the growing gap, cognitive and social, between those who do research and those who

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1032 Newman *et al* (2006) paper delivered at the 2006 HIV/AIDS Conference, Toronto, Canada, August 2006.

1033 As above.

1034 As above. Of the 266 participants, 19 % reported that an HIV vaccine will make safer sex less important: 'if you got the vaccine...you wouldn't need condoms'; 50 % were concerned about confidentiality in receiving an HIV vaccine; 20 % reported having been refused service by medical providers 'they are not really going to consider if the whores, junkies and faggots are getting information about the vaccine unless it affects them'; and 30 % feared discrimination as a result of receiving an HIV vaccine; and 40 % feared getting an HIV vaccine would cause difficulties in getting health insurance.

1035 Farmer (2002) 360 *The Lancet* 1266.

are participants'.[1036] These social gaps underpin the growing 'outcome gap' that characterises transnational research projects.[1037]

Farmer emphasises the importance of an understanding of the context in which research takes place, and comprehension of the disparity that exists between the knowledge and world-views of researcher and research participant. Without an understanding of context, and without an understanding that counselling sessions, in some instances, may add little to a participant's understanding of the subject matter of the trial, informed consent remains an empty gesture: a mere formality without substance. In the case of HIV vaccine efficacy trials in South Africa, the importance of context should not be underestimated: trials are likely to take place in settings where resources are stretched.

The following section analyses informed consent as a cultural concept in South Africa.

5.4 Informed consent as a cultural construct

Informed consent has been criticised by some as a concept, based on 'uniquely Western notions of individual rights and autonomy',[1038] presupposing an autonomous individual who is able independently to reach decisions about her participation in research:[1039]

> informed consent represents a struggle to find patients' voice[es] in medical decisionmaking (*sic*) and to level the playing field between patients and their physicians. The voice discovered, however, echoes a notion of autonomy based on Western cultural values.

A number of theorists argue that informed consent should be dispensed with altogether in some contexts. Their argument is based on relativist grounds that informed consent standards are not universally valid, and are not known in community-orientated societies in which personhood is defined by membership of a community.[1040] It is asserted that the notion of informed consent is an imposition in the form of 'medical-ethical imperialism' on developing countries.[1041]

1036 As above.
1037 As above.
1038 Meier (n 334 above) 545; see also Alora and Lumitao (2001) *Beyond a Western Bioethics: Voices from the Developing World* 15 - 17.
1039 Gordon (1996) 23 *Fordham Urban L J* 1328. See also Barry (n 10 above) 1083.
1040 As above. See also Levine in CIOMS *Ethics and epidemiology: International guidelines*; Dyckman 'The myth of informed consent: An analysis of the doctrine of

Autonomy, it is said, is an attribute of liberal individualism. The participant reaches her *own* decision in a process which excludes her family, friends and community. Autonomy and informed consent, in this view, are based on cultural traditions relating to liberal individualism.[1042] Although a model of liberal individualism is appropriate in dealing with research participants who belong to a western tradition, it is not appropriate to rely on autonomy in dealing with non-western participants. Accordingly, autonomy is not a universal principle and is not applicable to cultures other than western ones.[1043]

In her excellent assessment of HIV vaccine trial participation in respect of ethical realities in South Africa, Keymanthri Moodley comments:[1044]

> [individual choice and informed consent] may prove to be a problematic standard in the Third World where *personal choice* is extremely limited, because in many African cultures the concept of personhood differs substantially from that in Western cultures. One's tribe, village or social group defines personhood. In certain African societies, selfhood cannot be extricated from a dynamic system of social relationships, both of kinship and of community as defined by the village.

Personhood in a traditional African sense, is relational in nature: persons exist only because of other persons.[1045] Moodley comments that in such a setting it is easier for traditional African societies to see research as an 'altruistic endeavour as opposed to an endeavour for personal benefit only'.[1046] However, Moodley emphasises (correctly to my mind) that, although individual informed consent may be difficult to obtain and special measures[1047] will have to be taken in an African context in which cultural values may require a tribal leader or elder's authorisation, the individual is still ultimately the one who is to give consent to participation:[1048]

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informed consent and its (mis)application in HIV experiments on pregnant women in developing countries (1999) 9 *Columbia J Gender and L* 91.

1041 Meier (n 334 above) 546. Ijsselmuiden and Fagan 'Research and informed consent in Africa – another look' (1992) 326 *New Engl J Med* 830 – 833. See especially the discussion by Macklin (n 295 above) 145 – 150.

1042 See eg Mackilin (n 295 above) 145 – 150; Christakis and Rox 'Informed consent in Africa' (1992) 327 *New Engl J Med* 1101 - 1102 and Ijsselmuiden and Fagan (n 1042 above) 830 - 833; Mkize 'Communal personhood and the principle of autonomy: the ethical challenges' (2006) 24 *CME* 26.

1043 Related to this is the point that some research participants belong to cultures which value paternalism and place great trust and reliance on the researcher or physician's expertise. They would thus need to have this attitude respected in the consent process.

1044 Moodley (2002) 27 *J Med and Philosophy* 199. Original emphasis.

1045 As above, 199.

1046 As above.

1047 Such as waiting periods before a consent form is signed so that the potential participant may discuss the study with family and elders (Moodley 200).

1048 Moodley (n 1044 above) 200. Original emphasis.

> What would be incompatible [with Western models of informed consent], however, would be where no one needed to ask the individual person because the tribal leader's authorisation was *sufficient* for studies carrying risk. Rather what is typically different in Africa is the need for family consent in addition to individual consent in biomedical research.

Molyneux *et al* find that '[t]he notion of informed consent was generally supported'[1049] by members of a rural community in South Africa and although '[t]here was widespread agreement by community members that chiefs and elders can give permission for research to be carried out in [an] area ... it was clear that these leaders cannot decide for specific households or individuals'.[1050] Other studies corroborate this finding, confirming that, at least in South Africa, informed consent is seen as an individual endeavour.

South African ethical guidelines reject the idea that informed consent should be given by anyone other than the individual participant, or that it should be dispensed with altogether where it is culturally inappropriate. Guideline 12.11.1 of the MRC Vaccine trial guidelines points out that it is customary in many South African communities to obtain the permission of community leaders or other designated authorities for investigators to enter the community to invite individual members to participate in research, such permission 'to enter communities should be distinguished from individual informed consent'.

Similarly, guideline 12.11.2 directs that the approval of other persons must 'never be used as a substitute for individual informed consent, which must always be obtained from the prospective participant'. The guideline states further that investigators should recognise that personhood in the African context is essentially defined by relationships, and that relationships will be important for many trial participants in South Africa; however, when there is a conflict between 'respect for individual autonomy and regard for the participant's relationships with other individuals and the community', 'every attempt' should be made to protect both values', but 'respect for individual consent should always receive priority'.[1051] Individual informed consent is unequivocally central in the MRC ethical guidelines.

Moreover, informed consent is a constitutional imperative in South Africa. This issue is discussed in greater detail above,[1052] suffice to mention here that section 12(2)(c) determines that '[e]veryone has the right to bodily and psychological

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1049 Molyneux *et al* (n 375 above) 433.
1050 As above, 451.
1051 Guidelines 12.11.3 – 12.11.5 MRC vaccine trial guidelines.
1052 See para 4.4.2 above.

integrity, which includes the right: ... not to be subjected to medical or scientific experiments without their informed consent'. The use of the words 'everyone' and 'their' in the subsection indicates that the Constitution regards individual informed consent as necessary: *everyone* must consent *personally*.

5.5 The role of ethical review

As far as informed consent to HIV vaccine trial participation in South Africa is concerned, it is important to remember that the primary function of a research ethics committee is the protection of research participants. Overseeing the informed consent process is an important aspect of an ethics committee's work.

As was pointed out before, in reaching its decision to approve a clinical trial protocol, the research ethics committee should focus on whether it is likely that informed consent by the participants will be achieved. This is executed by a carefully examination of the protocol and informed consent documents to discover if they meet the ethical and legal prerequisites. The committee must review the way in which the participant is to be informed about the proposed research and the precise way in which consent is to be sought.[1053] See above for a more detailed discussion of review in research.[1054]

5.6 Conclusion

This section examines informed consent in the context of South African HIV vaccine trial participation. It outlines the origins, application and nature of requirements for ethically and legally valid informed consent to HIV vaccine efficacy trials. The classification of HIV vaccine trials as either 'therapeutic' or 'non-therapeutic' research is discussed; and it is submitted that, in a South African context, Phase III preventive HIV vaccine efficacy trials are likely to contain both therapeutic and non-therapeutic elements.

Problems in obtaining informed consent in the South African HIV vaccine efficacy trial context, such as the likely lack of voluntariness and difficulties in comprehension, are pinpointed. In the second-last section, despite argument to the contrary, informed consent is viewed as central, a relativist or cultural construct idea is rejected. Nevertheless, cultural imperatives should be taken into account during

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1053 Guideline 9.8.1 MRC guidelines.
1054 See para 2.2.2 above.

the informed consent process. The role of ethical review in the evaluation of informed consent is commented upon.

It is difficult to ensure the informed consent of HIV vaccine trial participants in South Africa. Moodley remarks that the concept of informed consent in the South African context is 'riddled with intricacies'; and that,[1055]

> [i]n the aftermath of the apartheid era in South Africa, many people who are completely competent still relinquish their decision-making rights to authority figures, be they doctors, researchers or both. This is accentuated when researchers and study participants belong to different racial groups and where asymmetrical power relationships, based on the previous apartheid system, exist. Enormous efforts are required on the part of the medical profession and researchers to create the level of understanding necessary to meet the criteria of competence. Coupled with this is the need for empowerment of many patients, who, as a result of decades of oppression, have never learned how to exercise their decision-making rights.

6 CONCLUSION

The specific focus of the chapter is on informed consent in preventive HIV vaccine efficacy clinical trials in South Africa. It analyses the protection ethical guidelines on informed consent afford HIV vaccine trial participants and investigates the protection human rights instruments on informed consent afford them. The aim is a comprehensive understanding of the protections these instruments and guidelines offer and to ascertain the relationship between the systems.

Informed consent is a central value or principle in both ethical and human rights discourse. In the first document of ethics, the Nuremberg Code, it is the first principle; and is present as well in the first international human rights convention, the ICCPR. It is a human rights standard, reflected at the UN, regional and domestic levels.

The background to clinical research establishing vaccine efficacy in South Africa is represented and the scientific and epidemiological risks inherent to HIV vaccine trial participation are indicated with the conclusion that HIV vaccine efficacy trials pose considerable risks to participants, even if live virus material is not used in the production of a candidate vaccine.

The socio-economic and political contexts in which HIV vaccine trials in South Africa take place are brought forward. In South Africa preventive HIV vaccine trials will be centred in communities in which poverty, unemployment and gender inequality are the order of the day. These circumstances have a considerable impact on informed consent in the trials.

'Vulnerability' is assessed; within Ruth Macklin's definition of vulnerability, HIV vaccine efficacy trial participants in South Africa are vulnerable to exploitation. Then, processes and actors in human subject research in South Africa are introduced within the context of internationally collaborative research.

The third and fourth sections of the chapter describe the international and national ethical and human rights frameworks on informed consent relevant to preventive HIV vaccine efficacy trials in South Africa. It is found that ethical guidelines are more comprehensive and specific in the scope of the protection they offer, laying down the procedural requirements for informed consent to participation in research.

As far as human rights law is concerned, it is the task of national law to give substance to the international law norm, and to lend specificity to the general substantive standard. In South Africa, national law in the form of the National Health Act for the first time makes informed consent a legislative imperative, as does the Constitution. The Constitution is 'vague' and non-specific in its phrasing of the consent requirement; the Health Act, however, is much more specific in what is meant by 'informed consent'.

It is pointed out that South African national statute law contains conflicting requirements for informed consent. Moreover, the National Health Act has reintroduced confusing and discredited terms, such as the distinction between 'therapeutic' and 'non-therapeutic research', and is not in line with ethical guidelines on informed consent. As well, the Draft health research regulations recently published for comment in terms of section 90 of the National Health Act, instead of clearing up the uncertainties and inconsistencies, create more confusion.

Human rights law considers informed consent as substantive, whereas ethical guidelines focus on procedural requirements as is indicated in chapter 3. The South African ethical guidelines, case law and legislation supply evidence of this distinction: they concentrate on who should give consent, whether it should be in writing, the extent of the information to be supplied to the participant, and so on.

It is submitted legislation should codify the substantive human rights in conjunction with procedural ethical guidelines. Such action would dissolve the distinction between the effects of human rights law and bioethics, subsuming both into a single system offering protection under the Constitution.

1055 Moodley (n 1044 above) 204.

In the next chapter, the conclusion of the thesis, the research question of the thesis is revisited, and the drawbacks to ethical discourse, if it is de-contextualised and is based on procedural notions of informed consent, are contrasted with the protections human rights law affords. Based upon the conclusions above, a possible synthesis between the two systems is suggested.

CHAPTER 6

CONCLUSION AND RECCOMMENDATIONS

Outline

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2 Two systems of protection: Bioethics and human rights law
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2.2 Bioethics
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3 Informed consent in respect of preventive HIV vaccine efficacy trials in South Africa
3.1 Introduction
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4 Conclusion and evaluation: Informed consent in context - an ethical guideline or a human right?

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5.1 Introduction
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5.4 Recommendations regarding informed consent in respect of preventive HIV vaccine efficacy trails in South Africa
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5.6 Recommendations proposing a multi-disciplinary approach to informed consent in South African HIV vaccine efficacy trials

1 INTRODUCTION

As the final chapter the aim is to offer a synthesis so as to draw conclusions, and to offer recommendations. In pursuing this goal, the two systems interrogated in the thesis are viewed as mutually reinforcing rather than diametrically opposed, as is demonstrated by the preceding chapter.

The research question that is investigated is revisited:

Do human rights afford more adequate protection to participants in preventive HIV vaccine efficacy trials in South Africa than that which is afforded by ethical guidelines, and what is the relationship between human rights and ethical guidelines in the protection of participants?

The chapter is structured in the following way. First, the two systems under investigation in the thesis - bioethics and human rights - are reviewed and assessed in order to establish whether it is appropriate to use human rights, instead of ethical guidelines, to protect the interests of participants in HIV-related clinical research in Africa. Second, the focus falls on informed consent in preventive HIV vaccine efficacy trials in South Africa in order to establish whether human rights law affords more adequate protection to participants in these trials, than that which is afforded by ethical guidelines, and to establish the nature of the relationship between human rights and ethical guidelines in the protection of participants. Conclusions that were drawn in the previous chapter, specifically those regarding ethical guidelines and human rights law on informed consent, are explored. Third, the research question of the thesis is tested, so that the strengths and weaknesses of each system (bioethics and human rights) are highlighted. Finally, recommendations are made regarding national law on preventive HIV vaccine efficacy trials and international human rights law in the form of a clinical research convention, as well as recommendations in respect of informed consent to HIV vaccine efficacy trail participation in South Africa.

2 TWO SYSTEMS OF PROTECTION: BIOETHICS AND HUMAN RIGHTS LAW

2.1 Introduction

Chapter 2 of the thesis establishes that the development of an effective preventive HIV vaccine offers the only hope of halting, or at least, slowing the epidemic. Not only does the possibility of developing a cure for AIDS within the next decade seem remote,[1] but ARV drug toxicity, acquired resistance to its components and difficulties in its administration – and that it remains unaffordable in many parts of the world – make the treatment of HIV with ARVs an ineffective long-term solution to the AIDS pandemic.[2]

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1 See para 3.5 of ch 2 above.
2 See paras 3.4 and 3.5 of ch 2 above.

Phase II and III clinical trials, which have the purpose of establishing the efficacy of various candidate vaccines against HIV, have begun in South Africa. By definition, these trials involve human subjects. It is crucial that ethical and human rights guidelines for the protection of research subjects are established and that they function effectively. Charles McCarthy observes; 'We must develop ethical and legal answers that are as sophisticated as the science that develops the vaccine itself'.[3]

Chapters 3 and 4 are largely conceptual in nature and investigate two systems that may apply to the protection of research participants in clinical trials: bioethics or clinical research ethics, and human rights law. Because of the conceptual bias, the analysis remains at a general level. The conclusions reached in these chapters are outlined below.

2.2 Bioethics

Chapter 3 of the thesis deals with bioethical discourse as it is applied to problem-solving in health care and clinical research. The foundational theory of bioethics – that of Beauchamp and Childress, elaborated in their work *Principles of biomedical ethics* – is investigated. Beauchamp and Childress do not regard their work as a complete moral or ethical theory but, rather, an analytical framework.[4]

Ethical norms derive from four ethical principles; namely, respect for persons (or respect for autonomy), beneficence, nonmaleficence, and justice. These ethical principles correspond to the four[5] ethical concerns or questions in research namely, which research qualifies as both scientifically valid and necessary research, which is in the best interests of the participants, and the autonomy of the research participant. These abstract principles (which express essential aspects of ethical theories, including utilitarianism, Kantian ethics, liberalism, communitarianism, ethics of care) are aimed at aiding in the process of reasoning about bioethical problems so that one arrives at an ethically 'correct' decision in a practical situation. The process of ethical reasoning that Beauchamp and Childress propose is a deductive (or top-down) approach; that is, the four general principles of bioethics are applied to

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3 McCarthy, quoted in Weisburd (1987) 131 *Science News* 329.

4 See para 2.4 of ch 3 above.

5 The discussion in ch 3 was limited to three of the four principles, as the third and fourth principles, beneficence and non-malefecence, were seen as inclusive of each other.

specific, practical problems.[6] This reliance on principles by bioethicists has led to the term 'principlism' being applied by various writers to their theory and methodology.

Chapter 3 reiterates Beauchamp and Childress's claim that the validity of the four bioethical principles is grounded in what they call 'common morality'. The common morality is not a moral theory of itself, but is defined as 'the set of norms that all morally serious persons share ... and [which] bind[s] all persons in all places'.[7] Beauchamp and Childress support a 'universal core of morality' to be distinguished from *community-specific* morality, which includes moral norms deriving from 'particular cultural, religious, and institutional sources'.[8] An important implication of the accepted universality of common morality is that Beauchamp and Childress's bioethical principles are (in theory) applicable to clinical research conducted anywhere in the world.[9]

In addition, a degree of *indeterminacy* is incorporated into Beauchamp and Childress's bioethical model: their four bioethical principles are general and abstract in nature and express no *exact content* that may lead to *specific* moral judgments and courses of action:[10]

> Principles may have a fairly determinate and undisputed meaning in core areas, but the precise interpretation and scope of application of the principles at the boundaries or in disputed contexts may be *indeterminate and uncertain*, particularly when the principle is divorced from its theoretical origins.

Bioethical principles have to be applied to practical situations, and they must be *balanced* when they prove antagonistic as they may be in conflict or be opposed to one another.[11] For instance, respecting people's autonomy (the principle of respect for persons) may be diagonally opposed to the idea of not causing them harm (the principle of beneficence).[12] These processes of *application* and *balancing* of principles are necessary if principles and rules are to be useful in resolving practical

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6 Also responsible for the term 'applied' ethics: 'Justification occurs if and only if general principles and rules, together with the relevant facts of a situation, support an inference to the *correct or justified judgment*' (Beauchamp and Childress (2001) 178). My emphasis.

7 Beauchamp and Childress 11.

8 As above.

9 As above.

10 Plomer (2005) 12. My emphasis.

11 Beauchamp and Childress (n 6 above) 17 – 19; Leontis (2006) 118.

12 Beauchamp and Childress use the example of a Jehovah's Witness refusing a blood transfusion for her child. The above-mentioned principles (autonomy and beneficence) must be now be *specified* in terms of all available details (medical, factual, cultural, religious, and so on) of the practical situation, and balanced in such a way that one of them may prevail in determining the course of action to be taken in resolving the ethical dilemma (Beauchamp and Childress 17 – 18).

problems in bioethics, both in medical practice and in clinical research.[13] However, the very application and balancing of principles to practical situations may depend upon underlying political or moral assumptions. For example, if the underlying political ideal is social solidarity, the realisation of the principle of autonomy yields different outcomes than what it would do were the underlying philosophy liberalism.[14]

Beauchamp and Childress's principlist model of bioethics forms the foundation of ethical guidelines related to both medical practice and clinical research as contained in the various ethical documents.[15] Ethical guidelines, derived from the bioethical principles which, in turn, derive from 'common morality', direct the actions of health care workers, researchers and research sponsors or agencies. The exact nature of the link between the various specific ethical guidelines in the ethics documents and the broad ethical principles remains uncertain.[16] For example, although autonomy, as the first of the four principles, is embodied in the ethical rule that informed consent should be sought for a medical or research intervention, the four principles in themselves are too vague to enable one to say exactly what the nature and extent of the informed consent must be.

On the consequences of Beauchamp and Childress's use of principlism in bioethics, Susan Wolf comments:[17]

> universal moral rules of principles posited for the abstract, generic person erase that person's gender (not to mention race, class, or other characteristics). This makes it difficult to query the significance of gender in the moral situation. It is only when a situation is appreciated in its particulars that the full moral problem and plausible tools for its resolution appear.

Wolf's criticism of bioethics points to an important limitation to the bioethicists' principlist approach – the approach is presumed on what the thesis nominates to be a 'disembodied' or 'decontextualised' person. Bioethics is too abstract to accommodate all decision-making in clinical research. Churchill asserts:[18]

> [b]ioethical disputes – as measured by the debates in journals and conferences in the United States – often seem to be remote from the values of ordinary people and largely irrelevant to the decisions they encounter in health care.

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13 As above; Leontis (n 11 above) 118.

14 See Plomer (n 10 above) 12. This is also to some extent true for human rights norms – see below.

15 See para 2.5 of ch 3 above; Leontis (n 11 above) 118.

16 See para 3.1 of ch 3 above.

17 Wolf (ed) (1996) 15; Leontis (n 11 above) argues a similar point.

18 Churchill (1999) 128 *Daedalus* 255.

This point will be re-examined later.

Further, chapter 3 investigates the protection afforded by the principles of bioethics, and the ethical guidelines they found, to participants in clinical research in Africa. Although the protection afforded by international and national ethics documents appears extensive at first glance, the chapter's survey of non-compliance with these guidelines[19] demonstrates that, in practice, ethical guidelines do not always function well in preventing the abuse of research participants in Africa.

This failure of ethical guidelines to protect the interests of research participants in Africa is attributed to two causes:[20]

First, ethical guidelines are just that – guidelines – they do not have the force of law, and, therefore, are difficult to enforce. In the case of transgression, fierce ethical debate may follow, but little else can be done. Though the editor of the *New England Journal of Medicine*, Marcia Angell, regards the HIV peri-natal transmission trials as unethical, she published the results of the trials in the journal. To a large extent, observance of ethical guidelines depends on the sanction of various professional bodies and research funding agencies. Other than a refusal to fund or publish unethical research, there is little to guard against unethical research. Meier comments:[21]

> The medical profession has been shown not to have the ability to police itself. Although physicians have formed international medical organizations to promote medical responsibility, there is little evidence to suggest that these organizations have regulated physician behaviour or protected the rights of subjects to free and informed consent.

And[22]

> The Nuremberg Code, Helsinki Declaration, and CIOMS Guidelines are not legally binding documents capable of placing legally enforceable obligations on states or individuals. They are not widely accepted or followed by physicians. Because they have no enforcement mechanisms, legal or medical, they have little effect on the regulation of human research.

Second, ethical principles are in many instances too general and ambiguous to be of much value in specific circumstances, unless converted into specific ethical guidelines. The HIV transmission trials in Uganda serve as a case in point. During

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19 See para 4.2.1 of ch 3.

20 For a more extensive discussion on the failures of ethical guidelines to protect the interest of research participants, see para 4.2 of ch 3.

21 Meier (2002) 20 *Berkeley J Intl L* 530.

22 As above, 531.

the debate on the ethics of these trials, both camps used similar ethical principles and guidelines in support of their arguments.[23]

Third, in bioethics the individual or society is *decontextualised* – bioethics fails to take account of the circumstances surrounding the problem under investigation – which may be poverty, social inequality, a lack of resources and a heavy burden of disease. These factors contribute to making health and HIV-related research in Africa an imperative, but they are also the cause of the situation being fraught with the potential for the abuse of research participants.[24]

2.3 A human rights-based approach

Chapter 4 proposes human rights law as an alternative system to be used for the protection of participants in HIV-related clinical research in Africa. Again, the importance of context is stressed – after all it is concluded in the previous chapter that a major problem in relation to bioethics or clinical research ethics is that the wide range of inequalities that exist in a research setting are not taken into account.[25] An unbridgeable gap in knowledge exists between the researcher and the research participant, moreover, attention is not paid to the unequal distribution of power created by poverty and other social circumstances such as exist in Africa.[26] The chapter quotes the comment by Paul Farmer and Nicole Gastineu Campos:[27]

> The majority of such international biomedical research has inequality as its foundation, and ethical codes developed in affluent countries are quickly ditched as soon as affluent universities undertake research in poor countries. Then come a series of efforts to develop alternatives (read, less stringent) codes 'appropriate' to settings of destitution.

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23 Ruth Macklin writes: 'Guidelines and principles from the previous versions of these now revised documents were cited both in support and in criticism of the trials in the controversy over the placebo-controlled AZT trials' (Macklin (2004) 19). Also see Angell (1997) 337 *N Engl J Med* 847; Lurie and Wolfe (1997) 337 *N Engl J Med* 853; Editorial (1997) 350 *The Lancet* 879; Varmus and Satcher (1997) 337 *N Engl J Med* 1003.

24 Ethical guidelines are also *undemocratic*:
'The ethical principles elaborated and adopted by a profession or a group of non-elected members may have little democratic legitimacy and their elaboration or implementation will not usually afford much opportunity for public scrutiny and accountability. Consequently, the ethical norms or principles adopted may fail adequately to represent and protect the interests of all affected parties' (Plomer (n 10 above) 12 - 13).

25 Farmer and Gastineau Campos (2004) 4 *Developing World Bioethics* 23.

26 Farmer and Gastineau Campos claim: 'It [the research enterprise] is also a fundamentally inegalitarian exercise in the sense that medicine and science are expanding rapidly, but in a social context of growing global inequality, which ensures that the fruits of medicine and science are not available to many who need them most' (25).

27 Farmer and Gastineau Campos 22.

Most bioethicists, however, deny this reality:[28]

> The word *power* is essentially absent from the vocabulary that scholars of medical ethics have constructed for their discipline and that has been accepted by almost everyone who does work in the field or tries to apply medical-ethical insights to the clinical context.

Chapter 4 considers whether justiciable human rights, by giving attention to issues of 'context', can function as an adequate alternative means to protect participants in clinical research in Africa. The origin and nature of human rights are explored and the philosophical background to the development of the notion of human rights is sketched.

Specific human rights provisions as contained in international human rights documents are applied to a clinical research setting in order to determine the measure of protection they offer participants in clinical research in Africa. In this regard the discussion demonstrates that these provisions are able adequately to accommodate many of the issues relevant to clinical research in Africa that, traditionally, are considered the exclusive jurisdiction of clinical research ethics, such as distributive justice, access to treatment and autonomy.

Chapter 4 illustrates that human rights better accommodate issues of 'context' such as unequal distribution of power in a research setting and the potential for the abuse of research participants. Human rights are inter-dependent and inter-related, unlike bioethical principles: the realisation of a right depends, as a whole or in part, on the realisation of other rights. Issues of 'context' are integral in the understanding of human rights: dignity or physical integrity in numerous ways are supported in the right to access health care. In *Government of the Republic of South Africa v Grootboom*[29] the Constitutional Court observed:[30]

> But section 26 is not the only provision relevant to a decision as to whether state action at any particular level of government is reasonable and consistent with the Constitution. The proposition that rights are interrelated and are all equally important is not merely a theoretical postulate. The concept has immense human and practical significance in a society founded on human dignity and freedom. It is fundamental to an evaluation of the reasonableness of State action that account be taken of the dignity of human beings.

Human rights provide a holistic approach: in human rights norms the research participant is situated within a specific socio-economic and political context; human

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28 Brody (1992) 12.
29 2001 (1) SA 46 (CC).
30 Para 83.

rights see research participants as complex beings who relate intimately to their environment – whether material, social, cultural, political or economic. If human rights norms which take cognisance of issues such as a lack of access to health care had been applied in the context of Ugandan MTCT trials discussed in chapter 3, the trials would have been observed to be illegal, on the grounds that, without the possibility of everyday access to health care there can be no question of autonomous choice or informed consent.

A major part to the thesis of chapter 4 is the comparison of the systems of human rights and bioethics. There are many similarities between bioethics and human rights, for example, both are the direct products of the mood of the mid-20th century, arising in response to humankind's horror at the events of World War II and the atrocities committed by National Socialism and Japanese Imperialism.

The Nuremberg Code, written in 1946 as the final part of the judgment delivered in the Nuremberg trials, contains the first comprehensive set of guidelines on how to conduct ethical research on humans.[31] Similarly, the Universal Declaration of Human Rights is the first comprehensive human rights document to be adopted by an international organisation.

The Nuremberg Code and the Universal Declaration of Human Rights are reactive – both are products of outrage and anger. In Edmund Cahn's words '"[j]ustice" ... means the active process of remedying or preventing what would arouse the sense of injustice'.[32] These two documents are also commemorative, they epitomise the sentiment 'lest we forget'.

As well as a shared historical background, bioethics or clinical research ethics and human rights have a common purpose: broadly, they aim to protect the individual or groups of individuals from harm.

However, there are also significant differences between the systems. Despite the shared objective each system has its own focus: ethical principles governing research on human subjects aim to regulate the relationship between researchers and research participants; human rights elaborate principles regulating the relations between the individual and the state or relations between individuals in a state.

The documents of the two systems are differently worded. Clinical research ethics documents are specific in their content and phrasing; human rights documents

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31 See para 3.1.1 of ch 3 above.
32 Cahn (1949) 13 – 14.

tend to be more general. For example, clinical research ethics codes give specific instructions as to procedural requirements, such as '[t]he subjects should be volunteers – either healthy persons or patients for whom the experimental design is not related to the patient's illness'[33]; human rights documents contain generalities, such as '[e]very individual shall have the right to enjoy the best attainable state of physical and mental health'[34]. Both expressions require interpretation to determine their application to a given situation, but the human rights principle demands a more extensive interpretation in order to discover the meaning of the value judgment implicit in 'best attainable state of health'.

Despite the necessity to be more precise and exact in phrasing, ethical guidelines are severely criticised for, in general, being too vague and ambiguous. Human rights, it is true, are phrased in yet more general terms, but are given content through interpretation in courts or other tribunals, with the consequence that their generality is not a serious failing, as is the case with ethical guidelines which are not litigated.

A crucial difference between the two systems lies in the nature of each: one consists of non-legal, non-binding ethical *principles*; the other of legally binding *rights*. It is true that human rights and ethical principles, equally, are systems which embody society's moral values, moral norms or its 'common morality', and it is further true that human rights *contain* principles of ethics. However, the values and norms in each system are codified very differently - as principles in the one and rights in the other.

Explicit in this difference between principles and rights, lies a crucial distinction between the two systems in terms of the enforcement mechanisms devised to monitor a system of non-binding principles as apposed to a system of legally binding rights.

In the case of ethical guidelines governing clinical research on human subjects, compliance with, and enforcement of, the system relies on professional sanction and other non-legal means. It is assumed that researchers are 'ethical' people who are to some extent trusted to uphold the guidelines of clinical research.[35] Because of the non-legal nature, to a large extent, observance of ethical guidelines

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33 Art III.2 Declaration of Helsinki.

34 Art 16(1) African Charter of Human and Peoples' Rights.

35 In the case of ethical guidelines, sanction for non-compliance depends on the discretion of human actors who are members of a professional class; in the case of international human rights law, the responsibility is placed on governments to ensure that violators of human rights are held accountable.

depends on the sanction of various professional bodies and research funding agencies. Other than a refusal to fund or a refusal to publish unethical research, there is little to guard against unethical research being conducted by unscrupulous agencies.

In respect of international human rights, monitoring and implementation mechanisms are in place. These monitoring systems are sophisticated and well-developed. International organisations, such as the United Nations, assume a duty to protect human rights. Similar institutions have been introduced at a regional level as well, and in some regional systems they include a court in which international human rights are litigated and enforceable against violators. At the domestic level, many states have promulgated constitutions which include justiciable bills of rights, making human rights immediately enforceable in a domestic court of law.

Chapter 4 explores the status of specific international human rights instruments in South Africa, indicating that the most important human rights treaties have been signed by South Africa, and that international human rights norms offer a justiciable framework for the protection of clinical trial participants in South Africa.

2.4 Conclusion

Chapters 3 and 4 of the thesis establish the nature and major tenets of two systems under discussion in the thesis – bioethics and human rights law. It is demonstrated that human rights law may be applied successfully to the situation of participants in HIV-related clinical research in Africa. Further, human rights law has important advantages over bioethics, not only because it has the force of law, but also because it positions the participant in research within a specific social context.

3 INFORMED CONSENT IN RESPECT OF HIV VACCINE EFFICACY TRIALS IN SOUTH AFRICA

3.1 Introduction

Chapter 5 specifically deals with informed consent in respect of preventive HIV vaccine efficacy trial participation in South Africa and investigates the effectiveness of ethical guidelines and human rights standards on informed consent for the protection of participants in these trials.

The origins, application and nature of requirements for ethically and legally valid informed consent in respect of HIV vaccine efficacy trials are elaborated. The classification of HIV vaccine trials as either 'therapeutic' or 'non-therapeutic' research

is investigated, and it is concluded that in a South African context Phase III preventive HIV vaccine efficacy trials are likely to contain both therapeutic and non-therapeutic elements, thus eluding classification as either therapeutic or non-therapeutic research.

Problems in connection with obtaining informed consent in the South African HIV vaccine efficacy trial context are raised - such as the likely lack of voluntariness and difficulties in comprehension. In the second last section of the chapter, despite arguments to the contrary, it is asserted that informed consent is not a relativist cultural construct, though cultural imperatives should be taken into account during the informed consent process. The role of ethical review in the evaluation of informed consent is commented upon. It is demonstrated that it is difficult to ensure the genuine nature of informed consent of HIV vaccine trial participants in South Africa, given the context in which these trials take place, that is, poverty, illiteracy, lack of access to health care and so on.

In this regard, the economic, social and political contexts of HIV vaccine efficacy trials in South Africa, as well as methodological and practical aspects of clinical trials, such as review procedures and investigator responsibilities, are delineated in the chapter. The discussion relates aspects of the South African economic, social and political context, such as dire poverty, women's inequality, stigmatisation, poor access to health care and political denial and inaction regarding HIV which increase not only certain communities' vulnerability to HIV infection, thereby accelerating the spread of the disease, but also those communities' vulnerability to exploitation and abuse during clinical research to establish the efficacy of HIV vaccines.

3.2 Informed consent in ethical guidelines

Informed consent is a requirement for ethical clinical research. It is contained in international and national ethical guidelines which are used by South African ethics committees in their evaluation of HIV vaccine research protocols.

International and national ethical guidelines on informed consent that may be appropriate to the protection of participants in HIV vaccine trials in South Africa are listed in chapter 5. It is ascertained that the international and national systems of ethical guidelines co-exist in South Africa and that informed consent is a well-established requirement for the ethical conduct of research and is dealt with extensively in both national and international ethical guidelines.

It is observed that although the ethical guidelines vary in the extent of the detail that is included regarding the nature of the consent that is required, they provide more detail than is given in the broad statement of a standard laid down by human rights law. Ethical guidelines, on the whole, give specific content to the broad guarantee of informed consent.

3.3 Informed consent in human rights law

International and national human rights law on informed consent is considered in chapter 5.

It is proposed that international human rights law protects the right to free and informed consent in medical research or experimentation. International human rights conventions, such as the ICCPR and the Protocol to the African Charter on Human and Peoples' Rights on the Rights of Women in Africa, make explicit provision for the right; while other international law instruments, as well as customary international law (such as the Universal Declaration of Human Rights) establish a broad range of obligations on the part of governments with respect to the informed consent of participants in clinical research in the form of guarantees with regard to equality, dignity, access to health care and physical integrity. Informed consent, as contained in international human rights law, offers protection against government intrusion upon individual freedom and autonomy. Positive action is insisted upon to ensure that informed consent is obtained from research participants.

Furthermore, according to section 233 of the South African Constitution, when interpreting domestic legislation, a court should prefer an interpretation of legislation which is in compliance with international human rights law obligations. In addition, legislation that meets the requirements of international human rights law must be developed and legislation can be used to reform policies and practices to bring ethical and legal guidelines on informed consent into compliance with international standards, should such compliance be lacking.

According to sections 231 and 232 of the Constitution, international law (whether treaties or customary international law) binds the Republic unless it is inconsistent with the Constitution or an Act of Parliament.[36] International (human rights) law, therefore, enjoys a status lower than that of the South African Constitution and Parliamentary legislation. It is, consequently, the task of national

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36 See para 6.5.1 of ch 4 above and secs 231(4) and 232 of the Constitution of the Republic of South Africa 1996.

law to give substance to the international law norm of informed consent to participation in research.

South African common law and case law on informed consent do not deal specifically with informed consent in a research setting, and it is therefore necessary to extrapolate general principles to the preventive HIV vaccine efficacy trial setting.

The analysis of South African common law and case law on informed consent shows that a researcher or health care worker who fails to obtain vaccine trial participants' informed consent may be liable for civil or criminal assault; *iniuria*; or negligence. Nonetheless, it is concluded that a conceptually sound approach dictates that research without informed consent constitutes not negligence, but an assault, as the relevant element of the delict or crime is that of wrongfulness or unlawfulness and not that of fault.

Furthermore, a researcher in the HIV vaccine trial context who does not perform trial-related procedures with the necessary degree of care and skill will be held liable for negligence.

In the case of damage suffered because of participation in a HIV vaccine trial, the flexible approach to causation needs to be adapted in order to take into account the unique situation of trial participants, where trial-related damage may not be immediately apparent.

In South Africa, national law in the form of the National Health Act for the first time makes informed consent a legislative imperative. The Constitution is 'vague' in its phrasing of the consent requirement; the National Health Act is much more specific in what is meant by 'informed consent'.

However, South African national statute law contains conflicting requirements for informed consent: especially regarding the position of children, the requirements for informed consent are unclear. The National Health Act has reintroduced confusing and discredited terms, such as the distinction between 'therapeutic' and 'non-therapeutic research', and is not in line with ethical guidelines on informed consent. In addition, the Draft health research regulations, instead of clearing up the uncertainties and inconsistencies, create more confusion.

South Africa enjoys a system of constitutional supremacy.[37] This means that domestic human rights law (contained in the Bill of Rights) protects the right of participants in HIV vaccine efficacy trials in South Africa not to be subjected to

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37 Sec 2 Constitution of the Republic of South Africa 1996.

medical experimentation without their informed consent.[38] Any preventive HIV vaccine efficacy trial should take as its point of departure the Constitutional guarantee of informed consent. Any ethical guideline, legislation or conduct which violates that guarantee, is void. Whether a violation has occurred in a particular situation is a question of fact to be determined by a court.[39]

A statutory body (such as a university or the MRC) or a private pharmaceutical company performing HIV vaccine efficacy trials is bound to respect the research participant's constitutional right to informed consent. In terms of section 8(2), '[a] provision in the bill of rights binds a natural or a juristic person if, and to the extent that, it is applicable, taking into account the nature of the right and the nature of the any duty imposed by the right'. The nature of the right not to be subjected to research without informed consent is not such that it cannot operate on the horizontal level (as apposed to, for example, the right to social security which by its nature can only operate on the vertical level, between the citizen and the state). Further, the duty imposed by section 12(2)(c) - to respect an individual's right not to be subjected to experimentation without informed consent - is not an onerous one,[40] and therefore it binds a statutory body, such as a university, as well as non-state actors such as a private pharmaceutical company.

Although guaranteed by international human rights law, the requirement that informed consent be given before medical treatment or scientific experimentation is mentioned explicitly in only two of the international human rights instruments under investigation in this thesis - the ICCPR and the Protocol to the African Charter on Human and Peoples' Rights on the Rights of Women in Africa.[41]

The fact that the right not to be subjected to experimentation without one's informed consent is not explicitly guaranteed may be due to two possible reasons. First, the right may be considered as implicitly included in other rights which are guaranteed, such as the right to human dignity, to physical and psychological integrity, to health and so on. Second, drafters of international human rights instruments may regard the right as falling within the ambit of ethical guidelines and

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38 Sec 12(2)(c).

39 A Court will have to determine whether the conduct in question constitutes 'medical experimentation', and whether informed consent was given by examining the facts of the case.

40 Such as would be duties imposed by socio-economic rights, such as the right to health care (sec 27).

41 Of course, the Council of Europe's Convention on Human Rights and Biomedicine explicitly guarantees the right to free and informed consent. This instrument does not, however, fall within the scope of this chapter of the thesis.

not human rights, and not 'worthy' of inclusion in a human rights instrument. If it is the case, it is extremely regrettable, as a unique opportunity to protect research participants has been missed.

Moreover, even in those cases where the right not to be subjected to medical experimentation without informed consent is mentioned in international (and national) human rights instruments, it is not given specific content. It is not, for example, indicated by either national or international human rights law who may consent, the formalities needed for valid consent, and so on. Compared to ethical guidelines on informed consent, human rights law is far less specific, setting a standard that must be adhered to, but not laying down any of the procedural requirements that must be met for the realisation of the right. This may be seen as either a strength or a weakness.

Finally, chapter 5 observes that informed consent in a research context has not been litigated under international human rights law; in the cases in which mention is made of informed consent, it is within the context of the torture of prisoners. Informed consent as an international human right rarely has been used as way of protecting the interests and rights of research participants.[42]

3.4 Conclusion

Ethical guidelines and human rights law on informed consent coexist in South Africa. Although South African ethics committees consider themselves bound by international and national ethical guidelines, legislation on informed consent, as contained in the new National Health Act, has the advantage that it creates enforceable obligations.

Moreover, section 12(2)(c) the South African Constitution affords protection to the right not to be subjected to medical or scientific experiments without informed consent. Because of its supreme nature, the Constitutional guarantee provides important protection of participants in HIV vaccine efficacy trials in South Africa, and should therefore be taken as a point of departure.

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42 See paras 5.5 and 6 of ch 5 above.

4 CONCLUSION AND EVALUATION: INFORMED CONSENT IN CONTEXT – AN ETHICAL GUIDELINE OR A HUMAN RIGHT?

The thesis investigates the following research question:

> Do human rights afford more adequate protection to participants in preventive HIV vaccine efficacy trials in South Africa than that which is afforded by ethical guidelines, and what is the relationship between human rights and ethical guidelines in the protection of participants?

As far as the first part of the research question is concerned ('do human rights afford more adequate protection'), the answer is shown to be 'yes' by the investigation in chapter 5 of ethical guidelines and human rights instruments with respect to informed consent in HIV vaccine trial participation in South Africa. The reasons for this conclusion are the following.

First, by their nature as rules of law, human rights offer the possibility of enforcement by the courts. Human rights law is rather more than non-enforceable 'guidelines' and 'principles'.

Second, bioethical discourse - specifically that which is represented by Beauchamp and Childress in their postulation of the major principles of bioethics – necessarily lacks context. Complex situations are analysed by bioethical discourse as without any consciousness of the social or cultural context in which they occur. The results of such an approach are postulated by Pam McGrath:[43]

> bioethical discourse can be seen as 'band-aid' tactics, offering some protection to the patient but minimal resistance to the hegemonic system. Such a bioethical discourse may, indeed, further legitimate the system by incorporating a publicly acknowledged ethical response. In a discourse where power is reified and disguised under the rubric of caring [...] the work of bioethicists may actually contribute to the naturalization of such power ...

Abstract bioethical principles envisage a disembodied and decontextualised human being – one who exists in a political, social and economic vacuum. Susan Sherwin asserts the following consequences (from a feminist perspective):[44]

> [Feminists] have questioned the usefulness of the concept of the abstract individual as the fundamental social and moral unit. They have argued that this concept masks particular details about persons that are often relevant to ethical evaluations, such as each individual's actual social and political location.

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43 McGrath (1998) 23 *J Med and Philosophy* 516 524.

44 Sherwin 'Feminism and bioethics' in Wolf (n 17 above) 52. Also see Leontis (n 11 above) 119.

A system which recognises the individual as part of a social context is able to account for the intricacies which are attendant upon HIV vaccine trials in South Africa. In taking cognisance of the claims, in chapter 5 the economic, social and political contexts of HIV vaccine efficacy trials in South Africa are described. Factors in the South African context, such as dire poverty, women's inequality, stigmatisation, poor access to health care and political denial and inaction deepen certain communities' vulnerability to HIV infection, thereby accelerating the spread of the disease, as well as to exploitation and abuse during HIV vaccine efficacy trials.

The thesis concludes that the principles of bioethics, embodied in the different international and national ethical guidelines, offer a circumscribed analysis of informed consent in HIV vaccine efficacy trials in South Africa (and correspondingly, of all clinical research endeavours around the world). Bioethics is primarily procedural in nature – it concentrates upon the procedures that have to be followed to adhere to its four principles. Bioethical discourse examines the ways in which informed consent is achieved, paying attention to whether it is in written form, whether it is embodied in a consent document, whether all material risks are revealed; whether it is ethically 'correct' to consult elders and other community leaders; and tests whether consent has been achieved by means of comprehension tests.

No understanding can be achieved of the broader social and moral ramifications of preventive HIV vaccine trials in South Africa if they are not *contextualised* - the investigation, therefore, must extend beyond looking at their technical procedures and constricted ethical reasoning to include their broader social, economic, and political reality. An understanding of the trials' larger context allows us to reflect upon ways in which the condition of HIV vaccine research participants' lives may be changed from survival to a dignified and 'autonomous' existence.[45] Nikolas Rose argues that 'autonomy and choice cannot be understood as based on politically innocent premises, but as products of systems in which subjects are . . . obliged to be free'.[46]

In this respect, human rights law, in the extrapolation to socio-economic rights, offers an alternative model to that of bioethics. Human rights are indivisible

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45 Leontis 119. See also Corrigan (2003) 25 *Sociology Health and Illness* 768, who argues a similar point in a different context.

46 Rose 'Governing 'advanced' liberal democracies' in Barry *et al* (eds) *Foucault and Political Reason* quoted in Corrigan (n 45 above) 771.

and interdependent;[47] they should be treated holistically in order to fully protect human welfare. As Craig Scott declares:[48]

> The term interdependence attempts to capture the idea that values seen as directly related to the full development of personhood cannot be protected and nurtured in isolation.

Socio-economic rights are 'concerned with the material dimensions of human welfare'.[49] Socio-economic rights are an acknowledgement that, without food, water, shelter, health care, education and social security, human beings cannot survive with dignity or develop to their full potential.[50] Socio-economic human rights attempt a description of the individual situated within a society; an individual situated within political, social and economic contexts. Human rights, thus, allow research participants to be treated truly holistically - as human beings.

In its understanding of the individual situated within a certain context, a human rights-based approach is able to acknowledge that, given a situation in which health care resources are scarce or even non-existent, the individual's 'informed consent' to participation in HIV vaccine trials, rather than constituting autonomous decision-making, may be a desperate attempt to access health care.

Human rights law - socio-economic human rights in particular – erects claims upon the state which have as their goals an adequate standard of living that would improve people's quality of life. Socio-economic rights pertain to the social and economic contexts - employment, education, health care, or even, clinical research – of real people and not imaginary autonomous - decontextualised - human beings.

Context is paramount in a human rights-based approach to informed consent to participation in clinical research, as a rights-based approach regards informed consent as wholly contingent upon the material conditions of the lives of research participants. The realisation of a threshold of socio-economic rights is a *sine qua non* for informed consent to participation in clinical research. The right of each and every person to a threshold level of material resources, if realised, affords the opportunity to make autonomous choices, such as giving 'free and informed consent'

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47 See para 2.3 of ch 4.

48 Scott (1989) 27 *Osgoode Hall L J* 769, 786, quoted in Liebenberg 'The interpretation of socio-economic rights' in Woolman *et al* (eds) (2005) 33-1.

49 Liebenberg 'The interpretation of socio-economic rights' in Woolman *et al* (eds) 33-1.

50 As above. Liebenberg writes: 'The danger exists that a Bill of Rights that privileges civil and political rights will become the exclusive instrument of the rich and powerful for protecting their vested interests. The inclusion of socio-economic rights as justiciable rights in the South African Bill of Rights makes the redress of poverty a matter of fundamental constitutional concern' (33-2).

to participation in preventive HIV vaccine efficacy trials. In its understanding of the individual situated within a certain context, a human rights-based approach is able to acknowledge that, given a situation in which health care resources are scarce or even non-existent, the individual's informed consent to participation in HIV vaccine trials, rather than constituting autonomous decision-making, is a means of accessing health care.

Human rights have a particular significance when claimed by the weakest members of society; those of a lower economic status and social worth most likely to be exploited in clinical research.[51] The question of socio-economic inequality cannot be avoided in assessing whether informed consent has been obtained in clinical research, especially with regard to the politics and ethics of the destitute in South Africa and the rest of the 'less-developed' world.

Poor people in many parts of rural South Africa are deprived of resources as basic as adequate nutrition and health care. There are few opportunities for formal education and the acquisition of professional skills, which would ensure them a measure of social and economic independence. In a vicious circle conditions of chronic poverty exacerbate, and are exacerbated by, these deprivations. Similarly, HIV is contracted and spreads within the circumstances of powerlessness, ill-health and misery.

A further limitation of the principlist bioethical model is that it does not offer an alternative to the *status quo*:[52]

> Of particular concern to bioethicists is the fact that ... rather than being an instrument for challenging oppression, ethics as it is usually pursued may actually be supportive of the oppressive *status quo*.

The account in chapter 3 of the Ugandan and other clinical trials in Africa demonstrates that, despite the existence of ethical guidelines, interpretation and implementation remain controversial areas and abuses still occur. The Ugandan

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51 Also see Ngwena 'Adjudicating socio-economic rights – transforming South African Society? A response to Linda Jansen Van Rensburg's paper' (2003) *Potschefstroom University Electronic L J*, who comments upon the judgments in socio-economic rights cases before the Constitutional Court:
'Protecting the vulnerable and weakest in our society as part of the transformation of post-apartheid and post-colonial South Africa fitted in well into the foundational values of the Constitution' (6) available at <http://0-www.journals.co.za.innopac.up.ac.za/WebZ/images/ejour/perblad/perblad_speced_2003_a11.pdf:sessionid=0:bad=http://www.journals.co.za/ejour/ejour_badsearch.html:portal=ejournal:clientid=2840> (accessed 28 February 2007).

52 Sherwin 'Feminism and bioethics' in Wolf (n 17 above) 49. Also see Leontis (n 11 above) 118 – 119.

trials were justified on the grounds that they were necessitated by the expense and infeasibility of the full course of AZT to prevent MTCT of HIV in Uganda. In their ethical analysis of the Ugandan trials, Lurie and Wolfe examine the 'standard of care' argument.[53] The version of the argument they contest implies that placebo-controlled studies are acceptable in the developing world as the standard of care here is either to rely on unproven treatment or to have no care at all.[54] In their view, this is a misunderstanding of the ethical concept of 'standard of care', as the standard of care that is used as a measuring stick should be that of the treatment available in the sponsoring country (in the developed world) and not that which is available in the developing world.[55] This type of bioethical reasoning departs from the wrong assumption: it does not question the *causes* for the lack of resources in the developing world; Lurie and Wolfe merely accept them as a given or part of the *status quo* – and advocate a 'standard of care' that conforms to what is regarded (in the developed world) as 'ethical'.

Instead, human rights law is capable of presenting an alternative examination which questions the *status quo* by offering an evaluation of research conducted in Africa which takes account of the socio-economic reality that surrounds or even prompts the research. Because it sees the individual holistically, as the bearer of rights which are inter-dependent and inter-related, a human-rights-based analysis regards the Ugandan trials as intrinsically linked to the surrounding circumstances, or even a result of those circumstances. A human rights-based approach, specifically that which concentrates on realising socio-economic rights, asks whether participants in HIV-related clinical research in Africa are able to access health care *independent* of their participation in the research.

Correspondingly, South African preventive HIV vaccine efficacy trial participants who live in dire poverty do not make an autonomous choice in deciding whether to participate in trials; Deborah Zion writes:[56]

> in an environment where the majority can neither read or write and is wallowing in poverty and sickness, hunger and homelessness, and where the educated, the powerful, the rich, or the expatriate is a semi-god, how can you talk of informed consent?

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53 See ch 3 para 4.2.2 (b) above and Lurie and Wolfe (1997) 337 *N Engl J Med* 853.

54 As above.

55 Lurie and Wolfe (n 53 above) 854.

56 Zion (1998) 'The ethics of AIDS vaccines' quoted by Moodley 'HIIV vaccine trial participation in South Africa: An ethical assessment' in Van Niekerk and Kopelman (eds) (2005) 174.

Chapter 5 indicates that HIV vaccine efficacy trials in South Africa will likely involve thousands of poor, unemployed and uneducated people with little or no access to health care, who thus constitute a tremendously vulnerable group. Any of the qualifications of vulnerability (as defined by ethicists such Ruth Macklin,[57] and in the South African and international research ethics guidelines) apply to them; specifically the conditions relating to the non-availability of health care resources. In such a situation, many prospective HIV vaccine trial participants cannot exercise valid informed consent, despite its guarantee in international and national ethical guidelines (and human rights instruments). No analysis which ignores the context in which vaccine trials take place is be able to adequately protect these trial participants' interests.

The thesis concludes that human rights law affords a viable alternative model to bioethical regulation in the protection of participants in HIV-related clinical research in Africa. It further concludes that, because of the reasons outlined above, human rights afford more adequate protection to participants in preventive HIV vaccine efficacy trials in South Africa than that which is afforded by ethical guidelines. In order to make clinical research more responsive to circumstance or 'context', bioethics should be inspired by the broader social, economic and political perspective that is provided by a rights-based analysis. It is proposed that a normative model derived from rights' principles adds value to the bioethical debate in the context of clinical research in South Africa and the rest of the world.

The second part of the research question remains, enquiring as to 'the relationship between human rights and ethical guidelines in the protection of participants'.

In exploring the relationship between human rights and bioethics, consideration should be given to Dworkin's comment that 'to suggest that the law has no role to play in the area of biomedical advance would be ... unrealistic. Yet blind faith in the dominant role of law would be equally unsound'.[58] Rather than suggesting that human rights discourse replaces bioethics, the thesis concludes by advocating an approach that integrates both systems. The answer to the second part of the research question, therefore, rejects the notion that human rights should replace

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57 See para 2.3.3 of ch 5 above.
58 Dworkin (1996) 2.

bioethics. In *Pharmaceutical Manufacturers Association of South Africa In re: Ex Parte Application of the President of the Republic of South Africa*[59] the Court observes that:[60]

> [t]here are not two systems of law, each dealing with the same subject matter, each having similar requirements, each operating in its own field with its own highest court. There is only one system of law. It is a shaped by the Constitution which is the supreme law, and all law, including the common law, derives from the Constitution and is subject to constitutional control.

Within a legal system in which the Constitution is supreme law, ethical guidelines and human rights law are not regarded as contesting systems, but rather are complementary. Nevertheless, the thesis argues in favour of the precedence of human rights law based on the directive that in interpreting legislation and developing the common law or customary law, every court, tribunal or forum must promote the spirit, purport and object of the Bill of Rights.[61]

Ethical guidelines and human rights law combine to afford protection under the Constitution and the Bill of Rights, and by drafting legislation that integrates ethical guidelines and human rights law effect will be given to the Constitutional guarantee in section 12(2)(c). Chapter 5 expresses the view that human rights law considers informed consent as substantive, whereas ethical guidelines focus on procedural requirements for informed consent. By combining both, such legislation may function to dissolve the distinction between the effects of human rights law and bioethics, subsuming both into a single system offering protection under the Constitution.

5 RECOMMENDATIONS

5.1 Introduction

The thesis examines bioethical and human rights-based aspects of HIV-related clinical research involving human subjects in Africa. Several examples of unethical practice in clinical research are presented in order to analyse the ethical problems they pose. The dominant bioethical framework, known as principlism, used for the ethical assessment of research practices, is explicated in terms of its responsiveness to fundamental ethical problems in research.

Finally, a model of autonomy, exemplified by an adherence to an integrated system of justiciable human rights and ethical guidelines is proposed as an

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59 2000 (3) BCLR 241 (CC).
60 Para 44.
61 Sec 39(2) Constitution of the Republic of South Africa 1996.

alternative normative framework to the principlist bioethical model in the evaluation of informed consent in preventive HIV vaccine efficacy trials in South Africa.

The thesis concludes with the following recommendations:

5.2 Recommendations regarding the importance of context in the evaluation of clinical trial protocols as well as an argument for attention to be paid to the realisation of (socio-economic) human rights

The principle of respect for persons, or respect for autonomy, and the ethical guidelines with regard to the informed consent of research participants should be contextualised. Typically, the autonomy of research participants is guaranteed in terms of the informed consent process. However, a research participant's ability to make autonomous choices has no practical import unless she can exercise real options. One cannot make a choice, exercise one's 'autonomy', if circumstances obviate choice.

In the context of HIV vaccine efficacy trials in South Africa, informed consent to trial participation is contingent upon prospective participants' being unconstrained by external eventualities or pressures, such as respect for authority[62] or the need to access basic health resources. These factors cannot be ignored when assessing whether consent to research participation is 'informed'.

The importance of context in the assessment by ethics committees of clinical research protocols, specifically HIV vaccine trials, cannot be over-emphasised. When assessing preventive HIV vaccine clinical trial protocols, ethics committees have to bear in mind the context in which the research is to take place. Abstract principles, such as autonomy, have little meaning in a society in which choice is limited by the material living conditions of research participants. Members of ethics committees need to question whether informed consent is possible in the actual situation in which the prospective participants find themselves.

To avoid transforming informed consent into a empty or procedural feature of research ethics (and human rights), a focus on trial participants' human rights requires clinical research to be part of a larger project of promoting and establishing

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62 See para 3.4.1 of ch 5 above.

access to health care that delivers legitimate and meaningful forms of remedy as an alternative to research.

Clinical research does not occur in a vacuum independent of the resources people have access to beyond the research setting. Therefore, to ensure that exploitation does not occur, clinical research must be accompanied by the delivery of a minimum of health care resources – guaranteed by a right of access to health in a national constitutional framework or bill of rights, and reinforced by a system of international human rights law.

Preventive HIV vaccine efficacy research in South Africa should only be allowed to take place if a programme for the future delivery of a successful HIV preventive vaccine is in place.[63]

Collaborative research in less-developed countries, such as South Africa, must be supportive of development in the areas of education and professional training in order to promote local economic and scientific independence.[64]

Lastly, informed consent should be seen as an integral part of clinical trials which have a goal of affirming the autonomy of trial participants. Autonomy is dependant on a capacity to make choices, including the choice to enrol in trials regardless of the opportunity they offer for treatment and health care.

5.3 Recommendations regarding the enactment of legislation on informed consent (and other aspects) in respect of HIV vaccine efficacy trails in South Africa

Specific legislation must be enacted to protect the interests of HIV vaccine trial participants in South Africa.[65] Existing legislation is contradictory, especially regarding the requirements for informed consent of children.[66] At present, various provisions dealing with the legal protection of trial participants are scattered through diverse pieces of legislation.[67]

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63 The Ugandan peri-natal HIV transmission trials were justified primarily on the basis of the state of economy in the hosting countries. However, even the shorter course of ARV (that was researched) as well as its successor, Nevirapine, remain unaffordable in many African countries, including Uganda. See ch 4 above.

64 Various writers, as well as the MRC Guidelines, argue this point.

65 In this regard, also see Strode *et al* 'HIV vaccine research – South Africa's ethical legal framework and its ability to promote the welfare of trial participants' (2005) 95 *SA Med J* 598, who advocate the enactment of legislation which includes provisions relating to conditions under which research may be conducted on vulnerable groups, informed consent, compensation for trial-related injuries, etc.

66 See para 5.4 of ch 5 above.

67 Strode *et al* 600.

International human rights instruments provide important protection of the right of informed consent, however, as indicated before in this chapter,[68] in sections 231 and 232 of the South African Constitution, international human rights law is given a lower status than that accorded to the Constitution or Parliamentary legislation. Therefore, it is necessary that national legislation on informed consent be enacted to translate the Constitutional guarantee in section 12(2)(c) into reality. There are important reasons why national legislation should be adopted:

- Legislation would be able to consolidate ethical guidelines, human rights law, existing legislation, common law and case law into a coherent whole which embodies constitutional principles and substantive rights.
- Legislation is likely to be more accessible to members of the public, members of ethics committees, researchers and research sponsors than different pieces of conflicting ethical guidelines and legislation.
- Legislation has a relatively certain content, which may be subjected to interpretation by a court of law.
- Legislation is able to hold violators accountable for transgressions.

The enactment of legislation should not only be limited to provisions on informed consent, but may touch on aspects such as risk, the vulnerability of certain groups, measures to protect participants form trial-related stigma, socio-economic pre-conditions for trial participation, requirements for internationally collaborative research, and so on.

It is important that such legislation be adopted not just in South Africa, but in other African countries as well. The account in chapter 3 of the thesis of Pfizer's Trovan experiments in Kano, Nigeria, shows that in general, clinical research in Africa is poorly regulated and there is little accountability for wrongs committed during research. Ethical guidelines are easily breached, and there is little recourse for victims. National legislation governing clinical research will be an important first step towards holding unscrupulous researchers accountable.

5.4 Recommendations regarding informed consent in respect of preventive HIV vaccine efficacy trails in South Africa

Chapter 5 of the thesis reports on empirical research which investigated the informed consent process in a phase II preventive HIV vaccine clinical trial held at the Chris

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68 See para 3.3 above.

Hani Baragwanath Hospital in Soweto.[69] The researcher, Samantha Smith, concludes that '[r]esults from this research study have thus identified significant compromises within the current informed consent protocols in HIV vaccine trials within this particular reviewed context'.[70] Although the results are very specific and, perhaps, not generalisable, Smith's study has important implications for the informed consent process in South African HIV vaccine efficacy trials. From the transcribed interviews with the participants it is clear that informed consent was not obtained from them. Smith comments:[71]

> [i]ssues of cultural inappropriateness and over-complex language that is not sufficiently translated into the native language of participants suggests that information transfer and ethical principles have been undermined within these sessions. It is thus important that new ways be developed to ensure the adequate transfer of information by trial sponsors as well as the adequate comprehension of information by prospective trial participants.

In the future particular attention should be paid to the methodology within the informed consent process.[72] The consent forms should be redesigned along the principles advocated by Campbell *et al*[73] and others, so as to ensure comprehension.[74]

It is imperative that the informed consent process is 'presented to participants in their strongest language and that protocol forms are sufficiently translated into all the relevant languages spoken within the South African context'.[75] Comprehension of trial-related information cannot be impeded by the poor language capabilities of the communicator.

Smith presses the need for study co-ordinators to undergo more thorough training in specific discourse and conversational techniques which aid comprehension. This training should equip them 'to read' prospective participants' behaviour and assist in the transfer of a maximum level of information.[76]

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69 See para 3.4.2 of ch 5 above.
70 Smith (2004) 83. See para 3.4.2 of ch 5 above.
71 Smith 79.
72 As above.
73 Campbell (2003) *Patient Education and Counselling* 1 - 10.
74 Smith 81.
75 Smith 80.
76 Smith 80.

5.5 Recommendation regarding a binding international clinical research convention

The power of human rights discourse to create a situation in which states acknowledge obligations enforceable upon them in an international forum, cannot be over-estimated.

Many states in Africa have none or few legislative provisions that protect participants in clinical research.[77] Meier remarks that African nations demonstrate a 'great reluctance to impose any restrictions upon human subject research, thereby creating a "medical race to the bottom", at the expense of human rights and human life'.[78]

In the context of the failure of domestic law, the role of international human rights law is significant. It is indicated above and in chapter 5, although international human rights law guarantees the right of informed consent to participation in research, two instruments applicable to research in Africa alone contain express provisions on informed consent; even they lack the specificity necessary to create binding obligations upon states and non-state actors.[79] The informed consent provision of article 7 of the ICCPR has never been litigated in an international forum.[80]

At present informed consent cannot be considered an international customary law norm; the elements which qualify it as such are lacking. There is no widespread or consistent state practice regarding informed consent around the world.[81]

There is thus an urgent need to establish an international human rights law convention on human rights and clinical research. Such a convention, drafted on the

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77 Meier (n 21 above) 532. See also Todres 'Can research subjects of clinical trials in developing countries sue physician-investigators for human rights violations?' (2000) 16 *New York L School J Human Rights* 737.
Meier remarks that this legislative vacuum is often intentional – desperate to bring international research collaboration to their dying populations, governments vie to limit legislation: 'to court these pharmaceutical corporations, African governments vie to minimise the regulation of the conduct of clinical research' (532).
Meier further refers to a study by Kelly *et al* which observes that Malawi, Tanzania, Zaire and Zambia all lack legal procedures to ensure informed consent (see fn 124 on 533).

78 Meier 532 - 533.

79 See ch 5, para 5.4. Also see Meier (n 21 above) 533 – 534; Meier (2004) 30 *American J L and Med* 419; Dykman (1999) 9 *Columbia J Gender and L* 91; Kelleher (2004) 38 *Columbia J L and Social Problems* 67.

80 See Fidler (2001) 42 *Harvard Intl L J* 299, 328-337.

81 Meier 535. See ch 5, para 5.4; Bassiouni *et al* (who support the contention that it is not a norm of international customary law); and Grodin *et al* (who are of the opinion that such a norm of international law already exists).

model of the European Convention on Human Rights and Biomedicine,[82] should contain a justiciable right which binds states and that prevents people from being subjected to clinical research without informed consent, and encourages the inclusion of a right not to be subjected to clinical research without informed consent in national constitutions.[83] Such a convention will grant participants in clinical research a right of recourse against clinical trial sponsors who act in disregard of their human rights.[84] Meier asserts that such an international treaty is superior to international ethical standards as it obligates states to provide penalties for the violation of rights and compensation for victims.[85]

5.6 Recommendations proposing a multi-disciplinary approach to informed consent in South African HIV vaccine efficacy trials

Disciplinary insularity results in an inward-looking gaze; the conviction of knowing all the answers.[86]

The thesis advocates a human rights-based approach for the protection of preventive HIV vaccine trial participants in South Africa. Nevertheless, the value of other disciplines and fields of study in assessing solutions to the problems inherent in obtaining informed consent cannot be ignored; neither can the contribution of an

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82 Opened for signature on 4 April 1997, entered into force on 1 December 1999. It has 19 states parties.
The European Bioethics and Human Rights Convention requires in art 5 that the subject receive appropriate information as to the nature and purpose of the intervention as well as its consequences and risks. For further commentary on the informed consent requirement in the European Bioethics Convention, see Meier (n 21 above) 528 - 529.

83 The problem of holding international corporations, who are non-state actors, and not bound by international human rights law, accountable for human rights violations committed by them, remains. By including a right not to be subjected to clinical research without a subject's informed consent in the domestic constitutions of states (as in the South African Constitution) it will be easier to hold such corporations accountable.

84 This argument is not without its limitations. Ford and Tomossy provide an insightful discussion into the limitations of international human rights instruments. See Ford and Tomossy 'Clinical trials in developing countries: The claimant's challenge' (2004) 1 *L, Social Justice and Global Development* 1-14.

85 Meier (n 21 above) 551. Joseph Decosas remarks: 'HIV in Africa is contracted and spread through a web of causations – economic, developmental, social – and when you start focusing on a single solution, like anti-retrovirals, you fail' (quoted in Friedman *New York Times* 21 March 2001).

86 Alain Badiou writes:
The Law (human rights, etc) is *always there*. It regulates judgments and opinions concerning the evil that happens in some variable elsewhere. But there is no question of reconsidering the foundation of this 'Law', of going right back to the conservative identity that sustains it' (Badiou (2002) 33) (original emphasis).

interdisciplinary approach be ignored. The research by Smith, a communication pathology therapist, discussed above, is a case in point. Her observations with regard to communication failures in information transfer afford an important critique of the informed consent process.

Similarly, the disciplines of theology, sociology, anthropology and economics offer valuable insights, specifically in establishing the context in which clinical research occurs. The social sciences provide critical approaches to the role of hegemonic discourse in sustaining the *status quo* – including the discourse of human rights; as well as modelling the economic and political systems through which poverty and inequality are produced.

The thesis expresses a considered preference; however, human rights law is proposed as an alternative to ethical discourse and is not maintained to be an exhaustive solution to the difficulties that have been raised. Rather, the thesis proposes a system which integrates human rights law and bioethics.

I began the thesis by quoting from Charles Dickens's *A Tale of Two Cities*:[87]

> It was the best of times, it was the worst of times, it was the age of wisdom, it was the age of foolishness, it was the epoch of belief, it was the epoch of incredulity, it was the season of Light, it was the season of Darkness, it was the spring of hope, it was the winter of despair, we had everything before us, we had nothing before us ...

In June 2007 we, like Dickens's character, Sidney Carton, are at a precipice. The development of a vaccine to stem the devastation of HIV/AIDS could indeed offer a glimpse of a 'spring of hope'. However, should HIV vaccine efficacy trials take place in South Africa without meticulous attention to ensuring that free and informed consent is obtained from participants, then we could face a 'the winter of despair'.

Informed consent in respect of HIV vaccine efficacy trial participation in South Africa will be considered ethical and legal only if trial subjects have access to health care and are not dependant upon participation in the trial for its delivery. Without a broad social and political perspective to inspire our understanding, we cannot 'talk of informed consent' in these trials.

I conclude in the words of Marcio Fabri dos Anjos,[88]

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87 Dickens (1964) 1.

88 Dos Anjos (1996) 21 *J Med and Philosophy* 629.

> First, to what level of quality can medical ethics aspire, if it ignores callous discrimination in medical practice against large populations of the innocent poor? Second, how effective can such theories be in addressing the critical issues of medical and clinical ethics if they are unable to contribute to the closing of the gap of socio-medical disparity?

And concur with the sentiment expressed by Paul Farmer:[89]

> Questions regarding social and economic rights are at the heart of what must become a new medical ethics.

89 Farmer (2005) 206.

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