CHAPTER 5

INFORMED CONSENT IN PREVENTIVE HIV VACCINE EFFICACY TRIALS IN SOUTH AFRICA

Outline

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

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.