Med Law (2012) 31:119-152

Medicine and Law

Genetics

ETHICAL, LEGAL AND SOCIAL ISSUES IN THE CONTEXT OF THE PLANNING STAGES OF THE SOUTHERN AFRICAN HUMAN GENOME PROGRAMME

Jantina de Vries,[*] Melodie Slabbert,[**] Michael S Pepper[***]

Abstract: As the focus on the origin of modern man appears to be moving from eastern to southern Africa, it is recognised that indigenous populations in southern Africa may be the most genetically diverse on the planet and hence a valuable resource for human genetic diversity studies. In order to build regional capacity for the generation, analysis and application of genomic data, the Southern African Human Genome Programme was recently launched with the aid of seed funding from the national Department of Science and Technology in South Africa. The purpose of the article is to investigate pertinent ethical, legal and social issues that have emerged during the planning stages of the Southern African Human Genome Programme. A careful consideration of key issues such as public perception of genomic research, issues relating to genetic and genomic discrimination and stigmatisation, informed consent, privacy and data protection, and the concept of genomic sovereignty, is of paramount importance in the early stages of the Programme. This article will also consider the present legal framework governing genomic research in South Africa and will conclude with proposals regarding such a framework for the future.

Keywords: Southern African Human Genome Programme; Ethics; Genomic Research; Informed Consent; Privacy; Stigmatisation;

[*] Postdoctoral Fellow, Department of Human Genetics, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa, Jantina.devries@uct.ac.za.

[**] Professor, Department of Jurisprudence, School of Law, University of South Africa, Pretoria, South Africa.

[***] Professor, Unit for Advanced Studies and Extraordinary Professor, Department of Immunology, Faculty of Health Sciences, University of Pretoria, South Africa; Professeur Associé, Department of Genetic Medicine and Development, University Medical Centre, Geneva, Switzerland.

Discrimination; Data Protection; Community Engagement; Benefit-Sharing; Access to Genomic Information; Secondary Use of Genomic Samples.

INTRODUCTION

The Southern African Human Genome Programme (hereafter the SAHGP) was officially launched in January 2011 in Irene (Pretoria), South Africa.[1] The aim of the project is to develop capacity in southern Africa for the sequencing, analysis and translation of genomic information of individuals of southern African origin. The medium-to-long term objectives are (1) to determine genetic risk factors and pathogenetic mechanisms of diseases that are important to southern African populations (e.g. infectious diseases and diseases of lifestyle); and (2) to establish a biorepository and build bio-informatic capacity across southern Africa in order to be able to generate and analyse genomic data generated locally and also to access and analyse data published in the public domain that could have an impact on southern African populations. In order to ensure that the SAHGP will be successful, it is essential that the ethical, legal and social aspects of human genomic research are well-considered and addressed. The purpose of this article is to identify and discuss some of the most pertinent ELSI issues in the context of southern Africa.[2] This investigation may be instructive for other developing jurisdictions contemplating the founding of similar genome programmes. It is submitted that lessons learned from developed countries may only be appropriate or relevant in a developing context when adapted to local conditions. Furthermore, regional-specific and historical issues will have an important impact on the roll-out of the programme.

The article will start with a consideration of the importance of understanding public perception around issues of genetics and genomics research. It will

1 Pepper MS. Launch of the Southern African Human Genome Programme. S Afr Med J. 2011; 101 (5): 287-288.

2 This article originated from a discussion held at the launch of the SAHGP by the working group dealing with ethical, legal and social issues related to the Programme. Several members of this group also contributed to a document which will form part of a report to the national Department of Science and Technology of South Africa regarding the structure and funding requirements for the SAHGP. The authors acknowledge with gratitude the input of the following colleagues to the discussion and last-mentioned document: Prof. Ames Dhai, Prof. Antonel Olckers, Prof. Jeffrey Mphahlele, Dr. Norma Tsotsi, Marietjie Botes and Roger Chennells.

then discuss the risk of genetic discrimination or stigmatisation as one of the outcomes of genomics research. This latter issue is of particular relevance in the southern African context. The article will then consider the most pertinent ethical and legal issues we have identified to be relevant for the SAHGP. First, the article will explore issues relating to informed consent and community engagement. Of particular importance here is to develop a method to ensure that research participants are aware that participation is voluntary, and that they understand the nature of their participation. Second, the issues of confidentiality and privacy protection merit close attention. The nature of genomic information – i.e. that it cannot be completely delinked from the individual – poses novel challenges for possibilities to protect the privacy of research participants. Third, issues around data storage, data access and secondary use will be examined. It is now commonplace in genomics research to store and share research data with scientists around the globe. So-called data sharing policies have increased the utility of genomic data, but have also raised novel ethical issues that will need to be considered in the context of the SAHGP. Fourth, the present legal framework governing genomics research will also be referred to. Particularly relevant in this context is the notion of "genomic sovereignty" as one of the guiding principles for the SAHGP.

PUBLIC PERCEPTION OF GENOMICS

The success of the SAHGP will to a large degree depend on public support for the project. Engagement is required around issues to do with genetics, the sequencing of the human genome, sampling strategies, selection of population groups, and the expected benefits of this project, which include, but are not limited to, healthcare. It is imperative for the success of the SAHGP that discussions are held with a broad range of southern Africans, and not just those in academia or government.[3] In this regard, a discussion of the ethical, legal, and social issues should proceed with an explanation of the difference between "genomics" and "genetics". Although both disciplines study human DNA, "genomics", which takes a wide-angle view, is a study of the entire genome, as well as the interactions among functional genetic variants and the environment,[4] whereas the focus of "genetics" is more specific, involving the

3 Slabbert, MN. 'Genes 'R' Us': A critique of genetic essentialism" Stellenbosch Law Review. 2006; 17(2): 251-265.

4 Pepper MS. The human genome and molecular medicine - promises and pitfalls. S. Afr. Med J. 2010; 100(1): 722-724.

study of single genes in isolation. Although both are ultimately important in the context of the SAHGP, the focus of the SAHGP is on the benefits that can be accrued from whole genome sequencing in terms of disease prevention, diagnosis and treatment.

In the context of the SAHGP, one of the most pertinent challenges in public engagement relates to common fears around genetic manipulation. In the context of agricultural genetics, fears about risks associated with genetic manipulation have led to the partial rejection of this technology, and this has also occurred in Africa.[5] Some feel that genomic research works against evolution, and that it would be preferable to allow Mother Nature take her natural course.[6] With regard to humans, the fear is related to the emergence of technologies that allow for the selection of particular favoured traits in embryos, leading to the emergence of "designer babies", selected, for instance, for the compatibility of their organs or tissues with siblings, or for traits such as intelligence. A second important concern, albeit more specific to humans, relates to human reproductive cloning. Although human reproductive cloning is regarded as unethical and is legally banned in the majority of countries including South Africa,[7] genetic technologies appear to raise concerns relating to human cloning. The SAHGP public engagement strategy will therefore need to take account of such fears, and not dismiss them as irrational.

Another public concern is that of stigmatisation and discrimination as a result of the disclosure of information. Disclosure may not only lead to the stigmatisation of an individual, but may have other legal ramifications in the public as well as the private contexts of finance, education, employment, insurance and health care. In the sphere of an individual's private life, disclosure may have a profound impact, including the question as to whether an individual has a legal obligation to disclose genetic risks to his or her family, spouse or partner.[8]

5 Mayet, M. 2005. "GM crops for Africa: No thanks!" Institute of Science in Society Report, accessed at http://www.i-sis.org.uk/GMCFANT.php (visited 10 May 2011).

6 WHO. Genomics and World Health: World Health Organization 2002.

7 The Human Tissue Act 65 of 1983 in section 39A expressly prohibits "genetic manipulation outside the human body of gametes or zygotes", whereas the National Health Act 61 of 2003 in section 57(1) prohibits the manipulation of any genetic material, including genetic material of human gametes, zygotes or embryos, as well as any activity, including nuclear transfer or embryo splitting, aimed at the reproductive cloning of a human being. Section 57 (and the rest of chapter 8 of the National Health Act) has not been enacted yet.

8 Slabbert, MN. Genetic privacy in South Africa and Europe: A comparative perspective (Part I). Tydskrif vir Hedendaagse Romeins-Hollandse Reg (Journal of Contemporary

It will be important to understand the pertinence of these fears in southern African populations. If they are found to be common, such concerns will have to be addressed in the SAHGP's public engagement strategy as they have the potential to undermine the success of the project. In the case of the SAHGP, "the public" is made up of a multitude of different stakeholders. One important group includes the populations that are going to be sampled. There is a need to engage with these stakeholders early on to discuss the project, and to build support. Failure to seriously engage with populations included in genomic studies can be detrimental to the success of such projects. It will be important to consider lessons learnt from, for instance, the failure of the Human Genome Diversity Project that was initiated in the United States in the early 2000s.[9] The values of respect for indigenous populations, and involvement in decisions around sample ownership, storage, and secondary use of data, should be carefully considered.

A second important "public" to consider, is policymakers at regional and national levels. Since policymakers will ultimately impact on the manner in which the outputs of the SAHGP will be applied to the peoples of southern Africa through the policies and legislation they design, it will be important for the SAHGP to interact closely with policy makers. A third and equally relevant group that the SAHGP needs to engage with is researchers from a wide range of disciplinary backgrounds in the southern African region. Crossovers between genetics and linguistics, anthropology and archaeology, for instance, can greatly facilitate the interpretation of data or the contextualisation of research findings. Similarly, the contribution of sociologists and anthropologists can help to identify and understand the social context within which the SAHGP will operate. Social scientists can also assist in developing appropriate responses to the ethical challenges outlined in the next section. Legal scholars, similarly, can help to understand the legal landscape of the SAHGP, and propose amendments to the existing legislation in a variety of contexts, for instance where this does not currently offer sufficient protection for research participants. As part of the SAHGP planning stages, it will be important to

South African Roman-Dutch Law). 2007; 70: 622-637.

9 Frank R. What to make of it? The (Re)emergence of a biological conceptualization of race in health disparities research. Social Science & Medicine. 2007;64(10):1977-83; Reardon J. Race to the Finish. Identity and Governance in an Age of Genomics. Princeton and Oxford: Princeton University Press; 2005; Marks J. Your Body, My Property: the Problem of Colonial Genetics in a Postcolonial World. In: Meskell L, Pels P, editors. Embedding Ethics: Berg Publishing; 2005.

develop a communication and engagement strategy that establishes interaction with academics in these areas.

GENETIC DISCRIMINATION AND STIGMATISATION

South Africa has moved a long way in promoting racial and ethnic equality since the end of the Apartheid era. It is of paramount importance that the SAHGP strives to be a mechanism to promote the values pertinent to the new democratic order in South Africa and to democracy in the region as a whole. The project will need to be respectful of the cultures of the different ethnic groups that live within the borders of southern African countries, and it needs to be inclusive of all those populations. If one of the aims of the SAHGP is to be of benefit to the southern African populations, then those benefits should equally apply to all the ethnic groups that together form its nation states. Similarly, if the ambition is to promote equality, then the project will need to be cognisant of existing disparities in academic opportunities between institutions of higher education in the southern African region, and seek to ensure that universities share in the resources and opportunities generated by the SAHGP.

One particular fear that is raised frequently in relation to genomics research is that it may increase stigmatisation or discrimination of the research participants, or their population groups.[10] The World Health Organization ascribes the potential for genomics research to cause discrimination or stigmatisation to the "predictive power" of genomics information to provide information related to the likelihood that an individual may develop a disease or condition. When such knowledge is of a harmful nature – for instance, it relates to conditions that are already stigmatised, such as HIV/AIDS – then such knowledge has the potential to cause harm. This is especially relevant in cases where genetic risk factors for a stigmatised condition vary in prevalence between population groups.[11] Potential harms that can come from genomics research are said to be increased social distance and social exclusion,[12] social

10 WHO, 2002; Goodman KW. Ethics, genomics, and information retrieval. Computers in Biology and Medicine. 1996;26(3):223-9.

11 Foster MW, Sharp RR. Ethical issues in medical-sequencing research: implications of genotype-phenotype studies for individuals and populations. Hum Mol Genet. 2006 April 15, 2006;15(suppl_1):R45-9.

12 WHO, 2002.

prejudice,[13] and increased discrimination.[14]

The potential for stigmatisation is often external to the original research project, in that it is considered most likely that the application of genomic data in ways that cause harm is undertaken by people outside the original research group.[15] This would imply that the risk of stigmatisation is more acute in data sharing than in primary genomic research. The implication is that data release and secondary use may need to be carefully governed in the context of the SAHGP.

An additional challenge is that genomics research offers us a catalogue of human history that is based on biological fact that need not necessarily be in accordance with social narratives of descent. In one recent case in the United States involving a Native American tribe, genomic research yielded a biological narrative of descent that was in conflict with the tribe's own understanding of its history.[16] The conflict between these social and biological narratives was experienced as deeply disconcerting by some members of the tribe.[17] On the contrary, genomic studies can also give biological support for social narratives of descent. For instance, the Lemba of southern Africa are Jewish, and have always claimed descent from early Jewish people in what is now Israel. Genetic studies found that some Lemba males carry Y chromosomes that show concordance with Y chromosomes found in descendants of the Jewish priesthood in Israel. Such evidence seems to support the Lemba narratives of origin.[18]

13 Mountain JL, Risch N. Assessing genetic contributions to phenotypic differences among 'racial' and 'ethnic' groups. Nat Genet. 2004.

14 Nuffield Council on Bioethics. Genetic Screening. London: Nuffield Council on Bioethics 1993.

15 Foster, 2006; Goodman, 1996.

16 Harmon A. Tribe wins fight to limit research of its DNA. New York Times. 21 April 2010; Editorial. The unexamined 'Caucasian'. Nat Genet. 2004;36(6):541.

17 Harmon, 2010; McGregor J. Racial, Ethnic, and Tribal Classifications in Biomedical Research With Biological and Group Harm. The American Journal of Bioethics. 2010;10(9):23-24.

18 Parfitt T, Egorova Y. Genetics, Mass Media, and Identity: A Case Study of the Genetic Research on the Lemba and Bene Israel. London: Routledge; 2005; Parfitt T. Constructing Black Jews: Genetic Tests and the Lemba – the 'Black Jews' of South Africa. Developing World Bioethics. 2003;3(2):112-8; Thomas MG, Parfitt T, Weiss DA, Skorecki K, Wilson JF, Roux Ml, et al. Y Chromosomes Traveling South: The Cohen Modal Haplotype and the Origins of the Lemba—the "Black Jews of Southern Africa" Am J Hum Genet. 2000;66(2):674-86.

The SAHGP will need to develop a strategy that accommodates these challenges, and that minimises the risk of adverse effects such as stigmatisation and discrimination. Such a strategy needs to ensure that population groups are sampled fairly and equally across southern Africa, and that greater caution is taken when including population groups that are already socially disadvantaged or discriminated against. It will also need to ensure that public engagement strategies discuss the relationship between biological and social narratives of descent, and seek ways to ensure that these can co-exist in harmony. Thirdly, the strategy will need to ensure that research results are not over-interpreted in terms of their social relevance, and that researchers are aware of the possibility that harmful research results could be generated from genomic studies. Articulating what these would be, and how they could be recognised, should be integral to the Programme.

ETHICAL AND LEGAL ISSUES

Informed Consent

Obtaining informed consent from research participants is essential to ensure that medical research does not harm them.[19] It also protects the autonomy of research participants and, possibly, could be used as a means of giving participants some control over sample and data use.[20] In order to be valid, consent needs to be given voluntarily, by a person who is sufficiently competent to understand the information provided therein and to make a decision, and the information that is to be supplied needs to be accurate and give the participant sufficient detail to make an informed decision, without being overly complicated or difficult. These requirements are not only recognised in ethical guidelines underpinning research involving humans but are firmly established as legal requirements in medico-legal literature.[21] Obtaining informed consent for genomics research is challenging for a number of reasons.[22] Although

19 Chokshi DA, Thera MA, Parker M, Diakite M, Makani J, Kwiatkowski DP, et al. Valid Consent for Genomic Epidemiology in Developing Countries. PLoS Med. 2007;4(4):e95.

20 Caulfield T, McGuire AL, Cho MK, Buchanan JA, Burgess MM, Danilczyk U, et al. Research Ethics Recommendations for Whole-Genome Research: Consensus Statement. Plos Biology. 2008 25 March 2008; 6(3):e73.

21 Van Oosten FFW. The Doctrine of Informed Consent in Medical Law. LLD, 1989: UNISA 17; Strauss SA. *Doctor, Patient and the Law: A Selection of Practical Issues*. Goodwood: Van Schaik,; 1991 3ff. See also *Castell v De Greef* 1994 (4) SA 408 (C) 420–421, 425, 426. Patient autonomy was statutorily reinforced by s 6 of the National Health Act.

22 Lunshof JE, Chadwick R, Vorhaus DB, Church GM. From genetic privacy to open

the ethical and legal bases for obtaining valid consent are incontestable, contextual differences between developed and developing countries present many problems. For example, it is debated whether the tenets of "Western" research ethics, mainly in the application of a written informed consent model, can truly be applied in the African context.[23] Moreover, communal forms of assent may in some instances prove to be as important as individual consent, whereas in others, gender inequality may mean that some women may be unable to give individual consent.

Other important legal questions are pointed out by Conley.[24] First, can research capable of generating the rich datasets that define public genomics, and that are necessary to unravel the genomic bases of complex traits, satisfy conventional privacy expectations of research subjects? Second, what should be done to ensure that informed consent is truly "informed" in light of these privacy concerns, considering that genomic datasets will be subjected to future data mining to answer research questions that cannot be specifically identified or consented to at the outset? Third, in view of the fact that certain genomic information inherently possesses both research and clinical value, what duties does a genome researcher have to identify and inform a participant of the clinical significance of genomic information? Is the legal duty of disclosure by researchers either a continuing one or only an initial one? To what extent should researchers be subject to legal regulations intended to regulate the practice of medicine that may simultaneously restrict their ability to disclose certain findings or to discuss the implications of those findings? These issues

consent. Nat Rev Genet. 2008;9(5):406-11; Mascalzoni D, Hicks A, Pramstaller P, Wjst M. Informed Consent in the Genomics Era. PLoS Medicine. 2008 September;5(9):e192; McGuire, Caulfield et al., 2008; Kaye J, Boddington P, De Vries J, Gowans H, Hawkins N, Heeney C, et al. Ethical, Legal and Social Issues Arising from the Use of GWAS in Medical Research. London: Wellcome Trust2009; Kaye J, Boddington P, de Vries J, Hawkins N, Melham K. Ethical implications of the use of whole genome methods in medical research. Eur J Hum Genet. 2010;18(4).

23 Tsotsi, NM. Informed consent in research in developing countries: Is there some unfinished business? 2009. Report submitted in partial fulfilment of the MScMed-degree. Faculty of Health Sciences, University of the Witwatersrand, 1-86; Tekola F, Bull SJ, Farsides B, Newport MJ, Adeyemo A, Rotimi CN, et al. Tailoring Consent to Context: Designing an Appropriate Consent Process for a Biomedical Study in a Low Income Setting. PLoS Negl Trop Dis. 2009;3(7):e482; Tindana PO, Kass N, Akweongo P. The Informed Consent Process in a Rural African Setting: A Case Study of the Kassena-Nankana District of Northern Ghana. IRB: Ethics and Human Research. 2006;28(3):1-6.

24 Conley, J. (2009) "Enabling responsible public genomics", available from http://works.bepress.com/cgi/viewcontent.cgi?article=1000&context=john_conley&sei-redir=1#search="1000genomes+project+consent+template" (visited 10 May 2011).

expose a tension between the societal benefits of public genomics research and the interests of individual participants in that research.

EXPLAINING GENOMICS

Perhaps one of the most challenging aspects in obtaining valid consent for participation in the SAHGP relates to the relatively low average levels of education and considerable poverty in many parts of southern Africa. The combination of these two factors is known to complicate the obtaining of informed consent in genomics research.[25] Understanding the nature of genomics research – for instance, that it deals with the entirety of a person's genomic material; that it may reveal information about family members; that the results point to relative not absolute risk factors, and so forth – is challenging at the best of times, even when research participants are highly educated.[26] There is no good proposal for how to best explain genomics to research participants, although some suggestions have recently been made.[27] These include, for instance, the recommendation that ways need to be sought to link the basic premise of the genomic study – namely, that it is genomic – to experiences that are common to research participants. Popular understandings of inheritance could be one way of embedding an understanding of genomics research in existing local knowledge. An example is linking an explanation of the genomic study to observed patterns of inheritance in families. However, it is dangerous to presume that because participants understand the nature of genetic inheritance, they will have understood the implications of participation in a genomic study.

It will be necessary to explore innovative methods to facilitate communication about the SAHGP. The talking book explaining what it means to be part of a clinical trial, produced by the Steve Biko Centre for Bioethics of the

25 De Vries J, Bull S, Doumbo OK, Ibrahim M, Mercerau-Puijalon O, Kwiatkowski DP, et al. Ethical Issues in Human Genomics Research in Developing Countries. BMC Medical Ethics. 2011;12(5); Gikonyo C, Bejon P, Marsh V, Molyneux S. Taking social relationships seriously: Lessons learned from the informed consent practices of a vaccine trial on the Kenyan Coast. Social Science & Medicine. 2008;67(5):708-20; Molyneux CS, Peshu N, Marsh K. Understanding of informed consent in a low-income setting: three case studies from the Kenyan coast. Social Science & Medicine. 2004;59(12):2547-59.

26 Lunshof, Chadwick et al., 2008.

27 De Vries, Bull et al., 2011; Nyika A. Ethical and practical challenges surrounding genetic and genomic research in developing countries. Acta Tropica. 2009;112(Supplement 1):S21-S31.

University of the Witwatersrand, is an example of a book that may be used in explaining genomics in the context of the SAHGP.[28] Collaboration with psychologists, educational specialists and anthropologists may be essential in the development of consent processes that are both ethically appropriate and respectful of local culture.

The perception of members of indigenous communities regarding the donation of certain samples should also be considered. In some societies, hair and other bodily materials may secretly be collected from intended victims to harm them through witchcraft. Where such beliefs are strong, people may collect their own loose hair, fingernail parings, and other body products and bury them to avoid this danger. Researchers who ask such a population for bodily materials may be perceived as intending to perform witchcraft.

Blood is also surrounded by mystique in many traditional African cultures, and the collection of blood is known to be controversial in Kenya and The Gambia.[29] The collection of blood for medical genomic studies in Africa often carries connotations of exploitative relations during colonialisation.[30] In southern Africa, blood is often collected to be used as a sacrifice, sometimes through special rituals. Donation of blood in some cultures is a serious issue that may require discussion and perhaps a neutralising ritual. But such views may not apply to all the populations and cultures of southern Africa. Before approaching the population, researchers need to know as much as possible regarding likely concerns about and reactions to their plans for sample collection. In the southern African context specifically, certain cultural beliefs may prevent the donation of tissues and blood.[31] In such cases, the SAHGP may need to explore the feasibility of collecting DNA from other sources, such as saliva.

28 Dhai A, Etheredge H, Cleaton-Jones P. A pilot study evaluating an intervention designed to raise awareness of clinical trials among potential participants in the developing world. Journal of Medical Ethics. 2010 April 1, 2010;36(4):238-42.

29 Fairhead J, Leach M, Small M. Where techno-science meets poverty: Medical research and the economy of blood in The Gambia, West Africa. Social Science & Medicine. 2006;63(4):1109-20; Molyneux et al, 2004.

30 Van Rinsum H, Tangwa GB. Colony of genes, genes of the colony: diversity, difference and divide. Third World Quarterly. 2004;25:1031-43; White L. Speaking with Vampires: Rumor and History in Colonial Africa. Berkeley and Los Angelos: University of California Press; 2000.

31 Slabbert MN, Pepper M. "A room of our own?" Legal *lacunae* regarding genomic sovereignty in South Africa. Tydskrif vir Hedendaagse Romeins-Hollandse Reg (Journal of Contemporary South African Roman-Dutch Law). 2010;73:432-50.

Where it is not possible to obtain truly informed consent, it may be necessary to complement consent with other governance mechanisms to ensure that the interests of research participants are appropriately protected.[32] In the context of one genomics project in Africa, the MalariaGEN project,[33] the realisation of limitations to consent as a mechanism to protect the interests of research participants led to the development of a restrictive data release policy.[34] It may be worthwhile to explore the relevance of such a policy in the context of the SAHGP.

TRAINING OF FIELDWORKERS

Relationships between members of the community, the participant's family and the research team play an essential role in determining decisions to participate.[35] Fieldworkers play an essential, yet complex role in obtaining informed consent. In practice, fieldworkers are often the people explaining the study to prospective participants, and it is therefore important that they understand the study well enough to do so, and to answer questions accurately. Fieldworkers are often drawn from the same communities as prospective research participants, to ensure that they are fluent in the local language and sufficiently aware of local customs and traditions. However, this also means that it may be more difficult for prospective participants to refuse participation. In addition, in some cases, fieldworkers' remuneration is dependent on the number of participants they recruit into a trial. This of course creates incentives for field workers to 'convince' prospective participants that they should participate. In order to ensure quality in obtaining informed consent for the SAHGP, care needs to be taken to adequately train the fieldworkers who will be tasked with collecting samples. This is not an easy task, considering the complexity of both genomics methodologies, as well as of components of the research project, such as secondary use and computer storage of data. Considerable attention will also need to be given to developing appropriate support structures for fieldworkers. For instance, fieldworkers should be

32 Parker M, Bull SJ, de Vries J, Agbenyega T, Doumbo OK, Kwiatkowski DP. Ethical Data Release in Genome-Wide Association Studies in Developing Countries. PLoS Med. 2009;6(11):e1000143.

33 The MalariaGEN Consortium. A global network for investigating the genomic epidemiology of malaria. Nature. 2008;456(7223):732-7.

34 Parker et al, 2009.

35 Gikonyo et al, 2008.

supported by more senior fieldworkers, who can help them to develop ways of communicating about the SAHGP in an efficient manner.

DATA SHARING AND FUTURE USES OF SAMPLES AND DATA

Genomic material is normally taken from a relatively small sample of human blood or saliva. Once it is extracted, genomic material can be duplicated to be used in other studies, although there is the risk of introducing variants in the duplication process which compromises the quality and therefore the validity of the material. It can also be frozen and used at a later date. But more significantly, once the sample is sequenced, there is no limit to the number of times the data can be used, or for which projects. This means that it is exceedingly difficult – if not impossible – to specify the exact studies for which samples are collected, or the timeframe during which samples and data will be used.[36] This raises considerable challenges for consent.[37] One way of dealing with this is by getting broad consent for "genomic studies", including consent for sample storage and future use.[38] However, broad consent raises a number of ethical challenges of its own.[39] One is whether "broad consent" respects the principle of veracity in consent.[40] Another is whether research participants and communities understand that they have given broad consent for the use of their genetic material in a wide range of studies. A recent case in the United States demonstrated that broad consent does not necessarily mean that samples can be used indiscriminately for all types of research. In the case of the Havasupai, the tribe had given consent for sample storage and secondary use, but they protested against the use of their samples in mental health research.[41] When challenged in court, the researchers and the sponsoring university were ordered to destroy the samples and to pay compensation to the tribal members.[42]

36 Lunshof, Chadwick et al., 2008; Kaye, Boddington et al., 2009.
37 Mascalzoni et al, 2008.
38 Lunshof, Chadwick et al., 2008; Mascalzoni, Hicks et al., 2008.
39 Hofmann. Broadening consent - and diluting ethics? J Med Ethics. 2009;35:125-9.
40 Lunshof, Chadwick et al., 2008.
41 Mello, MM, Wolf LE. The Havasupai Indian Tribe Case — Lessons for Research Involving Stored Biologic Samples. New England Journal of Medicine. 2010;363(3):204-7; Harmon 2010; Vorhaus DB. The Havasupai Indians and the Challenge of Informed Consent for Genomic Research. 2010; Available from: http://www.genomicslawreport.com/index.php/2010/04/21/the-havasupai-indians-and-the-challenge-of-informed-consent-for-genomic-research/ (visited 10 May 2011).
42 Harmon 2010.

Only very few empirical studies that aim to understand the intricacies of obtaining consent for genomic research have been conducted on the African continent, and there is almost no evidence to support a proposal for how to best address these challenges. Even so, the SAHGP will need to determine whether it is desirable or feasible to discuss these aspects of the genomic study with prospective research participants in the consent process. It will need to carefully weigh the value of veracity with the need to provide comprehensible and relevant information to participants. It will be necessary to engage with representatives of communities that will be targeted for recruitment to discuss what kind of information should be included in the consent form.

Data sharing is also relevant in considerations relating to benefit-sharing agreements and may be one of the benefits to which local communities (if the capacity exists) may have access.

DEVELOPMENT OF A CONSENT TEMPLATE

Considering the challenges involved in developing consent forms that are appropriate for the wide variety of cultures and customs of the peoples of southern Africa, it may be worthwhile for the SAHGP to consider developing a consent template. Such a template could list a number of agreed components of and suggested phrasing for the consent form, while allowing for local adaptation where appropriate. This is the route that the MalariaGEN project followed.[43] Guidance can be sought from existing consent templates for genomic studies that are publicly available, such as the consent template of the 1000Genomes project that was developed by a team of international experts in this area,[44] or alternatively, the consent form developed by the P3G Consortium, an initiative involving experts worldwide, undertaken with the aim of facilitating the development of project guidelines and policies in genomics.[45]

43 See www.malariagen.net and The MalariaGEN Consortium. A global network for investigating the genomic epidemiology of malaria. Nature. 2008;456(7223):732-7.

44 Available at http://www.genome.gov/Pages/PolicyEthics/InformedConsent/eMERGEModelLanguage2009-12-15.pdfz (visited 10 May 2011).

45 Available from http://www.p3gobservatory.org/repository/ethics.htm;jsessionid=0BAF0033551FA015ECE28611D8657B6E z9b9 (visited 10 May 2011).

COMMUNITY ENGAGEMENT

Considering the challenges to individual consent, growing consensus seems to be that consent should be preceded by community engagement activities. In many indigenous communities, the approval of a tribal or community structure is a crucial precursor to individual consent.[46] So-called community engagement complements informed consent and public engagement activities, and is an essential step in medical research in Africa.[47] In many instances, community engagement entails a number of sequential discussions with political and administrative individuals in healthcare facilities; with the tribal leaders and elders of population groups or communities; with opinion leaders such as teachers or health nurses; with religious leaders in communities; and with specific social groups in communities, such as for instance a women's interest group or a drama group. Within the SAHGP collaboration, there are a multitude of researchers with established expertise in processes of community engagement who should be consulted about the design of an appropriate community engagement strategy. The seeking of individual consent in the context of the SAHGP should be sensitive to the legal and social characteristics of the diverse local contexts in southern Africa.

FEEDBACK OF INCIDENTAL FINDINGS

One increasingly important topic of debate in genomics research relates to decisions regarding the feedback of incidental findings. These are findings that (a) were not part of the research question, (b) relate to a particular, traceable individual, and (c) are of health relevance.[48] An example is a finding that a

46 Tindana PO, Singh JA, Tracy CS, Upshur REG, Daar AS, Singer PA, et al. Grand Challenges in Global Health: Community Engagement in Research in Developing Countries. PLoS Med. 2007;4(9):e273; Tindana PO, Kass N, Akweongo P. The Informed Consent Process in a Rural African Setting: A Case Study of the Kassena-Nankana District of Northern Ghana. IRB: Ethics and Human Research. 2006;28(3):1-6.

47 Marsh V, Kamuya D, Rowa Y, Gikonyo C, Molyneux S. Beginning community engagement at a busy biomedical research programme: Experiences from the KEMRI CGMRC-Wellcome Trust Research Programme, Kilifi, Kenya. Social Science & Medicine. 2008;doi:10.1016/j.socscimed.2008.02.007; Rotimi C, Leppert M, Matsuda I, Zeng C, Zhang H, Adebamowo C, et al. Community Engagement and Informed Consent in the International HapMap Project. Community Genetics. 2007;10:186-98.

48 Bredenoord A, Onland-Moret CN, Delden JJMv. Feedback of Individual Genetic Results to Research Participants: in Favour of a Qualified Disclosure Policy. Human Mutation. 2011;32:1-7; Cho M, K. Understanding Incidental Findings in the Context of Genetics and Genomics. The Journal of Law, Medicine & Ethics. 2008;36(2):280-5; Wolf SM,

participant is a carrier of a genetic trait that predisposes to cancer, such as familial adenomatous polyposis (FAP).[49] FAP-carriers will develop polyps in the colon, which can be asymptomatic and undiagnosed until they develop into colon cancer. Regular screening and removal of polyps can prevent progression to cancer. This is an example of a serious but treatable condition, where genomic diagnosis of carrier status could prevent death. The SAHGP needs to develop a policy on whether and how to report such incidental findings back to its participants.

If samples are irreversibly anonymised after collection, it will be virtually impossible to trace them back to the individual to whom they are related. Yet from a legal and ethical point of view, information that could influence an individual's health or alter the course of a disease should not be withheld. In addition, the feeding back of an incidental genomic diagnosis with specific health implications to an individual who does not have access to relevant health care services to treat such a condition further complicates the matter. Whereas genomic information may be beneficial to the health of those who have access to treatment, the same information will not be helpful to those who do not, and may create anxiety and result in social ostracism and stigmatisation and therefore affect their quality of life negatively. The inclusion of a question in the consent form that requires participants to indicate whether they wish to be informed of incidental findings needs to be debated. Given the complexity of these issues, it will be important for the SAHGP to seek the advice of legal experts, ethicists, medical genetic counsellors and other specialists to establish a way of managing incidental findings.

In addition to incidental findings, it is considered part of ethical "good practice" to feed back research results to research participants and their communities. Although often neglected in medical research, there is ample evidence that research participants expect some form of communication about the research project after it is completed, at least in countries in the Western world.[50] It will

Lawrenz FP, Nelson CA, Kahn JP, Cho MK, Wright Clayton E, et al. Managing Incidental Findings in Human Subjects Research: Analysis and Recommendations. The Journal of Law, Medicine & Ethics. 2008;36(2):219-48.

49 Kaye, Boddington et al, 2010.

50 McGuire AL, Beskow LM. Informed Consent in Genomics and Genetic Research. Annual Review of Genomics and Human Genetics. 2010;11(1); Beskow LM, Dean E. Informed Consent for Biorepositories: Assessing Prospective Participants' Understanding and Opinions. Cancer Epidemiol Biomarkers Prev. 2008;17(6):1440-51; McGuire et al 2008.

be important for the SAHGP to consider how it will communicate findings from research to the participants that donated their samples.

PRIVACY AND CONFIDENTIALITY

Genomics research raises a number of important challenges related to the privacy of research participants.[51] The fact that genomic data is unique for an individual, combined with the wide availability of genomic data through the Internet, raises important questions about the meaning of privacy in genomics, as well as about the means of protecting it. A number of privacy challenges exist. Firstly, a possible threat to the privacy of personal information exists in instances where a person's genetic or genomic results are stored, processed or kept in a data bank, not only by institutions or persons in the insurance or financial sectors, health sector or the employment sector, but also in the context of the SAHGP. In South Africa, privacy and the confidentiality of health information is presently protected by the Constitution, statutory law, common law, relevant ethical guidelines[52] and the National Patients' Rights Charter. Soon, legislation protecting personal information specifically (e.g. the Protection of Personal Information Act 9 of 2009) will come into operation. The National Health Act 61 of 2003 also protects the confidentiality of health information.[53] The same act provides for relevant exceptions to the general confidentiality rule, as well as for limited grounds of access to health information.[54]

The regulation of access to records is another measure capable of directly or indirectly protecting confidentiality in personal records. The Promotion of Access to Information Act 2 of 2000 provides persons with the right of access to records of public bodies and private bodies, thereby giving effect to section 32(2) of the Constitution. This provides that national legislation be enacted to

51 Heeney C, Hawkins N, De Vries J, Boddington P, Kaye J. Assessing the Privacy Risks of Data Sharing in Genomics. Public Health Genomics 2011 14(1):17-25; Rothstein MA. Is Deidentification Sufficient to Protect Health Privacy in Research? The American Journal of Bioethics. 2010;10(9):3 – 11; Lowrance WW, Collins FS. Identifiability in Genomic Research. Science. 2007 3 August 007;317(5838):600-2.

52 Rule 13 of the Ethical Rules of Conduct for Practitioners registered under the Health Professions Act, 1974 (Government Notice No. R717 of 4 Aug. 2006); HPCSA; cf. in general, HPCSA Guidelines for Good Practice in the Healthcare Professions: Booklet 10: Confidentiality: Protecting and Providing Information (2008).

53 Section 14 of the National Health Act.

54 Section 15.

give effect to the constitutionally protected right of everyone to have access to information held by the state or another person, where such information is required for the exercise or protection of any rights. The privacy of third parties is protected by providing that a request for access to a record must be refused by a public or private body if such disclosure would involve unreasonable disclosure of private information about a third party, including a deceased person. The above-mentioned provisions relating to privacy and data protection all overlap to provide a multi-layered regime of protection of personal information. The exact extent to which genomic information will be protected in terms of this regime will need to be examined in more detail by the SAHGP.

Secondly, the question as to who will have access to genomic information will have to be answered. Should employers and insurance companies have access to the genetic and genomic information held by the SAHGP? To what extent should medical insurers be permitted to refuse claims based on arguments that those insured should have known whether they are susceptible to a given condition because the technology is available? In 2008 the United States government introduced the Genetic Information Non-discrimination Act[55] which attempts to address these issues specifically. Similar legislation protecting genetic information specifically has been enacted in Switzerland. As mentioned above, the extent to which the present legal framework addresses and protects genomic and genetic information in a range of contexts, e.g. employment, insurance, health care, etc, should be investigated in the context of the SAHGP, and if found lacking or insufficient, should be addressed.

On an individual level, the taking of a genetic or genomic sample of an individual, the genetic testing itself, the collection of and acquaintance with, as well as disclosure[56] or publication of the results without the person's

55 Copy of this act available at http://www.eeoc.gov/laws/statutes/gina.cfm (visited 13 May 2011).

56 E.g. where a person other than the person to whom the private facts relate, acquaints third parties with the private facts of the other person, as was the case in *Jansen van Vuuren v Kruger* 1993 4 SA 842 (A), where a doctor told his friends about a patient's HIV status. In the latter case, decided on common law principles prior to the coming into force of the 1993 Constitution, the court found that there was no ethical or legal duty on the practitioner to inform third parties and that his conduct was a breach of his patient's confidence. See also NM and Others v Smith and Others (Freedom of Expression Institute as Amicus Curiae) 2007 5 SA 250(CC). In the latter instance, the Constitutional Court held that the publication of the HIV-status of the applicants by the respondents constituted a wrongful publication of a private fact and that the applicants' right to privacy

consent[57] constitute an infringement of both the right to privacy in terms of the common law and the constitutional right to privacy.[58] In respect of the latter, it is possible to argue that a genetic test may be tantamount to a "search" in terms of section 14(a) of the Constitution.[59] Section 14(d) of the Constitution in addition refers to the "right not to have – the privacy of. . . communications infringed", which would protect the privacy of any communication between a person undergoing genetic testing and his or her health practitioner, e.g. relating to a genetic result. Such conduct may also infringe other protected personality interests, for example a person's identity. Identity is thus infringed by the untrue or false use of indicia of the identity, which in the case of the disclosure or publication of genetic test results, may possibly result in identifying a person with a specific genetic disease of which the probability of its manifestation is difficult to determine, or because of the unspecific nature of certain genetic conditions, and is not a true factual condition in relation to a person's health. Disclosing the fact that a person or close relative of a person, for example, has tested positively for a genetic condition associated with insanity (e.g. Huntington's disease) may lead to social ostracism and stigmatisation of such a person in the absence of definite certainty.

Unauthorised medical tests, which may include genetic tests, in the absence of justification, constitute in principle a violation of a person's body or *corpus* and

was breached by the respondents.

57 Consent here refers to informed consent as a defence against breach or violation of privacy. In *Castell v De Greef* (1994 4 SA 408 (A)) the court formulated the requirements for informed consent in a health care context. Although these principles were applied in the context of an invasion of physical integrity, there is no reason why these should not apply in the context of disclosure of personal information.

58 A similar example of an invasion of a person's constitutional personal autonomy privacy right and informational privacy right is the taking of a person's blood for testing without consent, see *S v Orrie* 2004 3 SA 584 (C) 589–590 regarding the taking of a DNA blood test for criminal investigations; *C v Minister of Correctional Services* 1996 4 SA 292 (T) on a blood test for HIV/Aids, or *Klein v Attorney-General WLD* 1995 3 SA 848 (W) regarding the restoring of previously erased computer information. Other examples are unauthorised medical examinations or tests. In the case of *M v R* 1989 1 SA 416 (O), Kotze J describes the wrongfulness in principle (except if a ground of justification, such as a court order exists) of a blood test: "[T]he taking of a blood sample which is normally in effect not much more than a prick of a needle, can be regarded technically as a violation of the right to privacy, as is contemplated in the law of personality". See, in general, Slabbert MN. Genetic privacy in South Africa and Europe: A comparative perspective. Tydskrif vir Hedendaagse Romeins-Hollandse Reg. 2008;71:81-100, 86-87.

59 Referring to the right not to have one's person searched, the violation of which should be reasonable and justifiable in terms of section 36 of the Constitution of the Republic of South Africa, 1996.

are hence an infringement of physical integrity. Protection of a person's *corpus* as a personality right is also entrenched by section 12 of the Constitution which protects a person's right to bodily and psychological integrity.[60] Section 12 of the Constitution also protects the right to be free from all forms of violence from either public or private sources,[61] not to be tortured in any way[62] and not to be treated or punished in a cruel, inhuman or degrading way.[63] The right not to be subjected to medical or scientific experiments is specifically mentioned.[64] Genetic tests yielding ambiguous or uncertain results may arguably be described as "medical or scientific experiments" in terms of this section. Fundamental rights protected by the Constitution are, however, not absolute and may be restricted or limited.[65] Any possible infringement of the above fundamental rights will need to be evaluated against the general limitation clause in the Constitution.[66] These legal issues are but a few examples that will need to be carefully considered by the SAHGP.

It has been suggested that should a researcher find a ground-breaking result, a procedure has to be established to enable one to contact the initial research participant, perhaps via a system of an "honest broker".[67] In this context it might as indicated above be useful to consider a standard clause in the consent form where a research participant can elect to approve of being contacted in the event of such eventualities.

60 Section 12(2) of the Constitution provides as follows: "Everyone has the right to bodily and psychological integrity, which includes the right – (a) to make decisions concerning reproduction; (b) to security in and control over their body; and (c) not to be subjected to medical or scientific experiments without their informed consent."

61 Section 12(1)(c) of the Constitution.

62 Section 12(1)(d) of the Constitution.

63 Section 12(1)(e).

64 Section 12(2)(c).

65 Section 36(1) of the Constitution provides that the rights may be limited only in terms of law of general application to the extent that the limitation is reasonable and justifiable in an open and democratic society based on human dignity, equality and freedom, taking into account all relevant factors that may include the nature of the right in question; the importance of the limitation; the nature and extent of the limitation; the relation between the limitation and its purpose, as well as less restrictive means to achieve the latter purpose.

66 Slabbert, 2008.

67 See, for example, Boyd AD, Hunscher, AD, Adam BA, et al The 'honest broker' method of integrating interdisciplinary research data. 2005. Proceedings of the AMAI Annual Symposium 902, available from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1560785/ (visited 15 May 2011).

DATA STORAGE AND ACCESS TO INFORMATION

The storage and re-use of samples and data is part and parcel of the way in which scientific research is now conducted. Originating in the context of the Human Genome Project, recent calls have been made to extend data sharing practices across other disciplines as well.[68] The objective here is that data could be re-analysed to confirm existing findings or findings from other studies, to be combined with other datasets, or to conduct new analyses. Similarly, samples can be stored with the objective of re-sequencing these when new technologies become available.

The storage and re-analysis of data and samples raises a considerable number of ethical and legal challenges.[69] Most important among these are possibilities to maintain (some form of) participant confidentiality, to ensure compatibility with consent given by research participants, and to ensure that data are not used in ways that may harm participants and their communities or population groups. Reporting of incidental findings to participants further complicates the matter.

With regard to maintaining participant confidentiality, a complicating factor is that genomic data is unique to a particular individual, and that it can therefore never completely be anonymised or de-identified.[70] For clarification about terminology around sample de-identification, see Knoppers and Saginur.[71] In addition, genomic data can be triangulated with other forms of data – for instance, hospital records or data from other studies – to facilitate the identification of individual research participants.[72] Several authors have

68 Walport M, Brest P. Sharing research data to improve public health. The Lancet. 2011;377:538-9.

69 Heeney et al 2011; Singh J, Daar A. Intra-consortium data sharing in multi-national, multi-institutional genomic studies: gaps and guidance. The HUGO Journal. 2009;3(1):11-4; Kaye J, Heeney C, Hawkins N, de Vries J, Boddington P. Data sharing in genomics: re-shaping scientific practice. Nat Rev Genet. 2009;10:331-5; Parker et al 2009; Chokshi DA, Parker M, Kwiatkowski DP. Data Sharing and Intellectual Property in a Genomic Epidemiology Network: Policies for Large-Scale Research Collaboration. Bulletin of the World Health Organisation. 2006;84(5):382-7.

70 Kaye, Boddington et al. 2009; Heeney, Hawkins et al. 2011.

71 Knoppers BM, Saginur M. The Babel of genetic data terminology. Nat Biotech. 2005;23(8):925-7.

72 Heeney, Hawkins et al., 2011; Malin B, Sweeney L. How (not) to protect genomic data privacy in a distributed network: using trail re-identification to evaluate and design anonymity protection systems. Journal of Biomedical Informatics. 2004;37(3):179-92; Sweeney L. Information Explosion. In: Zayatz L, Doyle P, Theeuwes J, Lane J, editors.

argued, therefore, that absolute promises about confidentiality and privacy are untenable within the context of genomics research and should therefore not be made. However, this does not absolve researchers from maximising efforts to ensure that research data is used appropriately, by people authorised to do so, and in ways that do not harm research participants or their communities.

In the context of the SAHGP, important questions are (a) how will data be de-identified, and (b) whether this will be irreversible. What is important is to consider whether genomic data should link to clinical data, now or in the future. If the latter is the case, then it will be impossible to irreversibly de-identify genomic data, and participants should be made aware of this.

SECONDARY USE OF SAMPLES AND DATA

Another very important area of ethical concern relates to secondary use of data and samples. As mentioned earlier, genomic material can be frozen and stored for extended periods of time, especially when divided into different aliquots to avoid repeated thawing and freezing. The advantage is that samples can be re-sequenced as technology is improved or when cost is reduced. The challenge is that research participants may not be aware that their samples are stored for extended periods of time. Another challenge is the development of an appropriate governance mechanism to ensure that sample re-use is compatible with consent and ethics approval. A further complicating factor is when samples are exported for analysis. The SAHGP needs to consider oversight of sample re-use in designing the governance structure.

With regard to secondary use of data, ethical issues arise in relation to consent and ethics approval, as well as with the potential for harm to arise out of the misuse of research data. With regard to compatibility to consent and ethics approval, it will be important for the SAHGP to monitor these carefully and keep detailed records of the types of research that data can be used for. With regard to the potential for harm arising out of inappropriate applications of the genomic data, it will be important for the SAHGP to specify the nature of this problem, and to define appropriate ways of dealing with this. To date, however, no examples exist anywhere in the world where genomics data was wilfully abused to generate harm for research participants.

Confidentiality, Disclosure, and Data Access: Theory and Practical Applications for Statistical Agencies: Urban Institute, Washington; 2001; Rothstein 2010.

The SAHGP will need to ensure that issues around sample and data re-use, as well as around data sharing, are constantly monitored and evaluated by the governance body. The notions of enduring or presumed consent which are used elsewhere in the world to address the secondary use of samples and data are not legally acceptable and compatible with the present legal framework regarding informed consent in South Africa.

PATENTS, COMMERCIALISATION AND BENEFIT-SHARING

Aspects regarding commercialisation and intellectual property rights in respect of information derived from genetic sequencing impact on the translation of genetic discoveries into health benefits and require detailed consideration. Who will own the data generated from DNA sequencing in the context of the SAHGP? Should the individuals from whom this information is obtained be entitled to royalties from DNA-based products and technologies? The Intellectual Property Rights from Publicly Financed Research and Development Act 51 of 2008 will govern this to some extent in South Africa.[73] Some research, however, may be conducted without public funds, thus falling outside the scope of the last-mentioned Act. Not all research holds the promise of intellectual property rights, yet benefit-sharing may still be relevant. The idea of benefit-sharing has its origin in the perception of injustice that may emerge from inequalities of power between the global medical industry and the resource-rich, yet less developed countries. As a mechanism to restore equilibrium to the asymmetry between researcher and participant in the spirit of deontological considerations of fairness, benefit sharing has become a specific principle of research governance consistent with social justice.[74]

The idea that genetic and genomic material is sacred, priceless or non-commercialisable, flows from various understandings of humanist and religious accounts of human bodily integrity, emphasised in UNESCO's 1997 Declaration on the Human Genome and Human Rights that describes the human genome as the "heritage of humanity".[75] However, in the context of

73 This act only applies to publicly-financed research.

74 Slabbert, MN. The legal regulation of access and benefit-sharing with regard to human genetic resources in South Africa. Tydskrif vir Hedendaagse Romeins-Hollandse Reg. 2011 (in press).

75 See UNESCO, Universal Declaration on the Human Genome and Human Rights, General Conference Res 29 C/Res16, reprinted in Records of the General Conference, UNESCO, 29th Sess, 29 C/Resolution 19, 41 (1997) (adopted by the UN General Assembly, GA res

human genetics and the potential for considerable profits to be generated from this field of research, it seems hypocritical to demand altruistic donations from participants in poor and developing countries, whilst industry-led researchers from developed countries reap all the benefit, especially if the purpose of the "genetic mining" in less developed countries is to produce products aimed solely at affluent populations of industrialised countries. Also, promising a share of benefits to participants seems to contravene ethical principles that the body or human genome should not give rise to financial gain. In addition, the ethical validity of consent given under the promise of benefits to be gained is also questionable. The flipside of this is of course that although there is ethical objection to making a profit from genetic material, human DNA may in reality be considered as already commercialised, and as such, appropriate compensation for individuals in exchange for commercial access to their DNA would be in accordance with respect for human rights.

It would be useful to separate the issues of ownership of the data, which would include patent and other intellectual property rights to generated data, from the issue of when and how it would be appropriate to offer any form of benefit-sharing to participants. On the one hand, any excessive offer of benefits would fall foul of the prohibition against "undue influence", in other words, encouraging participants for reasons that affect their judgement, yet on the other hand one would need a mechanism to deal with those rare cases where genetic samples might lead to the kind of discovery or technology for which a benefit-sharing process might be appropriate.

Relevant in this context is the importance of carefully drafted Material Transfer Agreements. A generic MTA in terms of genomics is suggested for use in the context of the SAHGP. One of the issues that could be contractually negotiated, for example, is that of the analysis of data outside South Africa's borders so that local capacity and expertise is strengthened, access to data is ensured and that consideration is given to benefit-sharing.

GENOMIC SOVEREIGNTY

Genomic sovereignty is the capacity of a people, a country or nation to own, and control both access to and use of, samples, data and knowledge concerning

152, UN GAOR, 53rd Sess, UN Doc A/RES/53/152 (1999)).

or emanating from genomic material.[76] South Africa is a resource rich nation, and has one of the greatest biodiversities in terms of natural fauna and flora on the planet. South Africa also boasts a high degree of diversity with regards to its human population.

South Africa's biodiversity has been recognised for many decades, and a significant amount of biological material (human, animal and plant) has left the country during this time.[77] This material has provided an important source of genetic/genomic information which has been used effectively for the advancement of science. Regrettably, while successful careers and academic and commercial endeavours have benefited from this knowledge, very little recognition has been given to the source of the material in terms of access to the information derived or in terms of benefit-sharing (commercial and other) to the communities from which the material was derived.

In a country with the potential to build skilled resources, it is important that resources are built locally. For example, understanding the pathogenesis of disease in an indigenous population is best done by the people of that area. Southern Africa has some very specific patterns of diseases that need to be recognised, studied and analysed in a local context taking into consideration the population structures of the region. Retention of genetic/genomic material within the borders of southern African countries and analysis of this material by locally skilled individuals using locally-developed resources, alone or in collaboration with external partners, is seen as a key factor in promoting the notion of sovereignty.

Legislation in South Africa that affects this area includes the Biodiversity Act 10 of 2004 which, amongst other things, regulates bio-prospecting activities and access to and benefit-sharing from indigenous biological resources. However while this Act deals with animals and plants, genetic material of *human* origin is specifically excluded and the Act is silent on the issue of genomic sovereignty. The National Health Act 61 of 2003, which replaced the Human Tissue Act 65 of 1983, is also silent on the issues of access, benefit sharing and genomic sovereignty. In addition, there are no national guidelines

76 See, in general, Slabbert and Pepper 2010. See also Benjamin R. A Lab of Their Own: Genomic sovereignty as postcolonial science policy. Policy and Society. 2009;28(4):341-55.

77 See, for example, McGown, J. Out of Africa: Mysteries of Access and Benefit Sharing. Edmonds Institute and African Center for Biosafety. 2006, and McGown, J. Pirating African Heritage. 2009. African Center for Biosafety.

governing genomic research and its legal or ethical ramifications that succeed in balancing the protection of human genetic information with the promotion of international collaboration that may increase the development of local scientific capacity.[78]

Thus, although Chapter 6 of the Biodiversity Act does attempt to regulate benefit-sharing and bio-prospecting regarding indigenous biological resources, including genetic material of animals and plants, as mentioned above legislation in this respect regarding humans is completely lacking. It is also interesting to note that in 1995 the Convention for Biological Diversity,[79] of which South Africa is a signatory, specifically excludes human genetic resources from its ambit. The present international legislative framework governing genomic research is a fragmentary one, consisting of various statements, guidelines and documents that address general principles and activities. None have a clear mandate or authority to formulate an internationally accepted position or norms and standards to oversee the governance of international collaborative genomic research.[80]

Concern has been expressed regarding the above unregulated practices regarding genetic/genomic material of human origin in South Africa.[81] The following proposals, contained in the National Biotechnology Advisory Committee (to the South African Minister of Science and Technology) position paper on genomic sovereignty, are suggested to address some of these issues:

1. The notion of genetic sovereignty should be debated more widely in open public fora;
2. Measures should be put into place to regulate and monitor the flow of genetic/genomic material into and out of the country;
3. The development of bioinformatics skills should be regarded as a national priority;

78 Slabbert and Pepper, 2010.

79 Signed by 150 government leaders at the 1992 Rio Earth Summit, dedicated to promote sustainable development. The Convention, negotiated under the auspices of the United Nations Environment Programme (UNEP), entered into force on 23 December 1993. The three goals of the CBD are to promote the conservation of biodiversity, the sustainable use of its components, and the fair and equitable sharing of benefits arising out of the utilisation of genetic resources.

80 Slabbert and Pepper, 2010.

81 Available at http://www.nacinnovation.biz/wp-content/uploads/NBAC-position-statement-on-Genomic-Sovereignty-in-South-Africa.pdf (visited 30 May 2011).

4. The opportunity afforded by the current revision of Chapter 8 of the National Health Act, which has not been promulgated to date and which deals with "Control of use of blood, blood products, tissue and gametes in humans", should be used to address the legislative gap with respect to human genetic/genomic material.

In the absence of a clear regulatory framework and no specific insistence on access and benefit-sharing, there is nothing to protect the exploitation of genomic information of southern African populations.

CONCLUSION

In order to address the many critical issues that have been raised in this article, it is suggested that the SAHGP should institutionalise a governance body from the outset of its activities, which comprises relevant South African experts in the fields of law, ethics, medicine, genomic science, sociology, anthropology or other relevant fields. The tasks of this governance body would be:

1. to liaise with project researchers, international experts and other SAHGP governance bodies to identify, discuss and propose solutions for ethical and legal challenges in the SAHGP;
2. to facilitate the development of ethical guidelines and policies for the SAHGP;
3. to harmonise consent forms and ethical approval for the various projects contributing samples and data to the SAHGP repositories;
4. to monitor and evaluate the ethical aspects of the SAHGP.

In summary, this article has highlighted a number of intricate ethical, legal, and social issues relevant to the development of the Southern African Human Genome Programme. The complex interactions between these issues, against the background of an ethnically diverse population, requires careful consideration if the Programme is to be successful. To compound the present situation, the legal framework regarding genomic research is seriously defective and insufficient. In particular, safeguards need to be put into place to ensure that when human tissues or DNA leave their country of origin to be exploited elsewhere, this is done with the understanding that access to information and benefit returning to the local population are of paramount importance. It is hoped that this article will assist in facilitating public debate regarding the ethical, legal and social issues relevant to the SAHGP, as the

manner in which these issues will be addressed will ultimately determine the success of the Programme.

REFERENCES

Benjamin R (2009). A Lab of Their Own: Genomic sovereignty as postcolonial science policy. *Policy and Society* 28(4):341-55.

Beskow LM, Dean E (2008). Informed Consent for Biorepositories: Assessing Prospective Participants' Understanding and Opinions. *Cancer Epidemiol Biomarkers Prev*. 17(6):1440-51.

Bredenoord A, Onland-Moret CN, Van Delden JJM. (2011) Feedback of Individual Genetic Results to Research Participants: in Favour of a Qualified Disclosure Policy. *Human Mutation* 32:1-7.

Boyd AD, Hunscher AD, et al. The 'honest broker' method of integrating interdisciplinary research data. 2005. Proceedings of the AMAI Annual Symposium 902, available from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1560785/ (visited 15 May 2011).

Caulfield T, McGuire AL, et al. (2008). Research Ethics Recommendations for Whole-Genome Research: Consensus Statement. *Plos Biology* 6(3): e73.

Cho MK (2008), Understanding Incidental Findings in the Context of Genetics and Genomics. The *Journal of Law, Medicine & Ethics* 36(2):280-5.

Chokshi DA, Parker M, et al. (2006). "Data Sharing and Intellectual Property in a Genomic Epidemiology Network: Policies for Large-Scale Research Collaboration." *Bulletin of the World Health Organisation* 84(5): 382-387.

Chokshi DA. Thera MA, et al. (2007). Valid Consent for Genomic Epidemiology in Developing Countries. *PLoS Med* 4(4): e95.

Conley J. (2009), "Enabling responsible public genomics", available from http://works.bepress.com/cgi/viewcontent.cgi?article=1000&context=john_conley&sei-redir=1#search="1000genomes+project+consent+template" (visited 10 May 2011).

De Vries J, Bull SJ, et al. (2011). Ethical Issues in Human Genomics Research in Developing Countries. *BMC Medical Ethics*.

Dhai A. (2005). Research Ethics Review - protecting participants in research. *South African Medical Journal* 95: 595-597.

Dhai A, Etheredge H, Cleaton-Jones P (2010). A pilot study evaluating an intervention designed to raise awareness of clinical trials among potential participants in the developing world. *Journal of Medical Ethics* 36(4):238-42.

Editorial (2004). The unexamined 'Caucasian'. *Nat Genet*. 36(6):541.

Fairhead J, Leach M, Small M (2006). Where techno-science meets poverty: Medical research and the economy of blood in The Gambia, West Africa. *Social Science & Medicine* 63(4):1109-20.

Frank R. What to make of it? The (Re)emergence of a biological conceptualization of race in health disparities research. Social Science & Medicine. 2007;64(10):1977-83.

Foster MW, Sharp RR (2006) Ethical issues in medical-sequencing research: implications of genotype-phenotype studies for individuals and populations. *Hum Mol Genet*. 15(suppl_1):R45-9.

Gikonyo C, Bejon P et al. (2008). Taking social relationships seriously: Lessons learned from the informed consent practices of a vaccine trial on the Kenyan Coast. *Social Science & Medicine* 67(5): 708-720.

Goodman KW (1996). "Ethics, genomics, and information retrieval." *Computers in Biology and Medicine* 26(3): 223-229.

Harmon A (2010). Tribe wins fight to limit research of its DNA. New York Times. New York.

HeeneyC, Hawkins N, et al. (2011). Assessing the Privacy Risks of Data Sharing in Genomics. *Public Health Genomics* 14(1): 17-25.

Hofmann (2009). Broadening consent - and diluting ethics? *J Med Ethics* 35: 125-129.

Kaye J, Boddington P, et al. (2009). Ethical, Legal and Social Issues Arising from the Use of GWAS in Medical Research. London, Wellcome Trust.

Kaye J, Boddington P, et al. (2010). Ethical implications of the use of whole genome methods in medical research. *Eur J Hum Genet* 18(4).

Kaye J, Heeney C, et al. (2009). Data sharing in genomics: re-shaping scientific practice. *Nat Rev Genet* 10: 331-335.

Knoppers BM and Saginur M (2005). The Babel of genetic data terminology. *Nat Biotech* 23(8): 925-927.

Lowrance WW and Collins FS (2007). *Identifiability in Genomic Research. Science* 317(5838): 600-602.

Lunshof JE, Chadwick R, et al. (2008). From genetic privacy to open consent. *Nat Rev Genet* 9(5): 406-411.

Malin B. and Sweeney L (2004). How (not) to protect genomic data privacy in a distributed network: using trail re-identification to evaluate and design anonymity protection systems. *Journal of Biomedical Informatics* 37(3): 179-192.

Marks J (2005). Your Body, My Property: the Problem of Colonial Genetics in a Postcolonial World. Embedding Ethics. L. Meskell and P. Pels, Berg Publishing.

Marsh V, Kamuya D, et al. (2008). Beginning community engagement at a busy biomedical research programme: Experiences from the KEMRI CGMRC-Wellcome Trust Research Programme, Kilifi, Kenya. *Social Science & Medicine* doi:10.1016/j.socscimed.2008.02.007.

Mascalzoni, D, Hicks A, et al. (2008). "Informed Consent in the Genomics Era." *PLoS Medicine* 5(9): e192.

Mayet M (2005) "GM crops for Africa: No thanks!" Institute of Science in Society Report, accessed at http://www.i-sis.org.uk/GMCFANT.php (visited 10 May 2011)

McGown J (2006) Out of Africa: Mysteries of Access and Benefit Sharing. Edmonds Institute and African Center for Biosafety. Available at http://www.edmonds-institute.org/outofafrica.pdf (visited 14 June 2011).

McGown J. Pirating African Heritage. 2009. African Center for Biosafety. Available at http://www.scribd.com/doc/22444300/African-Center-for-Biosafety-09-Pirating-African-Heritage (visited 14 June 2011).

McGregor J. (2010). Racial, Ethnic, and Tribal Classifications in Biomedical

Research With Biological and Group Harm. *The American Journal of Bioethics* 10(9): 23-24.

McGuire AL, Caulfield T, et al. (2008). Research ethics and the challenge of whole-genome sequencing. *Nat Rev Genet* 9(2): 152-156.

McGuire AL, Beskow LM. (2010) Informed Consent in Genomics and Genetic Research. Annual Review of Genomics and Human Genetics 11(1).

Mello MM and Wolf LE (2010). The Havasupai Indian Tribe Case — Lessons for Research Involving Stored Biologic Samples. *New England Journal of Medicine* 363(3): 204-207.

Molyneux CS, Peshu N, et al. (2004). Understanding of informed consent in a low-income setting: three case studies from the *Kenyan coast. Social Science & Medicine* 59(12): 2547-2559.

Mountain JL, Risch N. Assessing genetic contributions to phenotypic differences among 'racial' and 'ethnic' groups. *Nat Genet*. 2004.

Nyika A. (2009). Ethical and practical challenges surrounding genetic and genomic research in developing countries. Acta Tropica 112(Supplement 1): S21-S31.

Nuffield Council on Bioethics. Genetic Screening. London: Nuffield Council on Bioethics1993.

Parfitt T. (2003). Constructing Black Jews: Genetic Tests and the Lemba – the 'Black Jews' of South Africa. *Developing World Bioethics* 3(2): 112-118.

Parfitt T. and Egorova Y (2005). Genetics, Mass Media, and Identity: A Case Study of the Genetic Research on the Lemba and Bene Israel. London, Routledge.

Parker M., Bull SJ, et al. (2009). "Ethical Data Release in Genome-Wide Association Studies in Developing Countries. *PLoS Med* 6(11): e1000143.

Pepper, MS (2010). The human genome and molecular medicine - promises and pitfalls. *S. Afr*. *Med J.* 100(1): 722-724.

Pepper MS. (2011). Launch of the Southern African Human Genome Programme. *S Afr Med J.* 101(5): 287-288.

Reardon J (2005). Race to the Finish. Identity and Governance in an Age of Genomics. Princeton and Oxford, Princeton University Press.

Rothstein MA (1998). Genetic Privacy and Confidentiality: Why They Are So Hard to Protect. *The Journal of Law, Medicine & Ethics* 26(3): 198-204.

Rothstein MA. (2010) Is Deidentification Sufficient to Protect Health Privacy in Research? *The American Journal of Bioethics* 10(9):3 - 11.

Rotimi C., Leppert M, et al. (2007). Community Engagement and Informed Consent in the International HapMap Project. *Community Genetics* 10: 186-198.

Singh J. and Daar AS (2009). Intra-consortium data sharing in multi-national, multi-institutional genomic studies: gaps and guidance. *The HUGO Journal* 3(1): 11-14.

Slabbert MN (2006). 'Genes 'R' Us': A critique of genetic essentialism *Stellenbosch Law Review* 17(2): 251-265.

Slabbert, MN (2007). Genetic privacy in South Africa and Europe: A comparative perspective (Part I) Tydskrif vir Hedendaagse Romeins-Hollandse Reg (*Journal of Contemporary Roman-Dutch Law*) 70: 622-637.

Slabbert MN (2008). Genetic privacy in South Africa and Europe: A comparative perspective (Part II) Tydskrif vir Hedendaagse Romeins-Hollandse Reg (*Journal of Contemporary Roman-Dutch Law*) 70: 81-100.

Slabbert MN (2011). The legal regulation of access and benefit-sharing of human genetic resources in South Africa Tydskrif vir Hedendaagse Romeins-Hollandse Reg (*Journal of Contemporary Roman-Dutch Law*) (in press)

Slabbert, MN. and Pepper, M. S (2010). "A room of our own?" Legal *lacunae* regarding genomic sovereignty in South Africa" Tydskrif vir Hedendaagse Romeins-Hollandse Reg (*Journal of Contemporary Roman-Dutch Law*) 73: 432-450.

Strauss SA. *Doctor, Patient and the Law: A Selection of Practical Issues*. Goodwood: Van Schaik; 1991.

Sweeney L. (2001). Information Explosion. Confidentiality, Disclosure, and Data Access: Theory and Practical Applications for Statistical Agencies. L.

Zayatz, P. Doyle, J. Theeuwes and J. Lane, Urban Institute, Washington.

Tekola F, Bull SJ, et al. (2009). Tailoring Consent to Context: Designing an Appropriate Consent Process for a Biomedical Study in a Low Income Setting. *PLoS Negl Trop Dis*. 3(7):e482.

Tekola F, Bull SJ, et al. (2009). Impact of social stigma on the process of obtaining informed consent for genetic research on podoconiosis: a qualitative study. *BMC Medical Ethics* 10(1): 13.

The MalariaGEN Consortium (2008). A global network for investigating the genomic epidemiology of malaria. Nature 456(7223): 732-737.

Thomas MG, Parfitt T, et al. (2000). Y Chromosomes Traveling South: The Cohen Modal Haplotype and the Origins of the Lemba—the 'Black Jews of Southern Africa' *Am J Hum Genet* 66(2): 674-686.

Tindana PO, Kass N, et al. (2006). The Informed Consent Process in a Rural African Setting: A Case Study of the Kassena-Nankana District of Northern Ghana. IRB: *Ethics and Human Research* 28(3): 1-6.

Tindana PO, Singh JA, et al. (2007). Grand Challenges in Global Health: Community Engagement in Research in Developing Countries. *PLoS Med* 4(9): e273.

Tsotsi N (2009). Informed consent in research in developing countries: is there some unfinished business? Report submitted in partial fulfilment of the MScMed degree. Faculty of Health Sciences, University of the Witwatersrand, 1-86.

Van Oosten FFW. The Doctrine of Informed Consent in Medical Law. LLD, 1989: UNISA.

Van Rinsum H, Tangwa GB. (2004) Colony of genes, genes of the colony: diversity, difference and divide. *Third World Quarterly* 25:1031-43.

Vorhaus DB (2010). The Havasupai Indians and the Challenge of Informed Consent for Genomic Research. Available from http://www.genomicslawreport.com/index.php/2010/04/21/the-havasupai-indians-and-the-challenge-of-informed-consent-for-genomic-research/.

Walport M. and Brest P (2011). Sharing research data to improve public health. *The Lancet* 377: 538-539.

White L. (2000) Speaking with Vampires: Rumor and History in Colonial Africa. Berkeley and Los Angelos: University of California Press.

WHO (2002). Genomics and World Health, World Health Organisation.

Wolf SM, Lawrenz FP, et al. (2008) Managing Incidental Findings in Human Subjects Research: Analysis and Recommendations. *The Journal of Law, Medicine & Ethics* 36(2):219-48.