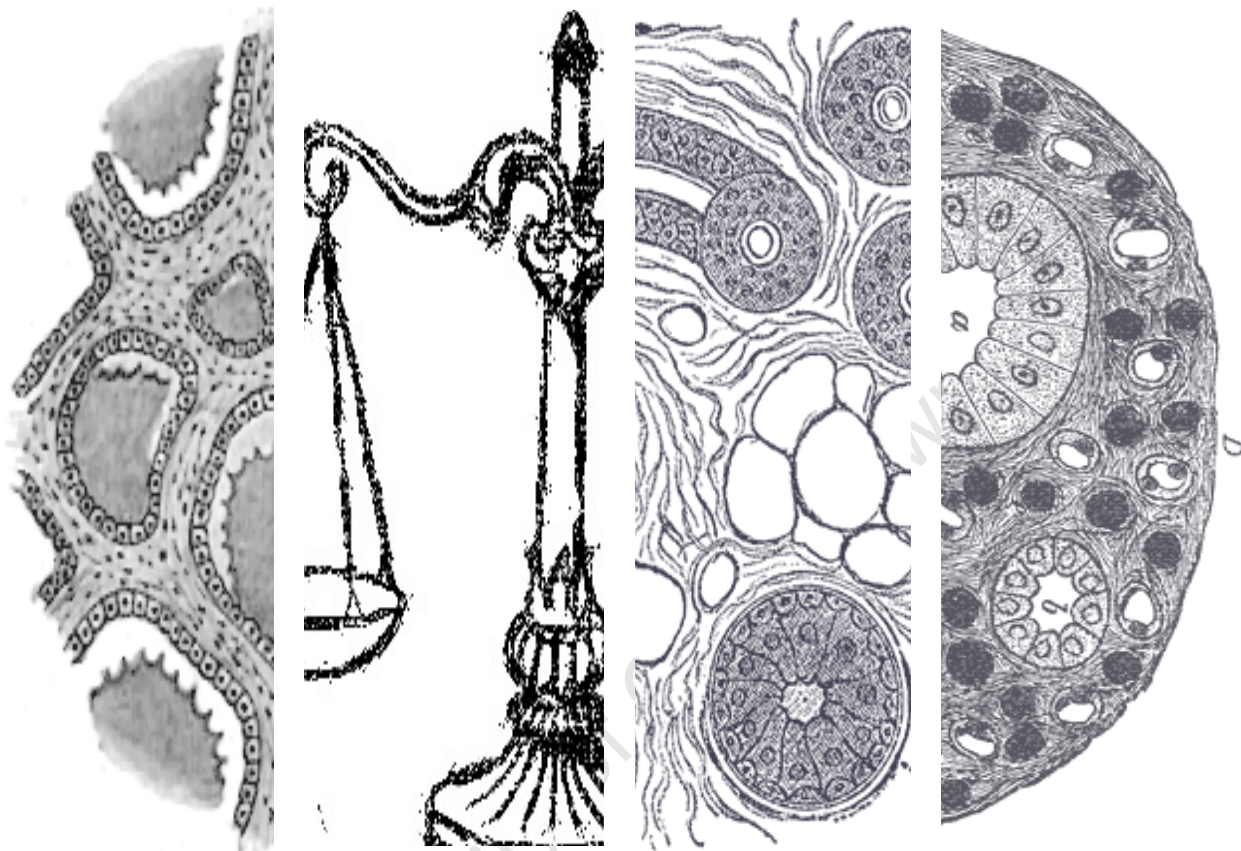


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Informed Consent and the Secondary Use of Biospecimens in Oncology Research

Legal and Bioethics Perspectives



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Research dissertation presented for the approval of Senate in fulfillment of part of the requirements for the degree of *LLM (Biotechnology, Ethics and Law)* in approved courses and a minor dissertation. The other part of the requirement for this qualification was the completion of a programme of courses.

I hereby declare that I have read and understood the regulations governing the submission of *LLM (Biotechnology, Ethics and Law)* dissertations, including those relating to length and plagiarism, as contained in the rules of this University, and that this dissertation conforms to those regulations.

.....
Pieter Miguel Erasmus

.....
Date

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CHAPTER 1

1.1 Introduction

Biospecimens¹ collected during routine oncology diagnostic and therapeutic interventions may be stored for future medical purposes. In accordance with legal and ethical principles, the patient provides informed consent for removal of the tissue for diagnostic or therapeutic reasons. Informed consent gives permission for the violation of bodily integrity that is inevitable with tissue removal. Simultaneously, informed consent may be provided for storage of surplus tissue for purposes such as future cancer research.² Usually, the nature

¹ The term 'biospecimen' refers to any quantity of tissue, blood, urine or other human-derived material, which includes cells (including sub-cellular structures such as DNA), tissue, organs, gametes, embryos, bodily waste and so on. A single biopsy has the potential to yield several of these biospecimens. The focus of this dissertation is on biospecimens harvested during diagnostic and/or therapeutic procedures in the oncology context specifically. 'National Cancer Institute Best Practices for Biospecimen Resources' (2007) published by the National Cancer Institute (NCI) available at http://biospecimens.cancer.gov/global/pdfs/NCI_Best_Practices_060507.pdf (accessed 29 March 2011) at 31.

² The National Health Act 61 of 2003 uses the term 'health research' in its definition section. The terms 'health' and 'medical' research will be used interchangeably in this dissertation. 'Health research' is given a very wide definition which

- '...includes any research which contributes to the knowledge of –
- (a) the biological, clinical, psychological or social processes in human beings;
 - (b) improved methods for the provision of health services;
 - (c) human pathology;
 - (d) the causes of disease;
 - (e) the effects of the environment on the human body;
 - (f) the development or new application of pharmaceuticals, medicines and related substances; and
 - (g) the development of new applications of health technology...'

In addition, the United States National Commission for the Protection of Human Subjects provides a more in depth description of 'health research', which the South African national policy on research ethics quotes on page 1 of Ethics in Health Research: Principles, Structures and Processes, as cited below at note 52. This description of 'health research' acts as a guide to the understanding of the term, and reads as follows:

'A research project generally is described in a protocol that sets forth explicit objectives and formal procedures designed to reach those objectives. The protocol may include therapeutic and other activities intended to benefit the subjects, as well as procedures to evaluate such activities. Research objectives range from understanding normal and abnormal physiological or psychological functions or social phenomena, to evaluating diagnostic, therapeutic or preventive interventions and variations in services or practices. The activities or procedures involved in research may be invasive or non-invasive and include surgical interventions; removal of body tissues or fluids; administration of chemical substances or forms of energy; modifications of diet; daily routine or service delivery; alteration of environment; observation; administration of questions or tests; randomization; review of records etc.'

and purpose of the research is spelled out so that the person is enabled to give *informed* consent for the use of tissue in research. However, the specific purpose of future research is seldom certain at the time of consent. This uncertainty and other factors result in complexities pertaining to the requirement of informed consent in these circumstances.³

The ethical dilemma is whether the formal consent requirements must be adhered to or whether it would be justifiable to use surplus tissue in oncology research without consent. A balance must be struck between respect for autonomy and societal interests in expanding oncology knowledge. If the patient did not consent specifically to use of the tissue for research purposes, then, strictly speaking, research cannot be done with that tissue. This is because the golden rule determines that research with humans as participants may take place only when informed consent has been given before such research begins. However, this rule may be over-zealously applied to the use of stored tissue. This is, firstly, because the person from whom the tissue was taken would not actually be a participant in the research and, secondly, once removed from the human body, the tissue is regarded as an object. Although, the law prevents free trade in body parts and human tissue, it is quite clear that human tissue is something different from a human being and that, consequently, informed consent requirements may differ considerably.⁴ Nevertheless, the informed consent requirements for human participation in research are apparently applied uncritically to the context where stored tissue is used in research. Sometimes an exception is made when only anonymised tissue samples are to be used. In other words, because the source of the tissue sample cannot be identified, the concern about informed consent is apparently diminished.

³ Fobelets G and Nys H 'Evolution in research biobanks and its legal consequences' in Dierickx K and Borry P (eds) *New Challenges for Biobanks: Ethics, Law and Governance* (2009) 19 at 19-21; Price D *Human Tissue in Transplantation and Research: A Model Legal and Ethical Donation Framework* (2010) at 169.

⁴ This complex topic could be the subject matter of a separate dissertation. Consequently, it is not dealt with in any detail here.

1.1.1 Utility of human biospecimens

The primary purpose of biospecimens is their use as tools in diagnosis and treatment of disease.⁵ For example, stored⁶ tissue samples, whether healthy or not, may be used as comparators to diagnose the state of cells under consideration.

However, stored oncology biospecimens are important resources for research endeavours. Biospecimens and their associated data⁷ provide information at a cellular level that facilitates research into detection, treatment and prevention of cancer. Enhanced understanding of the mechanics of cancer has the potential to improve current treatment regimens. In addition, biospecimens allow categorisation of cancer types according to molecular and histopathological structure, which enables effective treatment.⁸ Analytical tools and techniques in cancer research have improved as advances in biomolecular technology have been made, especially in developing personalised medicine.⁹ This enables a tailor-made approach, in which a treatment regimen is developed to address an individual patient or specific variant of disease. Such a personalised approach promises to bring treatment efficacy to new heights.¹⁰

⁵ Eiseman E and Haga SB 'Handbook of human tissue resources' (1999) published by the Research and Development Corporation (RAND) available at http://www.rand.org/pubs/monograph_reports/MR954.html#toc (accessed 23 March 2011) at 1; Salvaterra E et al 'Banking together: a unified model of informed consent for biobanking' (2008) 9 *European Molecular Biology Organisation Reports* 307 at 307.

⁶ The physical storage of human tissue is a science in itself and the scope of this dissertation does not allow for the in-depth discussion of it. However, for enrichment purposes, it suffices to mention that human tissue specimens can be stored in various ways, such as in paraffin blocks, frozen, as a tissue culture, formalin-fixed, in the form of slides or extracted DNA. These modes of storage allow for the microscopic study of the cellular and molecular structure of the tissue cells, which allow diagnosis by comparing a patient's tissue sample with stored tissue. Eiseman E and Haga SB (note 5) at 1; Price D (note 3) at 169.

⁷ Biospecimen-associated data refers to any information associated and collected with the biospecimen and includes research data, phenotype data, clinical data, epidemiological data and the biospecimen resource data. NCI (note 1) at 31.

⁸ NCI (note 1) at 1.

⁹ Oosterhuis JW et al 'Tumour banks: well-guarded treasures in the interest of patients' (2003) 3 *Nature Reviews: Cancer* 73 at 73.

¹⁰ An example of personalised medicine or targeted therapy is the use of the ErBB2-specific antibody called trastuzumab (marketed as Herceptin) in cases of ErBB2-positive breast cancers. ErBB2 refers to a specific biomarker (gene) that codes for the susceptibility to this strain of breast cancer. Simply put, if the ErBB2 gene mutates, the development of this particular strain of breast cancer is imminent. The use of targeted therapy potentially reduces the side effects that would occur if a non-targeted approach were followed. William R et al 'Integrating biobanks: addressing the practical and ethical issues to deliver a valuable tool for

Each year, cancer claims more lives than HIV/AIDS, malaria and tuberculosis combined and accounts for one in eight deaths worldwide.¹¹ In the developing world it is the third leading cause of death.¹² Consequently, it is somewhat surprising that, even though the burden of this disease is very high in South Africa, the Cancer Research Initiative of South Africa (CARISA)¹³ notes that local oncology research is highly fragmented with relatively low government participation.¹⁴

Although tissue and cell lines derived from non-human sources are also valuable for medical research, human tissue is essential in the research process, for example, to determine accuracy and confirm preliminary research findings. Medical research is first and foremost aimed at improving human health.¹⁵ Society has an interest in oncology research insofar as a potential collective benefit is at stake.

At a policy level, a balance must be struck between fostering society's interests (in advancing knowledge about oncology) and protecting the individual's interests (in preventing unethical use of tissue samples). Careful consideration must be given to informed consent requirements for secondary use of biospecimens, in particular whether they are essential in this context.¹⁶ Informed consent requirements concretise the right to self-determination or autonomy. The importance of tissue banks that source, store and provide

cancer research' (2010) 10 *Nature Reviews: Cancer* 646 at 646.

¹¹ This is based on statistics published in 2007 by the American Cancer Society: *Global Cancer Facts & Figures 2007*. See 'Situational/Landscape Analysis of South Africa and International Cancer Research' (2008) published by Cancer Research Initiative of South Africa (CARISA) available at http://www.carisa.org.za/documents/report_10-08-2008.pdf (accessed 7 February 2012) at 13-4. The World Health Organization has also identified cancer as a leading cause of death worldwide, accounting for 7.6 million deaths, in 2008. See also Cancer Fact Sheet 297 (Oct 2011) available at <http://www.who.int/mediacentre/factsheets/fs297/en/index.html> (accessed 1 Feb 2012).

¹² CARISA (note 11) at 13-4.

¹³ CARISA was founded by the Medical Research Council of South Africa (MRC) and the Cancer Association of South Africa (CANSAs) in 2005 in order to facilitate and coordinate local cancer research. CARISA (note 11) at 7.

¹⁴ Government research institutions conduct 38 per cent of local cancer research, while universities conduct a considerable majority of 60 per cent. CARISA (note 11) at 8.

¹⁵ Salvaterra E et al (note 5) at 307.

¹⁶ Fobelets G and Nys H (note 3) at 21.

access to samples and related data is clear.¹⁷ It is therefore apparent that the utility of biospecimens extends beyond diagnostic and therapeutic purposes.

1.1.2 Collection of biospecimens and the concept of secondary use

Tissue banks and repositories should be adequately stocked with human tissue for use in medical research projects if the South African oncology research enterprise is to flourish. By far the most common method of sourcing human biospecimens for research purposes is from surplus tissue taken during diagnostic or therapeutic procedures such as biopsies.¹⁸ In most cases, diagnostic and therapeutic surgical procedures yield more tissue than may be strictly required for current diagnostic confirmation. Storage of the surplus tissue allows further future diagnostic or therapy-related tests to be undertaken without having to perform a biopsy again.¹⁹ Other means of sourcing specimens include removal of tissue from persons with express consent for use in particular research, and samples gathered during autopsies.²⁰

Storage may be indefinite or for the lifetime of the donor patient. Indefinite retention of these biospecimens represents an important research resource²¹, even though the tissue was stored initially for the sole benefit of the patient.²²

The concept of secondary use applies to a situation where surplus tissue removed for diagnostic purposes and stored, is later utilised for research not anticipated at the time of removal. The question is whether use of this stored

¹⁷ Salvaterra E et al (note 5) at 307.

¹⁸ Eiseman E and Haga SB (note 5) at 1; Nienaber A 'Consent to and authorisation of the export and use of human biological specimens for future research – perspectives from three African countries' (2011) XLIV *CILSA* 225 at 225.

¹⁹ Van Diest PJ and Savulescu J 'For and against: no consent should be needed for using leftover body material for scientific purposes' (2002) 325 *BMJ* 648 at 648; Elger B 'Consent to research involving human biological samples obtained during medical care' in Elger B et al (eds) *Ethical Issues in Governing Biobanks: Global Perspectives* (2008) 89 at 89-90.

²⁰ Eiseman E and Haga SB (note 5) at 1.

²¹ In addition to possible medical research, other uses for stored tissue include its use for teaching and control specimens used for other patients' diagnostic and prognostic testing. Van Diest PJ and Savulescu J (note 19) at 648.

²² Vermeulen E et al 'Opt-out plus, the patients' choice: preferences of cancer patients concerning information and consent regimen for future research with biological samples archived in the context of treatment' (2009) 62 *J Clin Pathol* 275 at 275.

tissue may be legally and ethically acceptable, despite the absence of specific informed consent.²³ A strict view of informed consent requirements for research would oppose such use on the basis that consent must be express and specific. A different view may argue that the consent to removal and storage of tissue for diagnostic and therapy purposes ought to include consent for use of the tissue in research related to the disease under consideration;²⁴ that this practice accords with accepted trends for advancement of knowledge in oncology.

1.1.3 Focus of the dissertation

The focus of this dissertation is on legal and ethical perspectives on secondary use of stored oncology biospecimens harvested without express consent for use in research. The primary research question is whether specific informed consent is necessary for secondary use of biospecimens collected for diagnostic or therapeutic purposes.

The current South African legal and ethics frameworks are examined and compared primarily to those of Australia. Relevant international instruments are also studied. Other aspects to be explored include the validity of asserting that self-determination is curtailed even though the biospecimen has long been separated from the patient's body.

It will become apparent that the current position in South African law pertaining to informed consent and secondary use of tissue in research is rather rigid. Consequently, the usual view is that fresh consent should be sought for secondary use of biospecimens in research projects. But this seems to be unnecessarily formalistic. The aim is to identify an appropriate alternative model of consent for secondary use of biospecimens in research.

The scope of discussion excludes consideration of genetic-specific nuances that may affect informed consent. It suffices to mention that where DNA is involved, privacy-related issues are a concern.

²³ Price D (note 3) at 168; Van Diest PJ and Savulescu J (note 19) at 648.

²⁴ Van Diest PJ and Savulescu J (note 19) at 648; Elger B (note 19) at 89-90.

The following section highlights particular difficulties associated with seeking fresh consent for secondary use in research. Thereafter, less strict consent models are reviewed.

1.2 Difficulties in acquiring new informed consent for secondary use of biospecimens

Getting specific informed consent for secondary use of stored biospecimens presents particular difficulties.²⁵ As mentioned earlier, the strict view of informed consent regards giving consent to use surplus tissue for research purposes at the same time as giving consent for tissue removal for diagnostic purposes as unacceptable. This is because the purpose of the future research is uncertain,²⁶ which, it is argued, undermines the proper exercise of autonomy. This section briefly describes some of the difficulties and possible solutions. In each case, however, the difficulties flow from a particular view of surplus tissue, viz that it continues to 'belong' to the donor patient despite having been separated from the body. Were this view to change, the difficulties would fall away.

Seeking specific informed consent for secondary use of stored biospecimens presents logistical difficulties in that donors may no longer be traceable or alive.²⁷ Apart from being a costly procedure, it could lead to a decline in available biospecimens for research,²⁸ which creates a burden for research. What follows is a brief discussion of the more important ethics difficulties.

²⁵ Stored tissue samples may have been obtained during medical care, or may form part of existing tissue collections. The ethical and legal questions related to the use of redundant samples obtained in the diagnostic and/or therapeutic contexts without informed consent for secondary research are not completely different from those arising from the secondary, unanticipated research use of samples taken for storage in a biobank primarily established for research. Elger B (note 19) at 89-90.

²⁶ Price D (note 3) at 170.

²⁷ Elger B and Caplan AL 'Consent and anonymization in research involving biobanks' (2006) 7(7) *European and Molecular Biology Organization Reports* 661 at 662; William R et al (note 10) at 648-9; Oosterhuis JW et al (note 9) at 75.

²⁸ Elger B and Caplan AL (note 27) at 662; Oosterhuis JW et al (note 9) at 75

1.2.1 Uncertainty

The patient's ability to provide informed consent for future research is limited by the lack of specificity and clarity regarding the proposed research.²⁹ Even if the future research is quite carefully planned and described at the time of consent, its purpose or focus may change over time,³⁰ due to scientific development that renders the proposed research out-dated and pointless. The previously given specific consent would be rendered futile.

Support³¹ exists for re-contacting patients to obtain specific informed consent once the research objectives have been finalised. Logistical matters make this solution impractical or even impossible if patients cannot be traced or have died. Furthermore, re-contacting is a lengthy and costly procedure.³²

It is axiomatic that informed consent to research participation requires clarity about what is expected of the participant. Consequently, the research and its interventions, the expectations of participants and the balance of risk of harm versus likelihood of benefit must be explained to the potential participant. In the case where stored surplus tissue is sought to be used, without prior mention of possible research on the samples, it is evident that donor patients had no opportunity to consider consent for this utilisation of their tissue samples.

A possible solution to this problem is to devise a consent process that includes discussion of the possibility of research on stored samples and to get permission at the same time that consent to removal of tissue is obtained. On the other hand, if the removed tissue was no longer associated with a particular person, the issue vanishes.

1.2.2 Lack of awareness about research

A second difficulty identified by scholars³³ is a lack of awareness amongst patients about the possibility that surplus tissue might be used for research

²⁹ Elger B (note 19) at 89-90.

³⁰ Fobelets G and Nys H (note 3) at 23-7.

³¹ Ibid.

³² Ibid.

³³ Elger B (note 19) at 89-90.

purposes. In other words, patients are often unaware that redundant tissue stored pursuant to diagnostic or therapeutic procedures may be used for future research.

This lack of awareness is seen to undermine the right to self-determination, exercised by providing specific informed consent. Whether this strict view is valid could be tested. For example, if there is persuasive evidence that, in general, most patients are hesitant to permit use of stored redundant tissue for research, then specific informed consent would be indicated. However, if most patients are willing to allow their stored tissue to be used in oncology research without further informed consent, then this would support the view that specific informed consent is unnecessary. Whether such empirical evidence exists in South Africa is unclear.

1.2.3 Vulnerability

In the third instance, certain authors³⁴ suggest that obtaining informed consent for secondary use from the patient in a clinical context is inappropriate because the patient is in a vulnerable state of mind at the time. Arguably, however, this vulnerability is easily addressed. Oncology-related biopsies are seldom emergencies. Patients can be informed of the possibility of research in advance of the clinical procedure. This would provide time to reconcile or not, with the possibility of use for research.

1.2.4 Perverse incentives and DNA

Other scholars have identified two further difficulties.³⁵ Firstly, the increase in demand for both diseased and healthy biospecimens for research purposes may incentivise pathology laboratories to store redundant biospecimens collected during diagnosis without the knowledge or informed consent of the patients.³⁶ In other words, suspicions are that, as a matter of business practice, supply of and demand for biospecimens may influence the manner in which they are sourced. However, suspicion is not a good basis for decision-making.

³⁴ Ibid.

³⁵ Fobelets G and Nys H (note 3) at 23-7.

³⁶ Ibid.

Factual evidence should be sought to demonstrate whether the suspicion is well-founded.

Lastly, a concern is that advances in genetic research and the very personal information encoded in DNA may challenge the usual processes of obtaining informed consent. Subsequent use of DNA is often not included in informed consent to removal of tissue for diagnostic purposes.³⁷

Legal and ethical norms and principles affect practical matters like collection of tissue, decisions about its subsequent use and whether patient data should be delinked from the sample.³⁸ In what follows, various instruments are examined to expose current trends.

1.3 Consent models

Internationally, no consensus exists about consent and secondary use of stored biospecimens.³⁹ Consent models vary from a very restrictive, specific informed consent only model to more liberal broader consent models.⁴⁰ The various models are described in the following section. The South African approach represents the strictest point on the spectrum of chosen jurisdictions. New specific informed consent is required where stored surplus tissue is to be used for research purposes unanticipated in the original consent,⁴¹ unless the research is to use only completely anonymised tissue samples.

Australia follows a relatively liberal consent model in the context where stored biospecimens are used for research purposes.⁴² In essence, a tiered model is used that ranges from specific consent for particular circumstances, to broader extended⁴³ and unspecified⁴⁴ consent in other circumstances. Donor

³⁷ Ibid.

³⁸ Fobelets G and Nys H (note 3) at 32-3.

³⁹ Salvaterra E et al (note 5) at 307.

⁴⁰ Ibid.

⁴¹ Nienaber A (note 18) at 242-3.

⁴² See Australian National Statement at 2.2.14. 'National Statement on Ethical Conduct in Human Research' (2007) published by the National Health and Medical Research Council (NHMRC), Australia available at http://www.nhmrc.gov.au/files_nhmrc/publications/attachments/e72.pdf (accessed 11 August 2011) (hereafter 'National Statement').

⁴³ Extended consent allow biospecimens to be used for research closely related to that envisaged during original consent, or for a specific sphere of research.

patients elect the form of consent, depending on factors like the availability of information regarding the future research at the time of consent.⁴⁵

Three broad categories of consent model are described. Two are polar opposites: the strictest (new informed consent is required)⁴⁶ and the most flexible (no specific informed consent is required).⁴⁷ Remaining possibilities fall into the middle, where the broader consent models prevail.⁴⁸

1.3.1 Strict model: new informed consent required

The South African legal and ethics landscape forms the point of departure.⁴⁹ Affirmation of the basic requirement of informed consent for medical research appears in the Constitution of the Republic of South Africa,⁵⁰ the National Health Act⁵¹ and in the Department of Health's Ethics in Health Research: Principles, Structures and Processes.⁵² This axiomatic requirement is also present in the other ethics guidelines like those of the Medical Research Council,⁵³ the South African Medical Association,⁵⁴ the Health Professions Council of South Africa,⁵⁵ as well as the various international guidelines to which South Africa subscribes.⁵⁶

⁴⁴ Unspecified consent provides researchers with the freedom to use the biospecimens in any medical research.

⁴⁵ See discussion in Chapter 3 part 3.2.2 below.

⁴⁶ See part 1.3.1 below.

⁴⁷ See part 1.3.3 below.

⁴⁸ See part 1.3.2 below.

⁴⁹ The South African legal-ethics framework is discussed in more detail in Chapter 2 below.

⁵⁰ Constitution of South Africa, 1996.

⁵¹ National Health Act 61 of 2003 and its Regulations.

⁵² 'Ethics in Health Research: Principles, Structures and Processes' (2004) published by the Department of Health, South Africa available at <http://www.doh.gov.za/docs/factsheets/guidelines/ethnics/> (accessed 7 June 2011) (hereafter 'Ethics in Health Research').

⁵³ See 5.1 of 'Guidelines on Ethics for Medical Research: General Principles' (2002) published by the Medical Research Council of South Africa (MRC) available at <http://www.mrc.ac.za/ethics/ethicsbook1.pdf> (accessed 8 June 2011).

⁵⁴ See especially Annexure 4 of the 'Standard Operating Procedures and Guidelines for the Ethics Evaluation of Clinical Trials in Humans' (2011) published by the South African Medical Association (SAMA) available at <http://www.samedical.org/assets/files/doctors-corner/law-and-ethics/SAMAREC/SAMAREC%20SOP%20&%20Guidelines%20July%202011.pdf> (accessed 1 February 2012).

⁵⁵ See especially part 6.3 of the 'General Ethical Guidelines for Health Researchers' (Booklet 6) (2008) published by the Health Professions Council of South Africa (HPCSA) available at http://www.hpcsa.co.za/downloads/conduct_ethics/rules/generic_ethical_rules/booklet_6.pdf (accessed 2 February 2012).

⁵⁶ For example the Declaration of Helsinki, the Belmont Report, the International Guidelines for

The Constitution⁵⁷ specifically entrenches informed consent for medical research by stating that

‘[e]verybody has the right to bodily and psychological integrity, which includes the right not to be subjected to medical or scientific experiments⁵⁸ without their informed consent.’⁵⁹

The National Health Act⁶⁰ strengthens this requirement by stating that research involving human participants may only ensue once written consent has been provided. Informed consent means that potential participants must be informed of the nature, objectives and expectations of the research, as well as any positive or adverse health effects that the research may entail.⁶¹ However, these requirements do not shed much light on requirements for secondary use in research of stored biospecimens.

Furthermore, It is important to bear in mind that previously removed tissue used in research is not a ‘participant’. The biospecimens⁶² used for secondary research purposes no longer form part of the person. It is unclear from the Constitution and legislation how the consent requirement would address the separateness between the stored biospecimen and the person from which it was initially removed.

The Regulations to the National Health Act⁶³ indicate that written informed consent is required for removal of biospecimens for ‘medical’ purposes, which definition includes ‘health research’.⁶⁴ The regulations therefore affirm the strict requirement of specific consent.

Ethical Review of Epidemiological Studies by the Council for International Organizations of Medical Sciences (CIOMS), and the World Health Organization (WHO) etc. *Ethics in Health Research* (note 52) at 55 (Appendix B).

⁵⁷ Constitution of South Africa, 1996.

⁵⁸ The term ‘experiments’ corresponds to the United Nations International Covenant on Civil and Political Rights (ICCPR). Dhali A and McQuoid-Mason D *Bioethics, Human Rights and Health Law: Principles and Practice* (2011) at 167-70.

⁵⁹ Constitution of South Africa, 1996 at s12(2)(c).

⁶⁰ National Health Act 61 of 2003 at s 71.

⁶¹ National Health Act 61 of 2003 at s 71(1)(b); Dhali A and McQuoid-Mason D (note 58) at 169.

⁶² The biospecimens stored pursuant to the initial removal from the patient for diagnostic and/or therapeutic purposes.

⁶³ Act 61 of 2003.

⁶⁴ See sub-regulation 4(b) of Draft regulation 7 to the National Health Act 61 of 2003. Draft regulation 7 ‘Regulations regarding the use of human DNA, RNA, cultured cells, stem cells, blastomeres, polar bodies, embryos, embryonic tissue and small tissue biopsies for diagnostic testing, health research and therapeutics’ GG 29526 5 January 2007.

The Ethics in Health Research⁶⁵ guidelines state that specific consent should be sought where stored biospecimens are used in research not originally consented to. Accordingly, donors would need to be re-contacted to provide new consent for the specific research use. This approach represents the strictest model on the spectrum.

1.3.2 The middle ground: broader consent models

The middle ground supports the idea that informed consent for removal of tissue for diagnostic purposes should include permission for use of the tissue in related future research, even though its nature may be uncertain at the time.⁶⁶ The broader consent approaches vary from actual consent to certain types of research;⁶⁷ to biomedical research in general; or, in the widest sense, to unrestricted use of stored biospecimens.⁶⁸ The donor patient should be free to choose the form of consent.⁶⁹

Three safeguarding criteria⁷⁰ are required for broader consent. Donor patients must be able to withdraw their consent, the personal information connected to the tissue samples must be kept confidential and a research ethics committee⁷¹ must approve each new research project.⁷² Interestingly, none of these criteria are innovative; they merely reiterate standard best practice in research ethics. Support for the broader consent standards flows from the

⁶⁵ Ethics in Health Research (note 52) at 41.

⁶⁶ Hoffmann B 'Broadening consent – and diluting ethics?' (2009) 35 *J Med Ethics* 125 at 125-9; Hansson MG et al 'Should donors be allowed to give broad consent to future biobank research?' (2006) 7 *Lancet Oncology* 266 at 269; William R (note 10) at 649; Elger B and Caplan AL (note 27) at 662-3.

⁶⁷ For example, consenting to oncology research only.

⁶⁸ Hansson MG (note 66) at 268; Oosterhuis JW et al (note 9) at 75.

⁶⁹ Hansson MG (note 66) at 268.

⁷⁰ Maschke KJ 'Alternative consent approaches for biobank research' (2006) 7 *Lancet Oncology* 193 at 194; Hansson MG (note 66) at 269; William R (note 10) at 649; Hoffmann B (note 66) at 125-9.

⁷¹ Research ethics committees may be found at most research and higher education institutions in South Africa. In terms of s 73(2)(b) of the National Health Act 61 of 2003, research ethics committees grant approval for any prospective research that involves human participants if the research proposal and protocol meet the ethics standards of the research ethics committee. Furthermore, research ethics committees must also review all such research undertaken ensuring that the research is conducted in a manner promoting health and the prevention and cure of disease and disability. Further functions include ensuring that research participants are treated with respect and that their informed consent has been duly acquired for the research endeavour. Ethics in Health Research (note 52) at 10; MRC (note 53) at 9.6.1.

⁷² Hansson MG (note 66) at 269; William R (note 10) at 649; Hoffmann B (note 66) at 125-9; Maschke KJ (note 70) at 194.

absence of risk of physical harm to the donor patient.⁷³ In order to be legitimate, broader models of consent depend on the adequacy of mechanisms to ensure confidentiality, consent withdrawal, and the prerequisite that research ethics committees perform their duties properly.⁷⁴

Certain authors⁷⁵ suggest that only the strict model is acceptable where biospecimens are identifiable. However, the same authors⁷⁶ suggest that an 'opt-out' system should be used, whereby consent for secondary use of biospecimens is assumed unless specifically objected to by the donor patient. An important qualification is that biospecimens must be de-identified or anonymised.⁷⁷

1.3.3 No Consent Required

The most lenient model on the spectrum supports the use in research of stored biospecimens previously removed for diagnostic or therapeutic purposes without seeking fresh informed consent. As will be seen below,⁷⁸ the identifiability of the stored biospecimen plays a decisive role in how the no-consent requirement is achieved. By way of introduction, it suffices to mention that, under certain circumstances, even where biospecimens are identifiable, a research ethics committee may waive the requirement of new, specific consent.⁷⁹ However, where the biospecimens are de-identified or anonymous, consent may simply not be required at all.⁸⁰ The international trends pertaining to this approach are discussed briefly below.

1.4 Normative instruments

As indicated earlier, no consensus exists on the consent requirement for secondary use of identifiable human tissue removed from humans. This section

⁷³ William R (note 10) at 649.

⁷⁴ Maschke KJ (note 70) at 194.

⁷⁵ Oosterhuis JW et al (note 9) at 75-6.

⁷⁶ Ibid.

⁷⁷ Ibid.

⁷⁸ See part 1.4.1 and 1.4.2 of this chapter below for a brief discussion of the no-consent categories.

⁷⁹ Elger B and Caplan AL (note 27) at 663.

⁸⁰ Salvaterra E et al (note 5) at 309.

outlines the approach in commonly used international and foreign ethics guidelines.

Principle 25 of The Declaration of Helsinki⁸¹ indicates that ‘normally’ consent should be sought for use of ‘identifiable human material or data’.⁸² Two important inferences may be drawn at this point. Firstly, under certain circumstances, no consent would be acceptable for secondary use of identifiable biospecimens in research. Secondly, identifiability is an important aspect and is discussed in more detail below. It may be pointed out here that the degree of identifiability has a material effect on the international approaches to consent.

Two sub-categories of ‘no-consent-situations’ may be identified: where a research ethics committee waives the need for consent relating to identifiable biospecimens and, secondly, de-identified or anonymised biospecimens.

1.4.1 Waiver of specific consent: Identifiable biospecimens

Research ethics committees may, under certain circumstances, waive the consent requirement.⁸³ In other words, a research ethics committee may authorise use of stored, identifiable biospecimens in research projects without consent from the original donors.

A trend is evident in the approach to waiver by selected international instruments. It should be noted that all seem to hold the view that severed biospecimens ‘belong’ to the donor patient.

⁸¹ The World Medical Association Declaration of Helsinki of 1964 (as amended in 2008) Principle 25 available at available at <http://www.wma.net/en/30publications/10policies/b3/index.html> (accessed 28 July 2011) (hereafter ‘Declaration of Helsinki’).

⁸² ‘For medical research using *identifiable* human material or data, physicians must *normally* seek consent for the collection, analysis, *storage and/or reuse*. There may be situations where consent would be impossible or impractical to obtain for such research or would pose a threat to the validity of the research. In such situations the research may be done only after consideration and approval of a research ethics committee’ [Emphasis added]. Declaration of Helsinki (note 81) Principle 25.

⁸³ Elger B and Caplan AL (note 27) at 663.

The Council for International Organizations of Medical Sciences (CIOMS) Guidelines⁸⁴ regard a waiver of consent as an exceptional measure. In terms of both the CIOMS and the Organization for Economic Co-operation and Development⁸⁵ (OECD) Guidelines, if the proposed research poses only minimal risk of harm to the donor patient and obtaining consent is impractical or impossible, then the research ethics committee may waive the requirement for specific consent.⁸⁶ Additionally, the OECD Guidelines require that the waiver not adversely affect the welfare of the donor patient.⁸⁷ Although no specific waiver guidelines are provided, the United Nations Educational, Scientific and Cultural Organization (UNESCO) Report⁸⁸ recognises the need for research ethics committee waiver when obtaining specific consent is not practicable. It requires relevant entities⁸⁹ to implement adequate waiver procedures.

On a regional level, the Council of Europe⁹⁰ has formulated specific guidelines pertaining to consent for use of identifiable biospecimens in research unanticipated during initial consent. A waiver of specific consent is permitted if the research ethics committee establishes that the original donor patient cannot be contacted, the research project addresses an important scientific interest and the research outcomes could not be achieved using biospecimens for which consent was obtained. Lastly, there must be no evidence that the original donor patient would have objected to the research.⁹¹

⁸⁴ 'International Ethical Guidelines for Biomedical Research Involving Human Subjects' (2002) published by the Council for International Organizations of Medical Sciences (CIOMS) available at http://www.cioms.ch/publications/layout_guide2002.pdf (accessed 4 February 2012).

⁸⁵ Australia is a member of this multi-national forum but not South Africa.

⁸⁶ 'OECD Guidelines on Human Biobanks and Genetic Research Databases' (2009) published by the Organization for Economic Co-operation and Development (OECD) available at <http://www.oecd.org/dataoecd/41/47/44054609.pdf> (accessed 7 February 2012) at Annotation 27; CIOMS (note 84) at Guideline 4 at 22-3.

⁸⁷ OECD (note 86) at Annotation 27.

⁸⁸ 'Report of the International Bioethics Committee of UNESCO on Consent' (2008) published by the United Nations Educational, Scientific and Cultural Organization (UNESCO) available at <http://unesdoc.unesco.org/images/0017/001781/178124e.pdf> (accessed 7 February 2012) at par 53.

⁸⁹ Regulations are to be implemented by countries, research ethics committees or professional societies. UNESCO (note 88) at par 53.

⁹⁰ See Council of Europe Committee of Ministers Recommendation Rec(2006)4 on research on biological materials of human origin (2006) available at www.coe.int/t/dg3/healthbioethic/texts_and_documents/Rec_2006_4.pdf (accessed 7 February 2012) at articles 21-2.

⁹¹ Council of Europe Recommendation Rec(2006)4 (note 90) at article 22.

In essence, therefore, the trend shows that research ethics committees may, under certain circumstances, waive the requirement of new, specific consent.⁹² The primary justifications for waiver are the impracticalities in recontacting donors to provide consent and the likelihood of only a minimal risk of harm to the donor. However, in the context of stored biospecimens, there is no risk of physical harm to the original donor in its use in research. This may result in expedience being the main consideration for waiver in the context of this dissertation.

1.4.2 No new consent: De-identified biospecimens

Where biospecimens are de-identified or anonymised, the general trend shows that, under certain circumstances, informed consent is no longer required.⁹³ The key factor is anonymity. This is confirmed by the World Health Organisation (WHO),⁹⁴ which states that biospecimens may be used in research without consent if two important requirements are met. The biospecimen must be anonymised and the research results must not be used to identify the original donor.⁹⁵

The CIOMS Guidelines also endorse no-consent use of anonymised biospecimens.⁹⁶ However, in addition to guaranteeing anonymity, the research ethics committee must find that the anticipated research seeks to answer a scientific question.⁹⁷ The Council of Europe too permits use of unlinked, anonymised biospecimens for research without consent.⁹⁸ Various jurisdictions⁹⁹ follow this trend of permitting research using non-identifiable

⁹² For a further discussion of the waiver of specific consent by research ethics committees, see parts 2.2.3 (South African context), 3.2.2 (Australian context) and 4.4 of this dissertation below.

⁹³ Salvaterra E et al (note 5) at 309.

⁹⁴ 'Genetic Databases: Assessing the Benefits and Impact on Human and Patient Rights' published by the World Health Organization (WHO) available at www.codex.vr.se/texts/whofinalreport.rtf (accessed 7 February 2012) at Recommendation 10.

⁹⁵ WHO (note 94) at Recommendation 10.

⁹⁶ CIOMS (note 84) at Guideline 4 at 22-3.

⁹⁷ Ibid.

⁹⁸ Council of Europe Recommendation Rec (2006)4 of the Committee of Ministers to member states on research on biological materials of human origin at article 23.

⁹⁹ Such as the United States of America, Canada, Germany, Norway and the Netherlands. Salvaterra E et al (note 5) at 309.

biospecimens without seeking new, specific consent where research was not originally consented to.¹⁰⁰

The trend therefore shows that anonymisation of biospecimens, which diminishes the risk of informational harm to the original donor, permits use of stored biospecimens previously removed during clinical procedures in oncology research without further consent from the original donor of the tissue.

1.5 Structure of the discussion

The next two chapters outline the foundations of the legal-ethics frameworks of South Africa¹⁰¹ and Australia.¹⁰² The general concept of informed consent and its role in medical research are discussed briefly. More specifically, it will be established whether the different legal-ethics frameworks address the requirement of consent pertaining to secondary use of biospecimens in research initially collected during diagnostic or therapeutic procedures. Where possible, specific reference is made to oncology. Furthermore, the critical comparative analysis¹⁰³ of the most important themes aims to evaluate the current legal-ethics landscapes, which may inform the conceptualisation of possible recommendations¹⁰⁴ to develop the current, rigid South African position.

¹⁰⁰ Knoppers BM and Saginur M 'Bio-banking' in Singer PA and Viens AM (eds) *The Cambridge Textbook of Bioethics* (2008) 166 at 168; Elger B and Caplan AL (note 27) at 663; Hansson MG (note 66) at 267.

¹⁰¹ See Chapter 2 below.

¹⁰² See Chapter 3 below. Australia is the primary comparative jurisdiction for the purposes of this dissertation.

¹⁰³ See Chapter 4 below.

¹⁰⁴ See Chapter 5 for the conclusions and recommendations.

CHAPTER 2

2.1 Introduction

This chapter provides a description of the current South African legal-ethics framework pertaining to the requirement of informed consent for the secondary use of biospecimens, previously obtained for diagnostic or therapeutic purposes, in medical research. The chapter is structured to provide, first, a brief exposition of the concept of informed consent and the values underpinning this requirement. Secondly, the relevant South African legal and ethics policy frameworks are identified and discussed; and lastly the most important features and possible flaws of the policy frameworks are identified.

2.1.1 General overview of informed consent

Before a person may participate in any medical research, an ethical and legal requirement is to obtain informed consent.¹⁰⁵ Authors¹⁰⁶ describe informed consent as a process of information sharing between persons and health care practitioners, based on mutual respect and participation. This promotes informed decision-making regarding participation in medical research.¹⁰⁷

The general requirements for informed consent in South African law are to be found in *Castell v De Greef*.¹⁰⁸ Although the case deals with medical treatment, the foundations of informed consent, relevant also for research, are outlined therein. A duty exists for a medical practitioner to disclose to the

¹⁰⁵ Section 71 of the National Health Act 61 of 2003; s 12(2)(c) of the Constitution of South Africa, 1996; Moodley K (ed) *Medical Ethics, Law and Human Rights: A South African Perspective* (2011) at 43; Dhai A and McQuoid-Mason D (note 58) at 169.

¹⁰⁶ Dhai A and McQuoid-Mason D (note 58) at 70.

¹⁰⁷ Dhai A and McQuoid-Mason D (note 58) at 71.

¹⁰⁸ *Castell v De Greef* 1994 (4) SA 408 (C).

patient 'material' risks¹⁰⁹ associated with proposed treatment before consent can be valid.¹¹⁰

A risk of harm is material where, in the circumstances at hand, a reasonable person in the patient's position would attach significance to the risk if warned about it.¹¹¹ It would also be the case where the medical practitioner is, or should be, aware that the patient would attach such significance to the warning of the risk of harm.¹¹² However, as Ackermann J¹¹³ notes, this obligation is subject to therapeutic privilege.¹¹⁴

Assuming that the consenting party has capacity¹¹⁵ to provide consent and does so voluntarily,¹¹⁶ the validity of the informed consent process rests on the presence of further elements.¹¹⁷ Four core elements have been identified:¹¹⁸ knowledge and awareness of the nature and extent of risk of harm; appreciation and understanding of the nature and extent of risk of harm; and consent to such risk of harm.¹¹⁹ Furthermore, the consent must be

¹⁰⁹ *Castell v De Greef* (note 108) at 426. See also Thomas R 'Where to from Castell v De Greef? Lessons from recent developments in South Africa and abroad regarding consent to treatment and the standard of disclosure' 2007 (124) *SALJ* 188-215.

¹¹⁰ Ackermann J bases this principle on the important Australian case of *Rogers v Whitaker* (1993) 67 ALJR 47, which reflects a similar outcome. See a short discussion of this Australian case in Chapter 3 below.

¹¹¹ *Castell v De Greef* (note 108) at 426.

¹¹² *Ibid.*

¹¹³ *Ibid.*

¹¹⁴ Therapeutic privilege denotes the situation where the harm caused by the disclosure of the risks to the patient potentially overshadows the harm caused by non-disclosure. For example, a disclosure of the risks may lead to the patient becoming so despondent that it prejudices treatment. Carstens P and Pearmain D *Foundational Principles of South African Medical Law* (2007) at 888; Dhai A and McQuoid-Mason D (note 58) at 74.

¹¹⁵ Competence in itself is a complex matter, but essentially refers to the ability to of an individual to provide consent. It requires that the patient is able to communicate a choice, understand the information given, and appreciate the medical consequences of the situation and reason about the treatment options available. Where competence is lacking, due to mental illness or minority, for example, proxy consent may be sought. Moodley K (note 105) at 44.

¹¹⁶ With regard to voluntariness, consent may not be induced by fear, duress, deceit, undue influence, financial gain and so on. Furthermore, certain categories of persons, such as those in dependent relationships and incarcerated persons, may, as a result of their position, potentially experience that their voluntariness be compromised. MRC (note 53) at 5.3.2.4.1.

¹¹⁷ It is not the purpose of this section to provide an in depth analysis of each element constituting informed consent. It is rather an opportunity to provide the reader with a broad idea of the wide scope of requirements necessary for informed consent.

¹¹⁸ *Castell v De Greef* (note 108) at 425.

¹¹⁹ *Ibid.*

comprehensive and 'extend to the entire transaction, inclusive of its consequences.'¹²⁰

Informed consent to medical research involving human participants is specifically entrenched in the Constitution.¹²¹ This constitutional imperative is confirmed in the National Health Act,¹²² which expressly requires written consent from research participants. Although not yet in operation, the Act¹²³ firmly requires that written consent be sought from a prospective participant before any research may be conducted on such a participant.

The consent requirement for research participation is explained by research ethics guidelines issued by entities such as the National Department of Health, the South African Medical Research Council (MRC) and other bodies.¹²⁴

The Ethics in Health Research: Principles, Structures and Processes¹²⁵ guidelines (hereafter Ethics in Health Research), inter alia, provide additional guidance on the standard of disclosure of information in the research context. The participant must be given detailed information, in understandable language, regarding certain core considerations. Firstly, the scope, nature, purpose and duration of the proposed research project must be made known to the participant.¹²⁶ Secondly, the participant must be informed of the nature, scope and consequences of the research intervention itself.¹²⁷ In the third place, the anticipated benefits and disadvantages of the research endeavour, as opposed to current standard treatment, must be communicated to the prospective participant.¹²⁸ Fourthly, information pertaining to foreseeable risks

¹²⁰ Ibid.

¹²¹ Section 12(2)(c) of the Constitution of South Africa, 1996. This provision was quoted in Chapter 1 part 1.3.1 above.

¹²² Act 61 of 2003 at Chapter 9 ('National Health Research and Information').

¹²³ Section 71(1) of Act 61 of 2003 reads as follows:

'[n]otwithstanding anything to the contrary in any other law, 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 objects of the research or experimentation and any possible positive or negative consequences on his or her health.'

¹²⁴ Carstens P and Pearmain D (note 114) at 894

¹²⁵ Ethics in Health Research (note 52).

¹²⁶ MRC (note 53) at 5.3.2.3.

¹²⁷ Ethics in Health Research (note 52) at 2.6; MRC (note 53) at 5.3.2.3.

¹²⁸ Ibid.

of harm, dangers and complications related to the proposed research must be relayed to the consenting party.¹²⁹ In the fifth place, the participant must be informed of any personal benefits, including those of a financial nature, that may accrue to the participants and researchers as a result of the research project.¹³⁰ Lastly, provision and withdrawal of consent is entirely voluntary.¹³¹

In the South African context, vulnerability of certain groups of participants is emphasised.¹³² Vulnerability may be a result of limited socio-economic development, reduced access to health services or illiteracy.¹³³ With this in mind, researchers should provide information in a 'clear, simple and culturally appropriate manner.'¹³⁴

2.1.2 Underlying values of informed consent

Up to this point, the general nature of and requirements for valid informed consent have been highlighted.

Scholars¹³⁵ identify certain ethics values underpinning informed consent. For purposes of this discussion, the right to self-determination as underlying value is emphasised. Self-determination or autonomy denotes the right to make decisions in matters affecting self.¹³⁶ In medical research the participants' right to choose is exercised by providing informed consent to the medical research.¹³⁷ In terms of the focus-point of this dissertation, it has been submitted¹³⁸ that autonomy would allow donors to have the right to veto the use of their biospecimens collected from their bodies for use in research or even specific areas of research. It is, in my view, doubtful whether this is justified, for reasons mentioned directly below.

¹²⁹ Ibid.

¹³⁰ Ibid.

¹³¹ MRC (note 53) at 5.3.2.3.

¹³² Ethics in Health Research (note 52) at 4.

¹³³ Ibid.

¹³⁴ Ibid.

¹³⁵ Magnusson RS 'Confidentiality and consent in medical research: some recurrent, unresolved legal issues faced by IECs' (1995) 17 *Sydney Law Review* 549 at 555; Carstens P and Pearmain D (note 114) at 883; Dhai A and McQuoid-Mason D (note 58) at 70.

¹³⁶ Dhai A and McQuoid-Mason D (note 58) at 70.

¹³⁷ Carstens P and Pearmain D (note 114) at 883; Magnusson RS (note 135) at 555.

¹³⁸ Magnusson RS (note 135) at 555.

Once removed, the biospecimen is no longer part of the person. Accordingly, as mentioned above,¹³⁹ such removed tissue is regarded as an object and not a 'participant' to research. Consequently, it is uncertain how this underlying value of autonomy should be given effect to where the bond between the donor and the removed tissue has been broken. In the light of this separation between donor and biospecimen, it may be unfounded to fulfil the donor's right to self-determination to the same extent as in the case of medical research on human participants. Strictly speaking, respect for a person would be impossible where research is conducted only on stored biospecimens.

2.2 Synopsis of the South African legal-ethics framework

This section provides an integrated view of the South African legal-ethics framework governing the requirement of informed consent from donors for secondary use of biospecimens initially taken for diagnostic and/or therapeutic purposes for subsequent research purposes.

2.2.1 International sphere and the South African Constitution

By way of introduction, a brief outline is given of some catalysts from the international sphere, that shape the current South African legal-ethics landscape. The South African Department of Health's Ethics in Health Research guidelines¹⁴⁰ explicitly recognise the Declaration of Helsinki,¹⁴¹ the Nuremberg

¹³⁹ See Chapter 1 at part 1.1 above.

¹⁴⁰ Ethics in Health Research (note 52) at 55.

¹⁴¹ Declaration of Helsinki (note 81). The South African Medical Association (SAMA) is a member of the World Medical Association; Moodley K (note 105) at 321.

Code¹⁴² and the Belmont Report,¹⁴³ as key texts contributing to development of the guidelines.¹⁴⁴

Principle 25¹⁴⁵ of the Declaration of Helsinki¹⁴⁶ is especially relevant here. As was previously shown,¹⁴⁷ where medical research is performed on *identifiable* human material or data, consent for collection, storage, use and reuse should be sought, as a matter of principle.¹⁴⁸ However, a research ethics committee may waive the consent requirement, where, for example, it is impractical or impossible to seek informed consent.¹⁴⁹ Furthermore, it may be argued that where the biospecimen is not identifiable, seeking informed consent for its use in research may be unnecessary.

The Constitutional provision, as established above,¹⁵⁰ clearly reinforces the strict principle that research involving human participants may only take place once written consent has been provided. However, it remains unclear how the Constitution would address the consent requirement where medical research involves stored biospecimens and not participants. In an attempt to address this uncertainty, a brief exposition of other relevant aspects of the South African legal framework follows.

¹⁴² The Nuremberg Code, developed in 1947 pursuant to the Nuremberg Trials, consists of ten principles. Principle 1 states that the ‘...voluntary consent of the human subject is absolutely essential’ for participation in a medical experiment. Available at http://www.accreditgcp.com/download/Nuremberg_Code.pdf (accessed 28 July 2011); Moodley K (note 105) at 320.

¹⁴³ The Belmont Report 1979, also firmly establishes the concept of informed consent as a requirement for participation to medical research. It also provides an analysis of consent under the elements of information, comprehension and voluntariness. Available at http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4178b_09_02_Belmont%20Report.pdf (accessed 28 July 2011) at Part C1.

¹⁴⁴ Apart from the three primary texts noted, certain other references that helped to develop the South African research ethics landscape include the CIOMS and WHO guidelines. These are referred to elsewhere in this dissertation. Ethics in Health Research (note 52) at 55.

¹⁴⁵ Principle 25 of the Helsinki Declaration was introduced in Chapter 1 part 1.4 above.

¹⁴⁶ Declaration of Helsinki (note 81) at Principles 24-9.

¹⁴⁷ See Chapter 1 part 1.4 above.

¹⁴⁸ Declaration of Helsinki (note 81) at Principle 25.

¹⁴⁹ *Ibid.*

¹⁵⁰ See s 12(2)(c) of the Constitution of South Africa, 1996 quoted, and briefly discussed, above in Chapter 1 part 1.3.1.

2.2.2 South African legislation

At present, the Human Tissue Act¹⁵¹ spells out requirements for informed consent for removal of tissue from living persons for research and other purposes. However, this Act¹⁵² will be repealed when Chapters 8 and 9 of the National Health Act¹⁵³ come into force.¹⁵⁴ It is therefore necessary, for comprehensiveness, to refer briefly to the relevant parts of the soon-to-be repealed Human Tissue Act¹⁵⁵ still in force. However, the focus of the discussion will be on the present form of the National Health Act.¹⁵⁶

2.2.2.1 Human Tissue Act 65 of 1983

In essence, this Act¹⁵⁷ provides that persons must provide written consent for the removal of tissue from their bodies, for 'medical or dental' purposes. These purposes include transplantation and the 'production of a therapeutic, diagnostic or prophylactic substance'.¹⁵⁸ Although it seems the list of purposes is not closed,¹⁵⁹ it is uncertain whether medical research is envisaged as a primary purpose for which tissue may be removed.¹⁶⁰

It is my view that it would in any case be ethically questionable to surgically remove tissue from a person solely for research purposes. This, of course, strengthens the argument for using stored surplus tissue from diagnostic or therapeutic procedures rather than sourcing them specifically for research purposes. In the oncology context, for example, the stored biospecimens used in research would most likely originate from biopsies or the therapeutic removal of malignant tissue.

¹⁵¹ Act 65 of 1983.

¹⁵² Act 65 of 1983.

¹⁵³ Act 61 of 2003.

¹⁵⁴ Only s 53 of Chapter 8 of Act 61 of 2003 is in force, but it is irrelevant to the scope of this dissertation. Nienaber A (note 18) at 242.

¹⁵⁵ Act 65 of 1983.

¹⁵⁶ Act 61 of 2003.

¹⁵⁷ Act 65 of 1983 at ss 18-9.

¹⁵⁸ Act 65 of 1983 at s 19(a).

¹⁵⁹ Due to use of 'including' in s 19 of Act 65 of 1983.

¹⁶⁰ Dhai A and McQuoid-Mason D (note 58) at 120.

2.2.2.2 National Health Act 61 of 2003

The present form of the National Health Act¹⁶¹ unequivocally states that where a medical practitioner¹⁶² excises tissue for any purpose stipulated in s 56, it is necessary for the person, from whom the tissue is removed, to provide written consent for the excision.¹⁶³ Regarding the actual purpose for the excision envisaged, s 56(1) refers to ‘medical or dental purposes as may be prescribed.’¹⁶⁴ There is no definition in the Act¹⁶⁵ as to what ‘medical’ purposes may specifically refer to. It would be necessary for the purposes of this dissertation to ascertain whether medical research is encompassed in such purposes.¹⁶⁶ To achieve some clarity, it is necessary to study the Draft-Regulations to the Act¹⁶⁷ to ascertain what ‘medical’ purposes may include.¹⁶⁸

Although not yet in force, Chapter 9 of the National Health Act¹⁶⁹ provides the consent requirements for medical research involving human participants. In essence, before any research may be conducted on human subjects, s 71(1)¹⁷⁰ requires written informed consent.¹⁷¹ This consent is provided once the prospective participants have been informed of the objects of the research and any positive or negative consequences the research may

¹⁶¹ Act 61 of 2003.

¹⁶² In terms of s 59(1) of Act 61 of 2003, only a registered medical practitioner or dentist may remove any tissue from a living person and use such tissue in accordance with the purpose stipulated in s 56. Furthermore, in terms of ss 54(1) and (2), the Minister of Health may designate specific institutions where such tissue is to be acquired from living or deceased persons for any purpose referred to in ss 58 and 64.

¹⁶³ Section 55 of Act 61 of 2003.

¹⁶⁴ Section 56(1).

¹⁶⁵ Act 61 of 2003.

¹⁶⁶ However, in terms of ss 56(2)(a) and (b) it is clear that unless the Minister expressly authorises it, certain tissue from certain persons may not be removed for any purpose whatsoever. An example of such a situation is the removal of a gamete of a person younger than 18 years. A detailed discussion of this falls outside the ambit of this dissertation.

¹⁶⁷ Act 61 of 2003.

¹⁶⁸ See part 2.2.2.3 directly below for an overview of the relevant draft regulations to Act 61 of 2003.

¹⁶⁹ Act 61 of 2003.

¹⁷⁰ Act 61 of 2003.

¹⁷¹ Section 71(1) should be read in conjunction with ss 6(1) and 7(1) of the Act, which fleshes out the informational aspect of informed consent for research involving human subjects. In essence, informed consent presupposes knowledge about: the consenting party’s health status (except in circumstances where such disclosure would be contrary to the party’s best interests); the range of diagnostic and therapeutic options available; the benefits, risks, costs and consequences associated; and the right to refuse health services and the implications of such refusal. In my view, this would be particularly relevant for clinical trials, but not for research on stored biospecimens.

have on their health.¹⁷² This provision resonates with the imperative set in, inter alia, s 12(2)(c) of the Constitution¹⁷³ and the Declaration of Helsinki, as discussed above.

2.2.2.3 Draft Regulations

In an attempt to ascertain the purposes for which tissue may be removed, the meaning of 'medical' purposes needs to be established. The relevant regulations¹⁷⁴ to the National Health Act,¹⁷⁵ which flesh out the general principles stipulated in the Act, are now reviewed.

Draft¹⁷⁶ Regulation 268¹⁷⁷ reinforces the requirement of written informed consent for removal of tissue. Biospecimens, *excluding* blood, blood products and gametes, may be used for 'the transplanting thereof in the body of another living person or for the production of a therapeutic, diagnostic or prophylactic substance'.¹⁷⁸ It is unclear whether medical research falls within the scope of this draft regulation.

Draft regulation 263¹⁷⁹ relates to the removal of biospecimens for 'genetic testing, genetic training, genetic health research and therapeutics'.¹⁸⁰ Even though it would seem that this draft regulation deals exclusively with genetic-based purposes, it is clear that human biological material may be removed for medical purposes including health research purposes.¹⁸¹

Also relevant for the purposes of this discussion is Draft regulation 7.¹⁸² This draft regulation deals with the harvesting of biospecimens for 'diagnostic

¹⁷² Section 71(1) of Act 61 of 2003.

¹⁷³ Constitution of South Africa, 1996.

¹⁷⁴ Regulations pertaining to the use of biospecimens are published by the Minister of Health, after consultation with the National Health Council, in terms of s 68(1) read with s 90(1) of the National Health Act 61 of 2003.

¹⁷⁵ Act 61 of 2003.

¹⁷⁶ It should be noted that the Regulations discussed below have been published in the Government Gazette on 5 January 2007 and again on 1 April 2011 for comment. They are not yet in force and will therefore be referred to as draft regulations. Nienaber A (note 18) at 244.

¹⁷⁷ 'Regulations regarding the general control of human bodies, tissue, blood, blood products and gametes' Regulation 268 GG 34159 1 April 2011 at 102.

¹⁷⁸ Draft regulation 268 (note 177) at sub-regulation 3(1)(a).

¹⁷⁹ 'Regulations relating to the use of human biological material' Regulation 263 GG 34159 1 April 2011 at 23.

¹⁸⁰ Chapter 1 of Draft regulation 263.

¹⁸¹ Draft regulation 263 (note 179) at sub-regulation 5(b).

¹⁸² Draft regulation 7 (note 64).

genetic testing, health research and therapeutics'.¹⁸³ It unequivocally states¹⁸⁴ that biospecimens removed from living persons may be used for specific 'medical' purposes, including '[h]ealth research referred to in section 69(3) of the Act.' Furthermore, sub-regulation 4(a) includes purposes such as genetic testing for carrier status¹⁸⁵ and susceptibility to disease¹⁸⁶ and diagnostic testing¹⁸⁷ which enables the use of the genetic information of the biospecimens. This is becoming increasingly important in medical research, especially in the context of oncology.

It may therefore be concluded that a person may provide written informed consent for the removal of a biospecimen for purposes including medical research, even though the Act,¹⁸⁸ when read in isolation, does not make it clear.

2.2.3 Ethics guidelines

The brief exposition of the relevant legal framework above has established that surplus tissue can be requested at the time of removal for biopsy or therapeutic intervention to be stored and used for certain research purposes. The donor therefore, during initial consent for the diagnostic or therapeutic intervention, provides consent for storage and use of excess tissue in certain research. However, as stated above,¹⁸⁹ difficulties such as uncertainty of what the future research projects are, hamper donors' ability to provide specific consent for such research. Neither the National Health Act¹⁹⁰ nor the draft regulations provide clear guidance as to how these challenges must be addressed. Accordingly, the South African ethics framework is studied to shed light on the matter.

¹⁸³ Draft regulation 7 (note 64) at 6.

¹⁸⁴ At sub-regulation 4(b).

¹⁸⁵ Draft regulation 7 (note 64) at sub-regulation 4(a)(ii).

¹⁸⁶ Draft regulation 7 (note 64) at sub-regulation 4(a)(iv).

¹⁸⁷ Draft regulation 7 (note 64) at sub-regulation 4(a)(i).

¹⁸⁸ Act 61 of 2003.

¹⁸⁹ See especially Chapter 1 above at part 1.2.

¹⁹⁰ Act 61 of 2003.

The Ethics in Health Research¹⁹¹ guidelines contain national policy on the ethical practice of research and set out the requirements for ethical review of proposed studies on human participants.¹⁹² The guidelines state that, generally, where biospecimens are collected for purposes including health research, informed consent is required.¹⁹³ All the usual requirements for informed consent, as mentioned above,¹⁹⁴ are necessary. Specific to biospecimen collection, is information about whether the biospecimens are to be stored for future use after completion of the current research¹⁹⁵ and information about the purpose of future use.

However, the focus remains whether tissue taken and stored without specific consent for use in research may nevertheless be used in research. The Ethics in Health Research guidelines require still, as a point of departure, that fresh consent be acquired for use of biospecimens in research.¹⁹⁶ In other words, where tissue samples are held in storage pursuant to, or in association with, diagnostic or therapeutic procedures, the consent of donors should be obtained.¹⁹⁷

However, this requirement of informed consent is not absolute. The Ethics in Health Research guidelines¹⁹⁸ acknowledge that the research ethics committee tasked with the review of a research project may waive the requirement for consent for secondary use of biospecimens in research. In deciding whether consent may be waived altogether, or waived subject to conditions, a research ethics committee may consider various factors, some of which are articulated in the guidelines.¹⁹⁹ The first factor that may be considered is the nature of existing consent relating to collection and storage of the sample and whether the research proposal is an extension of, or closely related to, a previously approved use of the tissue sample. Secondly, the

¹⁹¹ Ethics in Health Research (note 52).

¹⁹² Ethics in Health Research (note 52) at Preamble.

¹⁹³ Ethics in Health Research (note 52) at 40.

¹⁹⁴ See especially part 2.1.1 of Chapter 2 above.

¹⁹⁵ Ethics in Health Research (note 52) at 40.

¹⁹⁶ Ethics in Health Research (note 52) at 41.

¹⁹⁷ *Ibid.*

¹⁹⁸ *Ibid.*

¹⁹⁹ *Ibid.*

justifications presented for seeking waiver of consent may be considered. These include the practicability of obtaining consent. Furthermore, it may be considered what the intended arrangements are to safeguard the privacy of the donor, as well as the extent to which research use may pose a potential risk to the privacy of the donor. The extent to which the tissue sample is de-identified is also a relevant factor. Lastly, the possibility of commercial exploitation of derivatives of the biospecimens used in research may be considered.²⁰⁰

With these and other factors in mind, a research ethics committee may make a decision as to whether it is appropriate to waive, with or without conditions, the requirement of consent in specific circumstances. Therefore, where the research ethics committee is of the opinion that the requirement for consent may be waived, no new consent is sought from the person from whom the biospecimen was initially removed.

An analysis of the South African waiver mechanism is found in Chapter 4 below. It suffices to mention here that the waiver provision lacks clarity as to exactly when it is justifiable and the extent to which the factors play a role.

2.2.4 Consent in action: Local examples

For illustrative purposes, two practical examples are identified in the South African context. The first example is an ethics guideline for acquisition of informed consent for the collection and storage of biospecimens for research purposes. The Standard Operating Procedures,²⁰¹ issued by the Faculty of Health Sciences Human Research Ethics Committee at the University of Cape Town, addresses informed consent for use of biospecimens in retrospective studies.²⁰² In short, where subsequent research use falls within the scope of the

²⁰⁰ Ibid.

²⁰¹ 'Collection and Storage of Data or Biological Specimens for Research Purposes' (2009) published by Human Research Ethics Committee of the Faculty of Health Sciences at the University of Cape Town (UCT) available at <http://www.health.uct.ac.za/research/humanethics/sop> (accessed 22 June 2011).

²⁰² 'Retrospective study' is defined in the UCT Standard Operating Procedures as: '[a] study which uses specimens that already exist when Human Research Ethics Committee approval is requested. This includes tissue collected for diagnostic purposes and then stored; for example, pathology samples or the secondary use of specimens previously collected for another research proposal and subsequently stored in a tissue bank.' UCT (note 201) at 1-2.

original consent, additional informed consent is not required.²⁰³ Where this is not the case, researchers must acquire fresh consent from the original donor before commencing the new research project.²⁰⁴ However, in certain cases²⁰⁵ informed consent will not be required, for example, where the identity of the donor patient is unavailable to the researchers.²⁰⁶ The Standard Operating Procedures also provide a separate information sheet and consent form for storage and future use of biospecimens.²⁰⁷ Donors may choose to provide broader consent for use of their biospecimens in, inter alia, any future research ethics committee-approved research project.²⁰⁸

The second practical example is a one-page consent form for storage of pathology specimens specifically used for breast cancer patients at Groote Schuur Hospital in Cape Town.²⁰⁹ Patients undergoing mastectomies are informed that two specimens of malignant tissue may be stored: one for diagnostic and treatment use, and the other for possible future research purposes. Patients may provide consent for storage of the second biospecimen and its use in a breast cancer study involving the donor or for any other future research approved by a research ethics committee.²¹⁰

It is interesting to note that these examples allow donors to provide different levels of consent: from project-specific consent to broad consent

²⁰³ UCT (note 201) at 2.

²⁰⁴ *Ibid.*

²⁰⁵ Cases where the research ethics committee may decide to not require informed consent are where:

- ‘Samples will be used anonymously and the results will not place an individual, family or community at social, psychological or economic risk.
- If the link to identifiers exists but is not provided to the research team and the results will not place an individual, family or community at social, psychological or economic risk. The investigator holding the code or link must sign a written agreement that he or she will not release the identifiers to the research team. This written confirmation must be included in the submission to the Human Research Ethics Committee.
- If the samples can be linked to identifiers, the Chair or designee will decide on a case-by-case basis whether a protocol requires expedited or full committee review.’ UCT (note 201) at 2.

²⁰⁶ *Ibid.*

²⁰⁷ UCT (note 201) at 2-5.

²⁰⁸ UCT (note 201) at 3.

²⁰⁹ Groote Schuur Hospital (University of Cape Town) ‘Storage of Pathology Specimens’ consent form (hereafter ‘Groote Schuur consent form’).

²¹⁰ Groote Schuur consent form (note 209).

permitting use of stored biospecimens in any form of research ethics committee-approved research. This is in contrast to the strict legislative point of departure of the present form of the National Health Act²¹¹ not yet in force, which requires specific consent for a specific research project.²¹² However, in terms of the current legislation, a window of opportunity permits a more flexible approach. Accordingly, it is my view that the new legal framework, when in force, should expressly accommodate such broader forms of consent in the context of the secondary use of biospecimens in research. In other words, the relevant part of the National Health Act should be amended before being implemented. The nature of the broader consent is discussed further in Chapters 3 and 4 below.

2.2.5 Socio-cultural sensitivity

Although the South African regulatory framework recognises the importance of socio-cultural sensitivities in seeking informed consent, it will be apparent from the following chapter that it does not do so to the same extent as Australia.²¹³ However, provisions promoting socio-cultural sensitivity do appear in the South African context.

The most prominent of these provisions is in the South African Constitution.²¹⁴ It firmly entrenches the cultural, religious and linguistic rights of all persons, including indigenous peoples.²¹⁵ It would therefore follow that socio-cultural sensitivities should always be considered in South African medical research projects as a matter of constitutionality.

The Guiding Principles in Ethics in Health Research,²¹⁶ for example, require that “[c]ulture, language, beliefs, perceptions, and customs must all be considered”²¹⁷ in health research projects. Furthermore, when providing information for purposes of seeking consent from prospective participants, it

²¹¹ Act 61 of 2003.

²¹² See part 2.2.2 above for an overview of the South African legislative position.

²¹³ See Chapter 3 below.

²¹⁴ Constitution of South Africa, 1996.

²¹⁵ See ss 9, 10, 15, 30 and 31, to name a few. Constitution of South Africa, 1996.

²¹⁶ Ethics in Research (note 52).

²¹⁷ Ethics in Research (note 52) at par 2.1 entitled ‘Respects and Dignity’.

must be done in a 'simple and culturally appropriate'²¹⁸ manner. The MRC Guidelines²¹⁹ require that the social and cultural environment of the prospective participants be taken into consideration at all times when seeking consent. Accordingly, instead of focussing only on the individual interests of the prospective participant when seeking consent, the collective interests of the community and its cultural sensitivities must also be respected.²²⁰ The MRC correctly holds that this 'is of paramount importance for health research in an African context.'²²¹

At this point in the discussion it suffices to note that the South African ethics framework acknowledges the importance of taking cultural sensitivities into account when acquiring consent. However, questions that may arise in this context include how socio-cultural sensitivity per se should be addressed in South Africa where cultural diversity is particularly diverse. This question and other aspects are addressed in a critical comparative analysis in Chapter 4 below.²²²

2.3 Concluding remarks

This chapter provided a brief description of the South African legal and ethics frameworks governing the requirement of informed consent in general, and in the context of the secondary use of human biospecimens in medical research.

As a point of departure, informed consent is always required for any research activity involving human participants or human biospecimens. However, this stance amounts to an overgeneralisation because, in certain cases, obtaining informed consent in health research on biospecimens may prove to be impossible or impractical, or even unnecessary.

²¹⁸ Ethics in Research (note 52) at par 2.6 entitled 'Informed Consent'.

²¹⁹ MRC (note 53) at 3.1.2.

²²⁰ Ibid.

²²¹ Ibid.

²²² See Chapter 4 part 4.5 below.

With regard to the Constitution²²³ and the National Health Act²²⁴ and its Regulations, it was found that it is permissible, with consent of the patient, to remove tissue for health research purposes. The South African legislative framework therefore addresses the requirement of informed consent for the use of biospecimens in health research. However, regarding secondary use of biospecimens in health research, legislation does not provide a clear answer.

The ethics guidelines do offer some clarity in this regard. The principle is, again, that fresh consent is required for the secondary use of biospecimens previously obtained for diagnostic or therapeutic purposes in health research. Therefore, where medical research was not initially consented to, new consent is required for this new purpose. However, where the original consent covers health research purposes, no new consent is required. It was found that this requirement might at times be relaxed. The role of the research ethics committee is important in this context. Research ethics committees decide, upon considering various factors, whether the requirement of consent may be waived in totality, or subject to conditions, for the secondary use of such biospecimens in research.

²²³ Section 12(2)(c) of the Constitution of South Africa, 1996.

²²⁴ Act 61 of 2003.

CHAPTER 3

3.1 Introduction

3.1.1 Australia as a comparative jurisdiction

This chapter describes the Australian legal and ethics framework for informed consent²²⁵ in general and, more specifically, for secondary use of biospecimens in oncology research. The aim is to lay a foundation for comparative analysis²²⁶ of the position in South Africa and Australia, and to identify similarities and differences between the two jurisdictions. Subsequently, the appropriateness of these legal-ethics positions may be evaluated.

The choice of Australia as a comparative jurisdiction is based on a number of factors. The primary reason is that both jurisdictions share the same underlying values for informed consent. This is manifested in the South African landmark case *Castell v De Greeff*²²⁷ where the approach followed in *Rogers v Whitaker*,²²⁸ the Australian locus classicus on informed consent, played an important role in shaping the current South African law. The formulation of the disclosure requirement in *Rogers v Whitaker*²²⁹ ‘accords with the fundamental right of individual autonomy and self-determination to which South African law is moving.’²³⁰ Furthermore, this approach corresponds to developments in other jurisdictions such as Canada and the United States of America, as well as with the judicial views of continental Europe.²³¹

A second reason for Australia being a comparative jurisdiction is the considerable amount of medical research conducted in that country.²³² In

²²⁵ It is suggested by the Australian High Court in *Rogers v Whitaker* [1992] HCA 58 at par 15 that the term ‘duty to disclose’ may be preferable to the ‘somewhat amorphous’ phrase of ‘informed consent’. However, the term ‘informed consent’ will be used in this dissertation because it remains a widely used term. Breen KJ et al *Good Medical Practice: Professionalism, Ethics and Law* (2010) at 49.

²²⁶ The comparative analysis forms part of Chapter 4 below.

²²⁷ *Castell v De Greeff* (note 108) at 426.

²²⁸ *Rogers v Whitaker* [1992] HCA 58.

²²⁹ *Rogers v Whitaker* (note 228) at par 16.

²³⁰ *Castell v De Greeff* (note 108) at 426.

²³¹ *Ibid.*

²³² ‘About Australia: Research and Development’ (2008) fact sheet published by the Department of Foreign Affairs and Trade, Australia available at

oncology specifically, research has resulted in, inter alia, development of a vaccine for cervical cancer and improved detection methods for skin malignancies.²³³ The study of the consent model in a jurisdiction where oncology research yields such results is, in my view, of great interest.

Lastly, the study of the Australian legal-ethics framework presents certain logistical advantages. All Australian regulatory documents are in English and the latest versions are readily available on the Internet, making access easy.

Australia is a federation of autonomous States and Territories with eight State and Territory government systems in a Federal or Commonwealth government²³⁴ system.²³⁵ Where there is conflict between state and Commonwealth laws, the latter prevail to the extent of the inconsistency.²³⁶ The Federal Parliament does not have the express jurisdiction to promulgate statutes in the context of health law.²³⁷ Legislative capacity in the context of health law is in the jurisdiction of the state and territory parliaments,²³⁸ some of which are discussed below.²³⁹

However, an important federal statute is the National Health and Medical Research Council Act.²⁴⁰ This Act establishes the National Health and Medical Research Council (NHMRC), a statutory body, which is, essentially,²⁴¹

http://www.dfat.gov.au/facts/research_development.pdf (accessed 29 August 2011) at 4.

²³³ Ibid.

²³⁴ Each state and federal government system includes the three branches of government: the legislature, executive and judiciary.

'About Australia: Legal System' (2008) fact sheet published by the Department of Foreign Affairs and Trade, Australia available at http://www.dfat.gov.au/facts/legal_system.pdf (accessed 29 August 2011) at 1-2.

²³⁵ Ibid.

²³⁶ Breen KJ et al (note 225) at 354.

²³⁷ Federal Parliament does, however, enact law pertaining to pharmaceutical, sickness and hospital benefits. Breen KJ et al (note 225) at 354

²³⁸ Ibid.

²³⁹ See part 3.2.1 of this chapter below.

²⁴⁰ Act 225 of 1992 as amended (hereafter NHMRC Act).

²⁴¹ In short, The Chief Executive Officer (CEO) of the NHMRC issues human research guidelines after the Australian Health Ethics Committee (AHEC) has developed them and referred them to the Council of the NHMRC. AHEC, which is also established by the NHMRC Act, is the Principal Committee of the NHMRC, and in terms of s 10(2) of NHMRC Act, AHEC is tasked with developing the research guidelines. The CEO then, in terms of s 10(1) of the NHMRC Act, issues the guidelines on behalf of the NHMRC pertaining to ethical issues relating to health research involving humans. The culmination of this interaction between the various role-players in the NHMRC is the National Statement. National Statement (note 42) at 4.

responsible for formulating the National Statement on Ethical Conduct in Human Research (hereafter National Statement).²⁴² These important ethics guidelines are discussed below.²⁴³

3.1.2 Australian concept of informed consent

By way of introduction, the meaning of informed consent in the Australian context is discussed briefly. As noted above, the leading federal court decision in *Rogers v Whitaker*²⁴⁴ lays down the foundations of the Australian model of informed consent for medical treatment. Nevertheless, the model is relevant to the research context too. In essence, during the process of informed consent, the medical practitioner has a legal duty to disclose to the patient the necessary information and material risks associated with the procedure.²⁴⁵ In effect, the information provided, upon which patients base their decision, must be what reasonable persons in the patients' position would require to make an informed decision.²⁴⁶

The National Statement²⁴⁷ sets the national standard for the conduct, ethical review and design of all human research projects in Australia.²⁴⁸ The National Statement provides the other elements that constitute valid informed consent in the context of medical research involving human participants.²⁴⁹

²⁴² National Statement (note 42).

²⁴³ See part 3.2.2 of this chapter below.

²⁴⁴ *Rogers v Whitaker* (note 228). In essence, the facts of the case were that the patient, Whitaker, was claiming damages from her ophthalmic surgeon, Rogers, for damage caused during a procedure aiming to improve the function of the right eye. However, the procedure did not succeed, and in addition, Whitaker's left eye lost all function due to it contracting sympathetic ophthalmia.

²⁴⁵ *Rogers v Whitaker* (note 228) par16 describes the scope of a medical practitioner's duty of disclosure as the obligation:

'...to warn a patient of a material risk inherent in the proposed treatment; a risk is material if, in the circumstances of the particular case, a reasonable person in the patient's position, if warned of the risk, would be likely to attach significance to it or if the medical practitioner is or should reasonably be aware that the particular patient, if warned of the risk, would be likely to attach significance to it.'

Tickner K 'Rogers v Whitaker – Giving Patients a Meaningful Choice' (1995) 15 *Oxford Journal of Legal Studies* 109 at 109.

²⁴⁶ Tickner K (note 245) at 109.

²⁴⁷ National Statement (note 42).

²⁴⁸ National Statement (note 42) at 7.

²⁴⁹ National Statement (note 42) at 19. Human research amounts to research conducted with or about people, their data or tissue and the National Statement expressly includes the collection and use of organs, tissues or fluids within the ambit of human research. See also National Statement (note 42) at 8.

Similarly to South Africa, consent must be voluntary²⁵⁰ and based on sufficient information²⁵¹ with adequate understanding of the proposed research and implications of participation.²⁵² The participant must also have decision-making capacity and consent must be specifically for the proposed research.²⁵³ Satisfying the requirements may vary according to the nature of the research, specific requirements of law and ethics, as well as cultural sensitivities of persons who would participate in the research.²⁵⁴

This brief introduction above outlines the essential considerations where a prospective research participant in a specific research project must provide informed consent. However, the focus of this dissertation is to ascertain the consent requirement where oncology biospecimens initially excised for diagnostic or therapeutic reasons only, are used in research. The following section addresses this issue in the Australian context.

3.2 Overview of the Australian legal-ethics framework

3.2.1 Legislation

A brief survey of legislation²⁵⁵ serves to illustrate the consent requirements for use of biospecimens in research. The state and territory laws for Queensland,²⁵⁶ Tasmania,²⁵⁷ Victoria,²⁵⁸ Western Australia²⁵⁹ and New South Wales²⁶⁰ regarding consent for removal of biospecimens are quite similar. All distinguish between regenerative²⁶¹ and non-regenerative²⁶² tissue as a basis for which

²⁵⁰ This includes the provision of sufficient time for the participant to consider all the matters before making the decision. Breen KJ et al (note 225) at 50.

²⁵¹ As discussed above in terms of the common law position articulated in the *Rogers v Whitaker* case.

²⁵² National Statement (note 42) at 19.

²⁵³ Breen KJ et al (note 225) at 50.

²⁵⁴ National Statement (note 42) at 19.

²⁵⁵ Not all of the Australian states and territories will be studied. Reference will be made to legislation of Queensland, Tasmania, Victoria, Western Australia and New South Wales.

²⁵⁶ Transplantation and Anatomy Act 1979 (hereafter Queensland Act).

²⁵⁷ Human Tissue Act 1985 (hereafter Tasmania Act).

²⁵⁸ Human Tissue Act 1982 (hereafter Victoria Act).

²⁵⁹ Human Tissue and Transplant Act 1982 (hereafter Western Australia Act).

²⁶⁰ Human Tissue Act 1983 (hereafter New South Wales Act).

²⁶¹ ‘...means tissue that, after injury or removal, is replaced in the body of a living person by natural processes [of growth or repair].’ Save for the definition in the Victoria Act, which does not contain the words in the square brackets, all the other named Acts share this definition.

purposes the tissue may be removed. In essence, the removal of regenerative²⁶³ tissue involves a lower risk of harm than the removal of non-regenerative²⁶⁴ tissue, due to the fact that the body can naturally replace the regenerative tissue removed.²⁶⁵ Accordingly, the purposes for which regenerative and non-regenerative tissue may be removed, differ.

Essentially, the Acts²⁶⁶ state that an adult donor may provide written consent for removal of regenerative tissue²⁶⁷ for the purpose of transplantation into the body of another living person or for any other medical or scientific purpose.²⁶⁸ It seems that this includes research purposes. However, regarding non-regenerative tissue, the Acts²⁶⁹ permit removal of non-regenerative tissue only for transplantation. At first glance, it is apparent that medical research is not a purpose for which non-regenerative tissue may be removed.

The Queensland Act²⁷⁰ permits removal of a restricted number of types of non-regenerative tissue for research purposes, under limited conditions. In essence, removal of tissue is authorised for human research ethics committee-approved research for which consent has been obtained in terms of the National Statement.²⁷¹

In summary, thus, the donation mechanism permits removal of (healthy) non-regenerative tissue for transplant purposes, but not removal of (malignant) non-regenerative tissue for research purposes. At first glance, this seems prejudicial for oncology research. However, in practice, when malignant

²⁶² ‘...means tissue other than regenerative tissue.’ All named Acts share this definition.

²⁶³ For example, bone marrow or a segment of liver tissue. ‘Organ and Tissue Donation by Living Donors: Guidelines for Ethical Practice for Health Professionals’ (2007) published by the National Health and Medical Research Council (NHMRC), Australia available at <http://www.nhmrc.gov.au/files/nhmrc/publications/attachments/e71.pdf> (accessed 4 February 2012) at 7.

²⁶⁴ For example, a kidney. NHMRC (note 263) at 7.

²⁶⁵ NHMRC (note 263) at 5.

²⁶⁶ Section 10 Queensland Act, s 7 Tasmania Act, s 7 Victoria Act, s 8 Western Australia Act, s 7 New South Wales Act.

²⁶⁷ All the Acts exclude the following tissue in this context: blood, foetal tissue, ova and spermatozoa.

²⁶⁸ From the definitions section of the Tasmania Act, it is clear that this includes ‘...medical or scientific research...’.

²⁶⁹ Section 11 Queensland Act, s 8 Tasmania Act, s 8 Victoria Act, s 9 Western Australia Act, s 8 New South Wales Act.

²⁷⁰ Section 21B, entitled ‘Authorised donations’ applies to skeletal muscle and perioral (mouth) tissue.

²⁷¹ Section 21B Queensland Act.

biospecimens are removed, it is done primarily in the health interests of the patient and not for research. Accordingly, once the malignant tissue is removed during a clinical procedure, surplus biospecimens may be used in subsequent cancer research.

The New South Wales Act²⁷² deals with secondary use of tissue initially removed for diagnostic or therapeutic procedures. Importantly, the Act does not distinguish between regenerative and non-regenerative tissue. Consequently, the New South Wales Act²⁷³ provides that tissue previously removed during treatment may be used for 'scientific purposes' if the person has provided consent for its use in such purposes. Therefore, where tissue is to be removed for a medical purpose, the patient may consent for its use also in research during initial consent or subsequently.

3.2.2 National Statement of Ethical Conduct in Human Research

The National Statement²⁷⁴ represents the national²⁷⁵ ethics standards for medical research involving human participants.²⁷⁶ These guidelines inform the design, conduct and ethical review of all research involving human participants research in Australia.²⁷⁷

The National Statement²⁷⁸ specifically addresses participant²⁷⁹ consent for use of biospecimens in research. Hospitals and pathology laboratories must retain archival samples of tissue removed for diagnostic or forensic purposes.²⁸⁰ However, these biospecimens may prove useful also in medical

²⁷² At ss 21W and 21X.

²⁷³ Section 21X New South Wales Act reads as follows:

'[t]he use, for therapeutic, medical or *scientific purposes*, of tissue removed from the body of a person during medical...or surgical treatment, is authorised if:
(a) the person has given his or her consent in writing to the use of the tissue for that purpose, and
(b) the consent has not been revoked...' [Emphasis added].

²⁷⁴ National Statement (note 42).

²⁷⁵ I.e. Australia as a whole.

²⁷⁶ National Statement (note 42) at 7.

²⁷⁷ *Ibid.*

²⁷⁸ National Statement (note 42) at chapter 3.4.

²⁷⁹ The National Statement uses the term 'participant' even in the context of research using tissue samples. In my view this is incorrect because tissue samples are not participants per se. Accordingly, the term 'donor' will be used instead.

²⁸⁰ National Statement (note 42) at p39.

research. It is therefore necessary to ascertain what the consent requirements are to unlock the potential of these valuable biospecimen resources.

Firstly, potential donors²⁸¹ must have clear information about whether tissue samples will be identifiable.²⁸² Furthermore, where the research is expected to produce information regarding personal health of donors, the method for follow-up with participants must be explained in the research proposal.²⁸³ These requirements reflect the importance attached to identifiability of biospecimens and the effect this has on consent. Where biospecimens will be de-identified or anonymised, follow-up is irrelevant.

Secondly, three variants of consent may be used regarding use of biospecimens in future research.²⁸⁴ Donors may elect²⁸⁵ to provide specific,²⁸⁶ extended²⁸⁷ or unspecified²⁸⁸ consent. The latter two forms of consent enable donors to provide broader consent where the availability of information²⁸⁹ regarding the future research is limited at the time of consent.²⁹⁰ Furthermore, the broader consent may need to include storage of the biospecimens in a tissue bank.²⁹¹ However, in terms of unspecified consent, donors must also be informed of the potentially far-reaching implications of providing such consent.²⁹²

²⁸¹ The National Statement also recognises the fact that prospective donors may decline to provide informed consent as well as withdraw previous consent. Donors need not provide reasons for declining to consent for the use of their biospecimens in research. No disadvantage may accrue to a donor because of their decision. Where there is a withdrawal of previous consent, the withdrawing party is entitled to be informed of the consequences of such withdrawal. National Statement (note 42) from 2.2.19 to 2.2.20.

²⁸² National Statement (note 42) at 3.4.5.

²⁸³ National Statement (note 42) at 3.4.6.

²⁸⁴ National Statement (note 42) at 3.4.7 and 2.2.14.

²⁸⁵ See Chapter 4 part 4.3 below for a discussion of the possible bases of this choice.

²⁸⁶ Consent provided for a specific project under consideration. National Statement (note 42) at 2.2.14(a).

²⁸⁷ Consent provided in relation to the future use of biospecimens in research that is an extension of, or closely related to, the original project, or in the same general area of research (for example oncology research). National Statement (note 42) at 2.2.14(b).

²⁸⁸ Consent given for any future research use of the biospecimen. National Statement (note 42) at 2.2.14(c).

²⁸⁹ However, the information available must still provide the participant with an adequate understanding of the 'purpose, methods, demands, risks and potential benefits of the research.' National Statement (note 42) at 2.2.2.

²⁹⁰ National Statement (note 42) at 2.2.14(c).

²⁹¹ National Statement (note 42) at 2.2.15.

²⁹² In addition, unspecified consent and its terms must be clearly recorded. National Statement

However, where patients have consented to removal of biospecimens for diagnostic or therapeutic purposes, but not for storage and possible use in future research of the excess biospecimens, a human research ethics committee or other review body may waive the requirement to seek fresh consent for the envisaged research purpose.²⁹³ In order to validly waive the requirement of such specific consent, a human research ethics committee or other review body must be satisfied that the proposed research fulfils certain criteria.

The National Statement²⁹⁴ stipulates eight core factors that need to be fulfilled before specific consent may be waived. The most important are briefly mentioned: use of biospecimens in the research must carry no more than low risk of harm to the donor; potential benefits should justify risks of harm associated with not seeking consent; and it should be impracticable to obtain consent.²⁹⁵ Furthermore, the human research ethics committee must be satisfied that there is no known or likely reason for thinking that donors would not have consented if they had been asked; that there is sufficient protection of their privacy as well as an adequate plan to protect confidentiality of data.²⁹⁶

It is therefore clear that specific consent for secondary use of biospecimens in research is not an absolute requirement and may be waived in certain circumstances. However, where specific consent has been waived, the National Statement²⁹⁷ requires that human research ethics committees make publically available (for example in annual reports) descriptions of research projects where the consent requirement was waived. This measure helps to maintain public confidence in the research process.²⁹⁸

It is important to note that the waiver of specific consent would not be relevant where donor patients, in the Australian context, have already provided broader forms of consent allowing the storage and use in future research of excess biospecimens removed for diagnostic or therapeutic purposes.

(note 42) at 2.2.16.

²⁹³ National Statement (note 42) at 3.4.7.

²⁹⁴ National Statement (note 42) at 2.3.6 (a)-(i).

²⁹⁵ National Statement (note 42) at 2.3.6 (a)-(c).

²⁹⁶ National Statement (note 42) at 2.3.6 (d)-(f).

²⁹⁷ National Statement (note 42) at 2.3.8.

²⁹⁸ *Ibid.*

3.2.3 NHMRC Biobanks Information Paper

The Information Paper²⁹⁹ supplements the National Statement with regard to biobank issues.³⁰⁰ Unlike the National Statement, however, it is not a prescriptive guideline.³⁰¹ Instead, it identifies best practice via analysis of national and international literature.³⁰² Although a discussion of biobanks is not within the scope of this dissertation, the Information Paper provides insight into the consent requirement for secondary use of biospecimens in research.

The Information Paper recognises that requiring specific consent for future research use of biospecimens may be problematical due to uncertainty about the research purpose at the time of collection and initial consent.³⁰³ Accordingly, it notes that the National Statement endorses use of extended and unspecified consent at the time of tissue collection, as discussed above.

However, in terms of the broadest form of consent, unspecified consent, the Information Paper makes a valuable suggestion pertaining to the consent requirement for storing biospecimens.³⁰⁴ It suggests³⁰⁵ that unspecified consent in this context should comprise of two consent components, namely: specific consent for removal and storage of the biospecimen (for diagnostic or therapeutic purposes); and unspecified or broad consent for use of stored biospecimens in future, undetermined research. This is, in my opinion, a sound approach where biospecimens are identifiable and, in essence, corresponds with the Groote Schuur breast cancer example highlighted in the South African context above.³⁰⁶

²⁹⁹ 'Biobanks Information Paper' (2010) published by the National Health and Medical Research Council (NHMRC), Australia available at http://www.nhmrc.gov.au/files_nhmrc/file/your_health/egenetics/practioners/biobanks_information_paper.pdf (accessed 11 August 2011) (hereafter 'Biobanks Information Paper').

³⁰⁰ Biobanks Information Paper (note 299) at 4-5.

³⁰¹ Ibid.

³⁰² Ibid.

³⁰³ Biobanks Information Paper (note 299) at 24-5.

³⁰⁴ Ibid.

³⁰⁵ Ibid.

³⁰⁶ See Chapter 2 at part 2.2.4 above.

3.2.4 Oncology research example

For illustrative purposes, relevant features of an example of an institutional ethics guideline are highlighted. The Australasian Biospecimen Network (ABN), an organisation established in 2002, is a platform for discussion of technical, legal, ethical and managerial issues relevant to supply and use of human biospecimens in medical research.³⁰⁷ In particular, the ABN deals with consensual storage of surplus tissue excised during therapeutic procedures, and its supply for use in approved research.³⁰⁸ A subgroup of ABN, known as ABN-Oncology, collects various types of cancer biospecimens for oncology research,³⁰⁹ including the Australian Ovarian Cancer Study (AOCS).

The AOCS brochure and consent form³¹⁰ demonstrate how the informed consent requirement applies in oncology research. Patients may consent to their tissue being stored indefinitely at a specific biorepository for research purposes set out specifically in the consent form. In addition, consent may be provided for any 'future biochemical and genetic studies of cancer.'³¹¹ Participants in the AOCS are not necessarily informed of the actual future use of the biospecimens, but all future research is reviewed and approved by a human research ethics committee, as set out in the National Statement.³¹²

This approach resonates with the tiered model of consent endorsed by the National Statement. In addition to consenting to storage of identifiable³¹³ biospecimens for research purposes, prospective participants may provide consent that is specific (for a specific cancer research project) or a broader form (for any future cancer research).

³⁰⁷ 'Biorepository Protocols' (2007) published by the Australasian Biospecimen Network (ABN) available at www.abrn.net/pdf/ABN_SOPs_Review_Mar07_final.pdf (accessed 12 August 2011) at i.

³⁰⁸ ABN (note 307) at i.

³⁰⁹ *Ibid.*

³¹⁰ ABN (note 307) at 70-7.

³¹¹ ABN (note 307) at 76.

³¹² ABN (note 307) at 72.

³¹³ In terms of the AOCS, biospecimens are coded (labeled with a barcode) and access to the donor information is restricted i.e. indirectly identifiable. ABN (note 307) at 71.

3.3 Socio-cultural sensitivities

The Australian regulatory framework is committed specifically to understanding and accommodating socio-cultural sensitivities of Australian indigenous people, i.e. the Aborigines and Torres Strait Islanders,³¹⁴ especially when seeking consent for research involving Aborigines and Torres Strait Islander participants.

In addition to the National Statement, researchers involved with Aboriginal and Torres Strait Islander participants must³¹⁵ consult the Values and Ethics: Guidelines for Ethical conduct in Aboriginal and Torres Strait Islander Health Research³¹⁶ (hereafter Values and Ethics), published by the National Health and Medical Research Council (NHMRC). These guidelines have the same status and authority as the National Statement, which makes them authoritative for health research involving Aborigines and Torres Strait Islanders.³¹⁷

The view expressed is that, where a research process neglects to ‘understand differences in values and culture [it] may be a reckless act that jeopardises both the ethics and quality of research.’³¹⁸ In the context of research using biospecimens, the National Statement³¹⁹ requires institutional policies to take socio-cultural sensitivities into account when formulating policies pertaining to the collection, storage and use of human tissue in research. Socio-cultural sensitivity may be manifested through researchers

³¹⁴ The Aboriginal and Torres Strait Islander population constitutes an estimated 2.5 per cent of the Australian population. In general, the disease burden of Aborigines and Torres Strait Islanders is considerably larger than that of non-indigenous Australians. In the context of cancer, it was found that Aborigines and Torres Strait Islanders are 3 times as likely to be diagnosed with cervical cancer, and 1.6 times as likely to be diagnosed with lung cancer. ‘The health and welfare of Australia’s Aboriginal and Torres Strait Islander people: an overview’ (2011) published by the Australian Institute of Health and Welfare available at www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=10737418955 (accessed 20 January 2012) at vii-viii and 48.

³¹⁵ See National Statement (note 42) at 69.

³¹⁶ ‘Values and Ethics: Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health Research’ (2003) published by the National Health and Medical Research Council (NHMRC), Australia available at <http://www.nhmrc.gov.au/files/nhmrc/publications/attachments/e52.pdf> (accessed 11 August 2011) (hereafter ‘Values and Ethics’).

³¹⁷ Values and Ethics (note 316) at 2.1.

³¹⁸ Values and Ethics (note 316) at 1.3.1.

³¹⁹ National Statement (note 42) at 3.4.1(g).

having due regard for the welfare, beliefs, perceptions, customs and cultural heritage, both individual and collective, of those involved in medical research.³²⁰ However, what do these considerations entail and what guidance is available in this regard?

It is at this point when the Values and Ethics guidelines must be considered. These guidelines emphasise six core values as an additional lens through which researchers should view the informed consent process *inter alia*.³²¹ Although complex and sometimes overlapping in interpretation, the six values are: reciprocity,³²² respect, equality,³²³ survival and protection,³²⁴ responsibility,³²⁵ spirit and integrity.³²⁶ A detailed discussion of all these values falls beyond the scope of this dissertation. Instead, what follows is a brief overview of how the value of respect should inform the acquisition of consent from Aboriginal and Torres Strait Islander research participants.

Respect,³²⁷ as a value, is particularly important in the context of acquiring consent from Aborigines and Torres Strait Islanders.³²⁸ Respect for the socio-cultural characteristics of these indigenous groups may be demonstrated in a research project by considering a variety of factors. These include whether the diversity of the indigenous communities is addressed in

³²⁰ National Statement (note 42) at 1.10.

³²¹ Values and Ethics (note 316) at 2.2.

³²² In the medical research context reciprocity implies that the research outcomes should include equitable and valued benefits to the Aboriginal and Torres Strait Islander participants. Values and Ethics (note 316) at 2.2.1.

³²³ In this context, equality refers to the equal value of people, which translates to the right of Aborigines and Torres Strait Islanders to be different with their culture being appreciated and respected. Values and Ethics (note 316) at 2.2.3.

³²⁴ Researchers must not undermine the collective dignity and identity of the Aborigines and Torres Strait Islanders and must respect their cultural distinctiveness. Values and Ethics (note 316) at 2.2.5.

³²⁵ In the research context, responsibility lies with the researchers to do no harm to the Aborigines and Torres Strait Islanders. Researchers are also accountable to the individual participants and their communities especially in relation to the socio-cultural aspects of the Aboriginal and Torres Strait Islander way of life. Values and Ethics (note 316) at 2.2.4.

³²⁶ This is an over-arching value binding the other values. Researchers must respect the integrity of cultural inheritance for generations to come. In addition, in terms of the research process, researchers must demonstrate that the process itself does not undermine any of the other values discussed. Values and Ethics (note 316) at 2.2.6.

³²⁷ Respect, in this context, entails the recognition of the contribution of the Aboriginal and Torres Strait Islander participants and how the consequences of the research may affect them. Furthermore, it is the respect and recognition of the right of people to have different cultural values and norms. Values and Ethics (note 316) at 2.2.2.

³²⁸ The National Statement itself also endorses respect for the participants' customs and cultural heritage. Values and Ethics (note 316) at 2.2.2.

the manner in which decisions are made, how the individual and collective contribution of the community is acknowledged and how the research proposal engages with the community's knowledge and experience.³²⁹ Essentially, the community which the participants form part of, should be satisfied with the terms of the research project.³³⁰ Researchers need to note that acquiring consent may have a collective dimension in these circumstances. In addition to individual consent, other interested parties, such as community elders, may need to provide consent before research may commence.³³¹

It is clear from the above that cultural sensitivity towards research participants³³² is firmly entrenched within the Australian regulatory framework regarding medical research. This approach accords with the international³³³ principle of non-discrimination and respect for different cultures.³³⁴ A further discussion of the relevance of socio-cultural sensitivity in acquiring consent for the purposes of this dissertation is found in Chapter 4 below.

3.4 Concluding remarks

In this chapter, a snapshot of the important aspects of the Australian legal-ethics framework pertaining to the use of biospecimens in medical research was given. The general concept of informed consent in Australia was distilled from relevant common law, legislation and ethics guidelines. The legislative base for the excision of human tissue for various purposes was ascertained primarily from State and Territory law. Although there are subtle differences amongst the various States and Territories discussed, they all comply with the federal research ethics framework, the National Statement. The National

³²⁹ *Ibid.*

³³⁰ *Ibid.*

³³¹ *Ibid.*

³³² Although researchers need to be sensitive to all cultures, the focus in this discussion was on the indigenous Aboriginal and Torres Strait Islander Peoples.

³³³ For example, see OECD (note 86) at Best Practice 5.3, UNESCO International Declaration on Human Genetic Data article 7 and the Council of Europe Convention on Human Rights and Biomedicine article 11 all require that institutions dealing with the collection of biospecimens need to be sensitive of the specific socio-cultural issues present when dealing with minorities, indigenous or vulnerable groups. Biobanks Information Paper (note 299) at 16.

³³⁴ Biobanks Information Paper (note 299) at 16.

Statement supplements the legislative point of departure by addressing the consent requirements where human tissue is used in medical research. It was established that a more flexible, tiered consent model is used in Australian medical research using biospecimens. However, similarly to South Africa, the National Statement allows the possible waiver, by human research ethics committees and other ethics review bodies, of the specific consent requirement in the case of the secondary use of biospecimens in medical research.

The following chapter contains the main discussion of the research question and other important themes of the dissertation. The current chapter, as well as the preceding one, provided the foundation for the comparative analysis to follow. Relevant international trends will be identified in the comparison below and an assessment will be made on how the South African and Australian positions compare. The critical discussion will form a basis for exploring less rigid consent approaches in the South African context.

CHAPTER 4

4.1 Introduction

This chapter critically compares the legal-ethics frameworks described in the previous chapters, viz those of South Africa and Australia.³³⁵ Reference is also made to international trends as articulated in reports and guidelines from the Nuffield Council on Bioethics,³³⁶ the National Cancer Institute,³³⁷ CIOMS,³³⁸ OECD³³⁹ and UNESCO to enrich the analysis.³⁴⁰

A focussed approach to the analysis is followed. The primary question is whether informed consent is necessary for secondary use in medical research of biospecimens initially collected for diagnostic or therapeutic purposes. In order to analyse the question adequately, four selected subsidiary themes form the basis of the comparative analysis.

The first theme is the legislative approach to consent for removal of biospecimens and its adequacy in accommodating secondary use for research purposes. Secondly, an evaluation of the consent models for secondary use of biospecimens in research is provided. Thereafter, a critical analysis of waiver

³³⁵ As discussed above in Chapters 2 and 3, respectively.

³³⁶ The United Kingdom-based Nuffield Council on Bioethics is an independent entity that examines and reports on ethical issues in biology and medicine. It was established in 1991 by the Nuffield Foundation. The reports issued by the Nuffield Council have achieved an international reputation for advising policy makers and 'stimulating debate in bioethics.' See <http://www.nuffieldbioethics.org/about> (accessed 4 February 2012).

³³⁷ The United States-based National Cancer Institute (NCI), established in 1937, forms part of the National Institutes of Health (NIH) and the Department of Health and Human Services. It has published guidelines that may be applied voluntarily to biospecimen repositories. NCI (note 1) at A.2. See also <http://cancer.gov/cancertopics/factsheet/NCI/NCI> (accessed 4 February 2012).

³³⁸ The Council for International Organizations of Medical Sciences (CIOMS) is an international, non-governmental and non-profit organisation, established by the World Health Organisation (WHO) and the United Nations Educational, Scientific and Cultural Organization (UNESCO) in 1949. The CIOMS guidelines aim to guide countries in defining their national policy. These guidelines are not legally binding. CIOMS (note 84) at 1. See also http://www.cioms.ch/about/frame_about.htm (accessed 4 February 2012).

³³⁹ The guidelines issued by the Organisation for Economic Co-operation and Development (OECD) is the culmination of the interaction between member governments comparing policy experiences, seeking answers to common problems, identifying good practice and working to co-ordinate domestic and international policies. OECD (note 86) at 1.

³⁴⁰ The United Nations Educational, Scientific and Cultural Organization (UNESCO) guidelines are a means of disseminating the reflections of this organisation regarding specific bioethics principles. These guidelines are not legally binding. UNESCO (note 88) at 5.

mechanisms for research ethics committees is presented. And lastly, the role of socio-cultural sensitivity in seeking consent is discussed briefly.

4.2 Statutory consent for removal of human biospecimens

The legislative approach to consent for harvesting of biospecimens for research purposes was introduced above.³⁴¹ The two jurisdictions have different points of departure regarding consent for removal of human tissue biospecimens but, as will be seen, actually have very similar approaches overall.

As will be recalled, the South African approach emphasises the purpose for which tissue is removed. It remains uncertain whether medical research may constitute such a purpose.³⁴² However, a survey of draft regulations³⁴³ suggests that health research may constitute a purpose for which biospecimens may be removed. Therefore, in summary, the South African point of departure requires specific consent given in advance for use of biospecimens in research.

Relatively speaking, the Australian legislative framework is clear that medical research is included as a purpose for which biospecimens may be removed,³⁴⁴ provided the tissue is regenerative. In other words, a distinction is made between regenerative and non-regenerative tissue, i.e. the physical nature of the tissue is considered rather than the purpose for which it is removed. In terms of the State and Territory Acts, participants may generally consent to removal of regenerative tissue for research.³⁴⁵ In summary, the point of departure in Australian law is that consent, provided in advance, is necessary for use of biospecimens in research. However, the consent need not be specific. The National Statement provides that broader forms of consent are acceptable.³⁴⁶

³⁴¹ For the South African legislative position see Chapter 2 at 2.2.2. The Australian legislative provisions are discussed in Chapter 3 at 3.2.1.

³⁴² The National Health Act 61 of 2003 at s 56(1) in particular.

³⁴³ Particularly Draft regulation 7 to the National Health Act 61 of 2003, referred to above at Chapter 2 at 2.2.2.3.

³⁴⁴ See discussion in Chapter 3 above at 3.2.1.

³⁴⁵ See Chapter 3 at 3.2.1 above for more detail.

³⁴⁶ See Chapter 3 at 3.2.2 above and discussion at 4.3 below.

However, where use in research is not anticipated during the initial consent process, the legislative requirements for use in research of the harvested tissue are uncertain.

Australia's New South Wales legislature³⁴⁷ addresses the issue by requiring fresh consent for subsequent use in research of harvested tissue.³⁴⁸ It remains unclear, though, whether consent must be specific to a particular research project. For example, it is unclear whether consent for research use may be given simultaneously with that for diagnostic use or only once the research project is to commence. In my opinion, the meaning attached to consent in the National Statement, where consent may be specific, extended or unspecified, would be relevant here.³⁴⁹ In other words, the information available to the participant pertaining to the future research project will shape the form of consent provided. Nevertheless, it is clear that, in one form or another, consent is required for use of tissue in subsequent research.

The distinction between regenerative and non-regenerative tissue is not articulated in the New South Wales provisions.³⁵⁰ The absence of distinction may be significant, in my view, as it implies that, once removed for a diagnostic or therapeutic purpose, the nature of the tissue is not material to secondary use. If this inference is correct, then oncology biospecimens – non-regenerative by definition – can be used for research. Furthermore, once the tissue has already been separated from the donor, the distinction between regenerative and non-regenerative as basis for the purpose for which the tissue is excised may be superfluous.³⁵¹

The above discussion reveals that the legislation envisages consent for a specific research project, i.e. for 'specific, stipulated and pre-ordained purposes'³⁵² is favoured instead of broad consent for uncertain research uses.

³⁴⁷ At Part 3C of the Human Tissue Act of 1983.

³⁴⁸ At Chapter 3 part 3.2.1. See ss 21W and 21X(1) of the Human Tissue Act of 1983 of New South Wales.

³⁴⁹ National Statement at 3.4.7.

³⁵⁰ Part 3C of the Human Tissue Act of 1983, particularly at ss 21W and 21X(1).

³⁵¹ See above reference about the separation between donor and the tissue in Chapter 1.

³⁵² Price D (note 3) at 102.

It is not only the South African and Australian approaches that are inclined towards a more specific consent approach. The United Kingdom's Nuffield Council on Bioethics³⁵³ notes that the current England and Wales legislation maintains the rigid requirement regarding consent for tissue removal. Explicit detail must be provided about the intended research uses of the removed tissue before the (specific) consent will be valid.³⁵⁴ However, the Nuffield Council expresses³⁵⁵ its concern that valuable research endeavours may be unduly inhibited due to overly onerous consent requirements in legislation.³⁵⁶

The discussion shows that use of surplus tissue in research in circumstances where prior specific consent has not been given remains problematic. There is a lack of guidance in legislation as to what the requirement of consent jurisdictions makes specific provision for this scenario. It was seen that the South African and Australian legislative approaches focus on specific consent for specific research projects. It would follow that fresh consent is required for secondary subsequent research use. I believe this approach may be too rigid. Sourcing biospecimens for research may become very onerous and may prove detrimental to the interests of research.

4.3 Ethics provisions for consent to secondary use of biospecimens in research

By way of introduction, it is necessary to revisit and discuss the primary ethics frameworks outlining the consent requirements for the use of biospecimens removed for clinical purposes in research without advance consent. As will be recalled,³⁵⁷ the South African ethics point of departure is, again, that fresh

³⁵³ 'Response from the Nuffield Council on Bioethics to the Human Tissue Bill' (2004) published by the Nuffield Council on Bioethics available at <http://www.nuffieldbioethics.org/sites/default/files/files/NCOB%20response%20-%20HT%20bill.pdf> (accessed 7 February 2012).

³⁵⁴ Nuffield Council (2004) (note 353) at 1.

³⁵⁵ Nuffield Council (2004) (note 353) at 2.

³⁵⁶ In particular, the UK Human Tissue Bill, as it was at the time of the report. The Nuffield Council on Bioethics does, however, concur that consent is the cornerstone guiding the lawful removal and use of human biospecimens. Nuffield Council (2004) (note 353) at 3.

³⁵⁷ See Chapter 2 above at 2.2.3.

consent should be obtained where stored biospecimens, previously removed for any clinical purpose, is used in subsequent research not initially consented to.³⁵⁸ In the Australian context, it will be remembered³⁵⁹ that advance consent, in one form or another, permits use of biospecimens in research.³⁶⁰ A tiered consent model is followed. Consent may take three forms:³⁶¹ specific, extended or unspecified. Specific consent relates to an instance where specific medical research is envisaged during initial consent for removal. The broader forms (extended and unspecified consent), on the other hand, address instances where the precise nature of future use of biospecimens in research is unknown at the time of consent for removal. What follows is a brief critical analysis of the South African and Australian ethics provisions for consent to secondary use of biospecimens in research. The discussion will include reference to relevant international trends.

A question pertaining to the Australian tiered consent model is whether the donor chooses the form of consent, or whether it depends on the availability of adequate information about the future research project. It is my opinion that a combination of these two possibilities would govern the use of extended or unspecified consent. Even where sufficient information is available at the time of initial consent to support specific research use, the donor may wish to give extended or unspecified consent to permit more flexible use of the tissue in future research. Unspecified consent allows the most flexible use of tissue in research.

Specific consent to a specific research project has important limiting consequences regarding use of biospecimens for other secondary purposes. The Australian National Statement³⁶² states that where specific consent for a certain research project is given, use of the biospecimens for other purposes is

³⁵⁸ This provision is introduced in Chapter 2 above. Ethics in Health Research (note 52) at 41.

³⁵⁹ See Chapter 3 above at 3.2.2.

³⁶⁰ National Statement (note 42) at 2.2.14 and 3.4.7.

³⁶¹ National Statement (note 42) at 2.2.14 and 3.4.7. These three consent types were defined in Chapter 3 above. Their significance is discussed below in this section.

³⁶² National Statement (note 42) at 3.4.7 reads as follows:

‘Consent for the use of tissue may be specific, extended or unspecified...When consent is given for the use of human tissue in specific research only, that tissue *should not be used for any other purpose without the consent of the tissue donor...*’
[Emphasis added]

not permitted. Specific consent therefore potentially limits the purposes for which stored biospecimens may be used in future research. In these instances it follows that fresh consent would be required for purposes other than that originally specifically consented to. However, where extended or unspecified consent is given, the determination of the future purpose of the tissue is more flexible. The latter situation would therefore be favourable for both researcher and participant. The researcher can, within limits,³⁶³ use stored biospecimens where the demand exists, while the consenting party's choice is still respected, in principle.

4.3.1 International trends

In order to contextualise the South African and Australian positions within the broader international arena, certain internationally recognised guidelines are discussed briefly in what follows.

4.3.1.1 *The Nuffield Council on Bioethics*

The Nuffield Report³⁶⁴ provides some insight regarding the nature of the consent requirement for secondary use of tissue in research. In essence, the Nuffield Council's viewpoint regarding the matter is the following: when a patient initially consents to the removal of tissue for a medical procedure, it should include the possibility of subsequent storage of surplus tissue for any acceptable use.³⁶⁵ An 'acceptable' use is that which is 'regulated by appropriate ethical, legal and professional standards.'³⁶⁶

However, this may result in such consent being 'inevitably general.'³⁶⁷ In order to address this, hospitals, for example, are encouraged to ensure that tissue removal consent forms indicate clearly that initial consent for tissue removal includes consent for secondary use of surplus tissue in, for example,

³⁶³ Depending on whether consent is extended or unspecified.

³⁶⁴ 'Human Tissue: Ethical and Legal Issues' (1995) published by the Nuffield Council on Bioethics available at <http://www.nuffieldbioethics.org/sites/default/files/Human%20tissue.pdf> (accessed 7 February 2012).

³⁶⁵ Nuffield Council (1995) (note 364) at par 13-15.

³⁶⁶ Nuffield Council (1995) (note 364) at par 13.12.

³⁶⁷ Nuffield Council (1995) (note 364) at par 13.13.

oncology research.³⁶⁸ This approach is similar to the Groote Schuur example referred to above³⁶⁹ and is, in my view, a desirable approach. It should be sufficient, in my opinion, to inform the donor that the redundant tissue may be used in future research that complies with legal and ethics regulations. The donor may then agree to, or disagree and opt-out from, the stored biospecimens being used in research.

4.3.1.2 National Cancer Institute

The United States National Cancer Institute (NCI) provides recommendations in its Best Practices document³⁷⁰ about consent for use of tissue in oncology research. It recommends that the biospecimen resources³⁷¹ must ensure that research use of the tissue corresponds with the consent provided for it.³⁷² Donors may consent to a broader type of research instead of a specific research project, by using so-called tiered³⁷³ consent.³⁷⁴ This is similar to the different forms of consent discussed in the Australian context.³⁷⁵ Despite the obvious advantages of broader consent for researchers, the NCI³⁷⁶ is concerned that where consent is too broad, i.e. permitting a wide range of research uses, it would be 'burdensome and uninformative'³⁷⁷ for consenting parties when faced with lists of potential types of research. Although a tiered consent model introduces some flexibility, it is my view that specific consent by the donor for storage of the biospecimens for possible future research should be sufficient. In any case, in the oncology context, it is obvious that stored malignant biospecimens will be used specifically for cancer-related research. This, in my opinion, should address the concerns raised by the NCI.

³⁶⁸ Nuffield Council (1995) (note 364) at par 13-15.

³⁶⁹ See Chapter 2 above at 2.2.4.

³⁷⁰ NCI (note 1).

³⁷¹ Biospecimen resources denote a collection of human tissue specimens and associated data for research purposes. NCI (note 1) at A.1.

³⁷² NCI (note 1) at C.2.2.

³⁷³ The NCI notes that the proper functioning of a tiered consent model depends on an efficient system that tracks the level of consent provided by each respective donor of the stored biospecimens. NCI (note 1) at C.2.2.7.

³⁷⁴ Donors may also withdraw their consent ('opt-out') should they wish to exclude the use of their stored biospecimen in research. NCI (note 1) at C.2.2.7.

³⁷⁵ See Chapter 3 above at part 3.2.2 for an explanation of the Australian tiered consent model.

³⁷⁶ NCI (note 1) at C.2.2.7.

³⁷⁷ *Ibid.*

4.3.1.3 Council for International Organizations of Medical Sciences

According to the Council for International Organizations of Medical Sciences (CIOMS) Guidelines³⁷⁸ all biomedical research involving human participants requires specific informed consent.³⁷⁹ However, where stored biospecimens, previously taken during a clinical procedure, are earmarked for secondary use in research, seeking specific informed consent is not necessary if certain conditions are met.³⁸⁰ The research ethics committee must ensure that the following five³⁸¹ conditions are met, namely: the research project poses only minimal risk of harm to the donor; the donors' interests or rights will not be violated; their privacy and confidentiality or anonymity are guaranteed; that the research is designed to answer an important scientific question; and lastly, the research would be impracticable if informed consent were to be sought.³⁸²

It is apparent that the CIOMS Guidelines do not endorse a tiered consent model similar to the Australian and NCI frameworks. It is akin to the South African position that requires specific consent as a point of departure. It seems that the CIOMS Guidelines generally advocate specific consent unless the requirements stated above are fulfilled, in which case no further consent is required. From the requirements named above, it is unclear what the minimal risk may entail. A physical risk of harm is not possible once the biospecimen has been removed from the patient. Informational risk may be at stake, but the requirement of confidentiality or anonymity should, in my view, prevent this risk from materialising.

4.3.1.4 Organization for Economic Co-operation and Development

Similarly to the Australian approach, the Organization for Economic Co-operation and Development (OECD) Guidelines³⁸³ recognise the possibility of a tiered consent model for secondary use of biospecimens in research.³⁸⁴ The

³⁷⁸ CIOMS (note 84).

³⁷⁹ CIOMS (note 84) at Guideline 4 at 32.

³⁸⁰ CIOMS (note 84) at Commentary on Guideline 4 at 35-6 at the part entitled *Use of medical records and biological specimens*.

³⁸¹ *Ibid.*

³⁸² *Ibid.*

³⁸³ OECD (note 86).

³⁸⁴ OECD (note 86) at Annotation 28.

guidelines defer to national sovereignty by stating that, where applicable national law and authorities permit it, broader consent from a donor may be obtained for use of biospecimens in research unforeseen at the time of consent for removal.³⁸⁵ The Guidelines³⁸⁶ state that donors should be able to elect how broad their consent will be. However, where initial consent does not cover secondary use of the stored biospecimens in research, new consent should be obtained.³⁸⁷ This approach is similar to those of Australia and the NCI.

4.3.1.5 United Nations Educational, Scientific and Cultural Organization.

Similarly to the South African and CIOMS approaches, the United Nations Educational, Scientific and Cultural Organization (UNESCO) Report³⁸⁸ states that where a future research purpose goes beyond the ambit of initial consent, specific consent should be sought from the donors.³⁸⁹ Where this is not practicable, the Report³⁹⁰ requires regulations³⁹¹ to be implemented to waive the specific consent requirement.³⁹² The UNESCO Report therefore, as a point of departure, requires specific consent for the secondary use of stored tissue in research.

However, where stored biospecimens are permanently de-identified, prior 'overall'³⁹³ consent is acceptable in terms of the UNESCO Report. This approach is stricter than that of the CIOMS Guidelines, for example, which require no consent at all where biospecimens are anonymised. Where the stored biospecimens are anonymous there is no possibility of informational harm to the donor. Although prior overall consent is very flexible, it is my view that no consent should be required in these circumstances.

The position can be summarised to show that South Africa requires specific consent from the donor for use of stored biospecimens in future

³⁸⁵ Ibid.

³⁸⁶ Ibid.

³⁸⁷ OECD (note 86) at Best Practice 4.5 and Annotation 33.

³⁸⁸ UNESCO (note 88).

³⁸⁹ UNESCO (note 88) at par 53.

³⁹⁰ Ibid.

³⁹¹ Regulations implemented by countries, ethics review boards or professional societies. Ibid.

³⁹² No specific guidelines for the waiver of consent are suggested in the Report.

³⁹³ Overall or blanket consent may be condoned where the biospecimen is 'irretrievably unlinked' from the identity of the participant. Consent must therefore be linked to the purpose of a specific research endeavour. UNESCO (note 88) at par 54.

research. This has been described as a rigid approach. Australia, on the other hand, endorses a broader consent. In addition, international guidelines also vary between specific and broader consent. Also, where specific consent is provided for use in research, it is not possible to use that tissue for any other purpose. Fresh consent would have to be sought, unless a waiver of consent may be justified. The waiver-mechanism is discussed in the next section.

4.4 Waiver of consent

The requirement of consent for secondary use of biospecimens in medical research is not absolute. In certain circumstances, research ethics committees are permitted to waive the consent requirement for use of biospecimens in future research. In both South Africa and Australia the waiver mechanism is available to research ethics committees subject to consideration of various factors.

Research ethics committees consider various factors when determining whether a waiver of consent is appropriate or not. The South African provision is permissive: research ethics committees '*may* take into account'³⁹⁴ certain factors,³⁹⁵ whereas the Australian counterpart is peremptory: human research ethics committees '*must be satisfied*'³⁹⁶ that the listed factors³⁹⁷ are complied with before a waiver of consent may be granted.

A comprehensive analysis of the factors themselves is not the aim of this section. Instead, only certain commonalities and differences in the waiver factors are highlighted and discussed.

An element common to both jurisdictions is risk of harm. Use of the biospecimens, without consent, in a future research project should not pose more than minimal risk of harm to the participants. The South African

³⁹⁴ See Ethics in Health Research (note 52) at 8.5 at 41.

³⁹⁵ For example, the extent of the existing consent provided by donors, the practicability of seeking new informed consent and the measures in place safeguarding the privacy of donors. See the South African factors outlined in Chapter 2 at part 2.2.3 above.

³⁹⁶ See National Statement (note 42) at 2.3.6.

³⁹⁷ For example, no likely reason for donors to refuse to provide informed consent if asked and measures in place to ensure confidentiality. See the Australian factors outlined in Chapter 3 part 3.2.2 above.

provision refers specifically to risk of harm for 'privacy' and 'wellbeing'.³⁹⁸ The Australian counterpart, on the other hand, permits a waiver only where the risk of harm is low, i.e. where the only foreseeable risk is no more than mere 'discomfort' to the donor.³⁹⁹ However, when considering the context where stored biospecimens previously removed during clinical procedures are to be used in research, it is clear that the use of such tissue in research will inflict no physical harm to the donor. The biospecimen has already been separated from the donor.

However, the risk of informational harm is the most significant risk associated with the secondary use of stored biospecimens in research. The South African waiver factors recognise this by referring specifically to the risk to the privacy of the donor. Where the biospecimens are de-identified or anonymised, so that the identity of the donor is not linked with the information pertaining to the biospecimen, the risk of informational harm is avoided. However, where this risk is deemed low or negligible by a research ethics committee, a waiver of specific consent is justified.

The corresponding Australian waiver factor considers the risk of discomfort, which is a physical risk of harm. This is, in my view, an irrelevant consideration, because once the tissue has been excised, no further physical risk of harm to the donor is possible.

A second element worth considering is related to the existence of previous consent or the lack thereof. Both jurisdictions accept the impracticability of seeking consent for the secondary use of stored biospecimens in research as a valid factor.⁴⁰⁰ However, apart from this commonality, the two jurisdictions have divergent approaches. South African research ethics committees consider the nature of the existing consent related to the collection and storage of the biospecimen.⁴⁰¹ Furthermore, it is considered whether the proposed research is related to, or an extension of

³⁹⁸ Ethics in Health Research (note 52) at 41.

³⁹⁹ National Statement (note 42) at 2.3.6(a).

⁴⁰⁰ National Statement (note 42) at 2.3.6(c); Ethics in Health Research (note 52) at 41.

⁴⁰¹ Ethics in Health Research (note 52) at 41.

previously approved research.⁴⁰² The Australian human research ethics committees, on the other hand, consider whether the lack of consent is justified by the benefits of the research,⁴⁰³ as well as the likelihood of participants declining to provide consent if asked.⁴⁰⁴

The two approaches, although related, are viewed from different perspectives. The South African approach determines whether any previous consent, if given, has the potential to include the secondary use of the biospecimens in the proposed research project. Should the nature of the initial consent include secondary research, consent exists, although perhaps non-specific consent. However, where the initial consent excludes the possibility of the secondary use, it only reveals a lack of consent for such secondary use. Although the lack of such consent may suggest intolerance by the donor for secondary research, such secondary use in research may not have been envisaged during the initial consent. Accordingly, a lack of consent would not always be a manifestation of donors' intolerance to the secondary use of biospecimens in research. Therefore, a lack of consent per se is not, in my opinion, a factor that should weigh against a waiver of consent.

In the Australian context, on the other hand, human research ethics committees must establish whether the benefits of the research justify a lack of consent as well as the likelihood of persons refusing to provide consent. Human research ethics committees have to determine whether the potentially negative effect of a lack of consent is outweighed by the benefit of the research. It has been mentioned that the potential informational harm is the most prominent risk in using stored biospecimens in research. Therefore, if tissue is de-identified or anonymised, this risk is avoided and the negative effect of a lack of consent is negligible. This reasoning should justify a waiver of consent.

⁴⁰² Ibid.

⁴⁰³ National Statement (note 42) at 2.3.6(b).

⁴⁰⁴ National Statement (note 42) at 2.3.6(d).

The factors just mentioned are only some of the considerations taken into account.⁴⁰⁵ However, it suffices for the purposes of this critical analysis to limit the discussion to those addressed.

4.4.1 International trends

Certain relevant international trends are now considered.

4.4.1.1 The Nuffield Council on Bioethics

The Nuffield Report⁴⁰⁶ does not expressly address waiver of consent by a research ethics committee for the secondary use of biospecimens in medical research. It does, however, recognise that providing specific consent for the use of biospecimens in research is not always possible.⁴⁰⁷ Where the acquisition of such consent is impracticable, 'procedures that give equivalent protection'⁴⁰⁸ are required. What these procedures entail is not entirely clear from the Report.

4.4.1.2 Council for International Organizations of Medical Sciences

The CIOMS Guidelines⁴⁰⁹ regard waiver of informed consent by research ethics committees as 'uncommon and exceptional'.⁴¹⁰ Where the research poses no more than minimal risk for the participant and the acquisition of consent would make the research impractical, the research ethics committee may waive the requirement of seeking new, specific consent.⁴¹¹ However, where the biospecimens are anonymised, consent need not be acquired at all.⁴¹²

⁴⁰⁵ In addition to those mentioned above, when research ethics committees consider waiving the consent requirement, both the South African and Australian ethics guidelines recognise the need to consider the participants' privacy and whether the commercialisation of the derivatives of the biospecimens is foreseeable. National Statement (note 42) at 2.3.6(e)&(f); Ethics in Health Research (note 52) at 41.

⁴⁰⁶ Nuffield Council (1995) (note 364).

⁴⁰⁷ Nuffield Council (1995) (note 364) at 13.5.3.

⁴⁰⁸ *Ibid.*

⁴⁰⁹ CIOMS (note 84).

⁴¹⁰ CIOMS (note 84) at Guideline 4 at 32.

⁴¹¹ CIOMS (note 84) at *Commentary to Guideline 4 at Waiver of the consent requirement* at 34.

⁴¹² See the CIOMS discussion above at 4.3.1.3 of this Chapter.

4.4.1.3 Organization for Economic Co-operation and Development

In terms of the OECD Guidelines,⁴¹³ a waiver of consent by a research ethics committee is possible where certain requirements are met. Similarly to the CIOMS requirements above, the risk associated with the research must be deemed minimal to the participant.⁴¹⁴ In addition, the acquisition of consent must be impossible to obtain and the welfare of the participant not adversely affected.⁴¹⁵

From the above discussion, it may be concluded that specific consent for secondary use of tissue in research is not always required. Research ethics committees may waive the requirement under certain circumstances. It was ascertained that the factors to be considered when determining the appropriateness of a waiver are permissive in nature for South Africa, but peremptory for Australia. Certain waiver factors were compared. In essence, it was found that the risk of 'discomfort', as considered in the Australian context, is irrelevant in the context of this dissertation due to the separation between the donor and the tissue sample. However, both jurisdictions recognise the potential risk of informational harm that may ensue. Accordingly, research ethics committees should then consider the extent to which the biospecimens are identifiable and what measures are in place to ensure confidentiality of the donor.

4.5 Socio-cultural sensitivities

It is important for researchers to take possible socio-cultural sensitivities of donors into account when seeking consent for use of biospecimens in research.⁴¹⁶ In the Australian context, the National Statement draws researchers' attention to the importance of cultural sensitivity when obtaining consent in general⁴¹⁷ and for research using human tissue samples.⁴¹⁸ In short,

⁴¹³ OECD (note 86) at Annotation 27.

⁴¹⁴ *Ibid.*

⁴¹⁵ *Ibid.*

⁴¹⁶ Otlowski M et al 'Biobanks Information Paper 2010' (2010) 20 *Journal of Law, Information and Science* 88 at 105.

⁴¹⁷ National Statement (note 42) at 11-3 ('Values and Principles of Ethical Conduct') and at 19

researchers must take cognisance of 'beliefs, perceptions, customs and cultural heritage, both individual and collective, of those involved in research.'⁴¹⁹

Aborigines and Torres Strait Islanders are an important indigenous minority group in Australia, and the National Statement⁴²⁰ takes great care to accommodate Aboriginal and Torres Strait Islander sensitivities in research. The measures taken and how they integrate in the consent process were discussed in the previous chapter.⁴²¹

Certain international guidelines⁴²² actively support sensitivity to cultural differences in the context of seeking informed consent for health research. In addition to seeking individual consent, it may be appropriate for researchers to obtain prior permission for access to a community from a leader, to use local language or to have additional discussions with the relevant community.⁴²³

The South African ethics framework also addresses cultural sensitivities to some extent. As will be recalled,⁴²⁴ the Bill of Rights firmly entrenches socio-cultural rights of all persons.⁴²⁵ In response to this constitutional imperative, the Ethics in Health Research guidelines⁴²⁶ as well as the MRC Guidelines⁴²⁷ require researchers to be sensitive to culture, language, beliefs, customs and perceptions of potential research participants.⁴²⁸ In addition, persons must be treated in a way that respects their community too.⁴²⁹ The importance of taking cultural sensitivities into account when acquiring consent is therefore acknowledged in the South African regulatory framework.

('General Requirements for Consent'), amongst others.

⁴¹⁸ National Statement (note 42) at 3.4.1(g).

⁴¹⁹ Otlowski M (note 416) at 105.

⁴²⁰ National Statement (note 42) at 4.7 ('Aboriginal and Torres Strait Islander Peoples'). See also Values and Ethics (note 316).

⁴²¹ See Chapter 3 part 3.3 above.

⁴²² See, for example, CIOMS (note 84) at *Commentary to Guideline 4 at Cultural Considerations* p35 and OECD (note 86) at Best Practice 5.3 and Annotation 29.

⁴²³ CIOMS (note 84) at *Commentary to Guideline 4 at Cultural Considerations* at 35 and OECD (note 86) at Best Practice 5.3 and Annotation 29.

⁴²⁴ See brief outline at Chapter 2 part 2.2.5 above.

⁴²⁵ The Bill of Rights in ss 9, 10, 15, 30 and 31, to name a few, protect the cultural, religious and linguistic rights of all persons. Constitution of South Africa 108 of 1996.

⁴²⁶ See especially Ethics in Health Research (note 52) at 2.1 and 2.6.

⁴²⁷ See especially MRC (note 53) at 3.1.2.

⁴²⁸ See Chapter 2 above.

⁴²⁹ MRC (note 53) at 3.1.2.

Comparatively, the Australian ethics framework provides more detailed guidance on how to respect cultural sensitivity during the consent process involving Aborigines and Torres Strait Islanders.⁴³⁰ Whether such detailed guidance is necessary in the South African context may be questioned. Although health research guidelines, tailor-made to accommodate different cultural sensitivities, may prove useful, I believe they would be unable to capture enough helpful information due to the rich cultural diversity found in the South African context. Socio-cultural rights are already enshrined in the Constitution. It therefore follows that socio-cultural sensitivities must always be considered in South African research projects as a matter of constitutionality.

However, the context of this dissertation requires that clarity be provided regarding how researchers should respond sensitively towards donors of stored biospecimens used in research, rather than research participants per se. At the point when donors decide whether to consent to storage of biospecimens and their possible use in research, it is my view that researchers should provide information, in a culturally appropriate manner, to the donors regarding the possibility of research.

Consider the scenario where patients may provide consent for the storage and use in future cancer research of surplus malignant tissue.⁴³¹ In this situation, patients should be provided with adequate information about the possibility of future use of surplus biospecimens in a 'simple and culturally appropriate'⁴³² manner. Once informed, patients will be able to assess whether storage and use of their biospecimens in cancer research is consistent with their, and their community's, cultural beliefs. Should this not be the case, patients may opt-out by declining to provide consent for storage of their biospecimens. In my view, the essence of cultural sensitivity therefore lies in the manner of conveying information to patients. It must be done in such a way that they are in a position to assess whether what they are consenting to, is compatible with their cultural background and beliefs.

⁴³⁰ See especially Values and Ethics (note 316).

⁴³¹ Previously removed for diagnostic and/or therapeutic purposes.

⁴³² Ethics in Health Research (note 52) at par 2.6.

In conclusion, it was found that in applying the socio-cultural sensitivity in the South African context, the manner in which researchers display these socio-cultural sensitivities is most important in ensuring that adequate information regarding storage and secondary research is conveyed to patients. In essence, patients with specific cultural backgrounds must be informed by researchers with an understanding of the patient's particular culture, and in a way that they fully comprehend that their tissue is to be stored and possibly used in research. This would enable them to make an *informed* decision that corresponds to their socio-cultural set of values.

CHAPTER 5

5.1 Recapitulation

It has been argued that biospecimens collected during diagnostic and therapeutic interventions and stored for future use in research are important resources for cancer research. In line with legal and ethics requirements, the patient provides informed consent for removal of the biospecimens. In addition, informed consent may be provided for storage of surplus tissue derived from these diagnostic or therapeutic procedures for future cancer research. However, it has been established that the specific purpose of future research is rarely certain at the time of consent. This uncertainty as well as other factors,⁴³³ complicate the requirement of informed consent regarding stored surplus tissue and research not anticipated at the time of removal. Accordingly, the focus of this dissertation was to ascertain what the consent requirement should be where no prior consent was provided for the secondary use in research of stored biospecimens removed during diagnostic or therapeutic procedures.⁴³⁴

A strict view of informed consent requirements for research opposes use without express and specific consent. However, another view is that consent to removal and storage of tissue for diagnostic and therapy purposes arguably includes consent for use in research related to the disease under consideration, and that this practice corresponds with accepted trends for advancement of knowledge in oncology.⁴³⁵

Specific consent to a specific research project, it was observed, has limiting consequences regarding use of biospecimens for other secondary purposes. Where specific consent for a certain research project is given, use of the biospecimens for other purposes is not permitted. Specific consent therefore potentially limits the purposes for which stored biospecimens may be used in future research. In these instances it follows that fresh consent would

⁴³³ See Chapter 1 above at part 1.2.

⁴³⁴ See Chapter 1 above at part 1.1.2.

⁴³⁵ See Chapter 1 above at part 1.1.2.

be required for purposes other than that originally specifically consented to.⁴³⁶ However, where extended or unspecified consent is given, appropriateness of future use of the tissue is more flexible. The latter situation would therefore be favourable for both researcher and participant. The researcher could, within limits,⁴³⁷ use stored biospecimens where the demand exists, while the consenting party's choice is still respected, in principle.⁴³⁸ Importantly, these effects of providing specific and broader consent is plausible only under the assumption that donors are actually entitled to exercise control over tissue samples already separated from their bodies.

Internationally, no consensus exists about consent models for secondary use of stored biospecimens in research.⁴³⁹ Consent models vary from a restrictive, specific consent only model (such as in South Africa), to more liberal, broader, consent models (such as in Australia), to the most flexible model, where no consent is required under certain circumstances.⁴⁴⁰

Chapter 2 provided a brief description of the South African legal and ethics framework governing informed consent in general, and in the context of secondary use of biospecimens in medical research.⁴⁴¹ It was concluded that applying the informed consent requirement, as it is applicable to research involving human participants, to the context of the secondary use of biospecimens in research, would amount to an overgeneralisation. This is so because in certain cases obtaining informed consent in health research on biospecimens, as a secondary purpose, may prove to be impossible or impractical, or even unnecessary.

The South African ethics guidelines, however, do offer some clarity in this regard. Fresh, specific consent is required for secondary use in health

⁴³⁶ See Chapter 4 above at part 4.3.

⁴³⁷ Depending on whether consent is extended or unspecified.

⁴³⁸ See Chapter 4 above at part 4.3.

⁴³⁹ See Chapter 1 above at part 4.3.

⁴⁴⁰ See Chapter 1 above at part 1.3 and discussion of the consent models of South Africa and Australia in Chapters 2 and 3, respectively.

⁴⁴¹ The South African legislative framework addresses the requirement of informed consent for the removal of biospecimens for purposes including health research, it was found that legislation is unclear regarding the secondary use of biospecimens, previously removed during clinical procedures, in research. See Chapter 2 above for an exposition of the relevant South African legislative framework.

research of biospecimens obtained for diagnostic or therapeutic purposes. It was found that this requirement might at times be relaxed. The research ethics committee plays an important role here. It decides whether the consent requirement may be waived for secondary use of biospecimens in research.⁴⁴²

It was concluded that the South African legal-ethics approach may be too rigid. Sourcing biospecimens for research may become very onerous and may prove detrimental to the interests of oncology research.

Chapter 3 provided an exposition of important aspects of the Australian legal-ethics framework pertaining to use of biospecimens in medical research. It was established that a more flexible, tiered consent model is used, allowing patients to consent to use of their biospecimens in research projects not known at the time of consent. However, similarly to South Africa, the National Statement allows waiver of consent for secondary use of biospecimens in medical research.⁴⁴³

It was also shown that the consent models in international research ethics guidelines vary from specific to broader models.⁴⁴⁴

It was concluded that seeking fresh specific consent for secondary use of tissue in research is not always required. A survey of the relevant South African and Australian ethics guidelines, as well as international trends, revealed that research ethics committees may waive this consent requirement under certain circumstances.⁴⁴⁵ Furthermore, where research is to be performed on anonymised biospecimens, the trend showed that no consent whatsoever is acceptable.⁴⁴⁶

The manner in which researchers should respect the socio-cultural sensitivities of patient donors when seeking consent for storage and future use of biospecimens in research was addressed in both the South African and Australian contexts. In summary, it was concluded that socio-cultural

⁴⁴² See Chapter 2 above.

⁴⁴³ See waiver discussion above at Chapter 3 part 3.2.2.

⁴⁴⁴ See Chapter 4 at part 4.3.1 above.

⁴⁴⁵ See Chapter 4 above at part 4.4 for a discussion of the waiver provisions of South Africa and Australia, as well as how they compare to international trends.

⁴⁴⁶ See Chapter 4 at part 4.4.1 above.

sensitivity pertains to the manner in which adequate information regarding the purpose of storage and secondary research is conveyed to patients. In essence, patients with cultural backgrounds different from that of the researcher must be informed so that they can comprehend that surplus tissue will be stored and possibly used in research and what this means. This enables them to make an *informed* decision, corresponding to their own socio-cultural values, whether to permit use of their biospecimens in future research or not.⁴⁴⁷

5.2 An alternative consent model for South Africa

In the course of discussion, it was emphasised that the current position in South African law pertaining to informed consent and secondary use of tissue in research is rather rigid. Fresh consent is required for secondary use of biospecimens in research projects. It follows that sourcing biospecimens for cancer research may become very onerous, which may prove detrimental to the interests of research. It is therefore desirable to identify an appropriate alternative model of consent for secondary use of biospecimens in research.

It is submitted that the rigid, specific informed consent model should be relaxed to a more flexible model, in terms of which consent for removal of tissue for a diagnostic or therapeutic purpose includes permission for storage and use of surplus tissue in related future research, even though its nature may be uncertain at the time. Broader, non-specific consent could give options: consent to certain types of research only;⁴⁴⁸ consent to biomedical research in general; or, in the widest sense, consent to unrestricted use of stored biospecimens. Support for broader consent flows from the absence of risk of physical harm for the donor patient when surplus tissue is used.

However, in line with international trends, three safeguarding criteria should accompany this flexible model. The most important criterion is the entitlement of donor patients not to provide consent, or opt-out, thereby excluding use of their identifiable biospecimens in research. The other two

⁴⁴⁷ Socio-cultural sensitivity during the informed consent process was discussed in Chapter 2 at part 2.2.5 (South Africa), Chapter 3 at part 3.3 (Australia) and Chapter 4 at part 4.5.

⁴⁴⁸ For example, consenting to oncology research only.

criteria reiterate best practice in research ethics, namely that personal information connected to the tissue samples must be kept confidential; and each research project must be reviewed by a research ethics committee. The legitimacy of this flexible model depends on the adequacy of mechanisms to ensure confidentiality, consent withdrawal and properly functioning research ethics committees.

The recommendation of a more flexible model addresses situations where biospecimens are identifiable i.e. the identity of the donor patient may be directly or indirectly traced back from the tissue sample.

The current South African ethics framework is not clear on how the consent requirement is affected when the biospecimens are anonymous. However, where biospecimens are anonymised, the consent requirement should, in my view, be relaxed further. It was argued that, where biospecimens are anonymised, the potential risk of informational harm to the original donor is non-existent. Accordingly, the general international trend shows that consent is no longer required in these circumstances.⁴⁴⁹ Therefore, where the biospecimen is anonymised and research results cannot be used to identify original donors, consent for use of the tissue in related future research should not be required. This should be articulated more clearly in the current South African ethics framework.

Therefore, at a policy level, a balance must be struck between promoting society's interests (in advancing knowledge about oncology) and protecting the individual's interests (in preventing unethical use of tissue samples). At present, the rigid requirement of specific consent distorts this balance in the South African context. The more flexible use of a broader consent model described above could serve as a means to recalibrate the current imbalance between the interests of both biospecimen donors and society.

⁴⁴⁹ See Chapter 1 above at part 1.4.2.

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