Chapter 1

Literature review and backdrop to the debate on sharing of biomaterials and data.

1.1 Introduction

1.1.1 Background, literature analysis and critique

Biobanks, defined by the World Medical Association (WMA) as the collection of biomaterials (human samples) and associated data,[2] have evolved in response to advances in sample preservation infrastructure and data storage technologies.[3] This in turn has enabled the usage of biobanking as a resource for supporting scientific research and development through readily available biomaterials and their associated data. In the scope of this research, data refers to information that is associated with biomaterials in biobanks including but not limited to; biomaterial identifying numbers, demographic information of those that have donated biomaterials as well as disease information. The terms 'biomaterials' and 'samples' will be used interchangeably in this Research Report. Biobank researchers and those who manage biobanks are obliged legally and ethically to protect the samples and associated data. Good biobank governance is therefore crucial for sound ethical conduct and sustainability.

In South Africa (SA), the National Health Research Ethics Council (NHREC), is the regulatory authority established in terms of section 72 of the National Health Act 61 of 2003[4] for, among other roles, setting "ethical norms and standards for health research involving humans and animals" (National Department of Health Ethics in Health Research Principles, Processes and Structures, 2015, pg. 9).[5] However, none of the current regulations and laws in SA address the sharing of biobank samples and data where funding is concerned. This then necessitates inclusion in the current ethico-regulatory structures of biobanks, provisions for sample and donor protections, where the expectation is funding in exchange for biobank resources (samples and data). A donor is a person, living or deceased, from whom biomaterials have been withdrawn[5] while a research participant refers to "a person who subjects himself or herself to scientific or health research" (Health Professions Council of South Africa General Ethical Guidelines for Health Researchers Booklet 13, 2016, section 2.4.2).[6] In the context of this Research Report the terms "donor", "research participant" and "participant" will be used interchangeably.

International collaborative research must take into consideration ethical issues, for example: benefit sharing and justice as in fairness. When sharing of materials and data is contingent to

funding, this in itself could negate the ethical notion of benefit sharing and lean towards commodifying human materials and associated data. It is on this basis that an argument is made for the development of an ethico-legal framework that addresses sharing of biomaterials and associated data where funding is concerned. In this chapter, the historical background and current context with regard to sharing of biomaterials and data in exchange for funding in international collaborative research is briefly introduced, mainstream versus alternative viewpoints are considered and issues arising from the topic at hand and relevance for performing the study are discussed.

1.2 Historical background and current context pertaining to sharing of biomaterials and data in exchange for funding in international collaborative research.

Although the idea of biobanking is not new, the history of actual biobanks is relatively new and dates back to about 30 years.[7] Biobanking has developed so drastically that it was among the 10 world changing ideas in 2009 as published by Time magazine.[8] The development of biobanks over the years gave rise to ethico-legal controversies that have led to mainstream and alternative viewpoints on issues such as biomaterial and data sharing. Adding to such controversies is the development of genomic and biobank research initiatives in Africa that include the Human Heredity and Health in Africa (H3Africa) Consortium and Bridging Biomedical research across Africa and Europe (B3Africa) initiatives.[9] These initiatives have promised to transform the way researchers typically conduct in international health research in Africa through claims of fostering equitable research collaborations. This has been met with criticism by African researchers involved in similar types of collaborations with fears of being exploited by their counterparts from high income countries (HICs), for example exploitation by not being included in benefit sharing. H3Africa is a consortium that is involved in research and funding for research of genomic and environmental determinants of disease with the aim of health improvement in African populations.[10] The consortium developed a proposal requiring for samples collected in H3Africa projects to be shared for secondary use by one of its repositories.[11] This proposal created considerable controversy and suspicion that this was a way in which H3Africa research was making African samples available for researchers elsewhere. H3Africa then developed a policy framework to address such fears.[11]

1.3 Backdrop to the debate on biomaterial and data sharing

There are two broad notions with respect to sharing of biobank samples and data in international collaborations. They are: (1) those concerning exploitation of African researchers

and research participants or those from whom biobank samples have been collected by researchers or funders from high income countries[12] and (2) those concerning a move towards harmonization of biobanks as justification of sharing of biobank samples and data.[13]

1.3.1 Exploitation of African researchers and research participants or those from whom biobank samples have been collected

1.3.1.1 Exploitation of African researchers through inappropriate benefit sharing

The genetic diversity of African populations is at the centre of the controversy around sample and data mining.[14] As a result of this genetic diversity, African biomaterials have been in demand internationally with a unidirectional move of biomaterials out of the continent raising concerns about exploitation of vulnerable populations and countries. Parties involved in collaborative scientific activities should agree on sharing of financial and non-financial benefits arising from biomaterials and associated data.[15] The recommendation by the International Society for Biobanks and Environmental Repositories' (ISBER's) Best Practices is that biobanks should be guided by national, regional as well as international guidelines on benefit sharing and sample access before sample collection commences. Equitable benefitting and ownership issues arising from biomaterials and associated data use including intellectual property rights should be part of benefit sharing. Legislation pertaining to copyright, patents and intellectual property may differ among various countries. In South Africa, the Copyright Act No. 98 of 1978[16] provides protection for original work of literature and publications with eligibility for copyright while the Patents Act No. 57 of 1978[17] provides for granting of patents and the Intellectual Property Laws Amendment Act No. 28 of 2013[18] provides for intellectual property rights protection.

In biobank research collaborations, stakeholders for benefit sharing include the donors, researchers, non-participating individuals suffering from the disease or condition that is being studied as well as the society at large.[19] The argument in benefit sharing with a focus on overall public health ethics approach is that the knowledge generated should not be viewed as contributing to an individual but to the common good.[19] Even though profit-oriented research has the potential to erode public trust, the profit motive could be beneficial in supporting biobank infrastructure. The aspect of infrastructure support is a good reason to discuss monetary sharing of benefits. Sharing of benefits can be in the form of access to healthcare, financial benefit, technology transfer and building capacity, knowledge dissemination as well as access to research results.[20]

Developing countries often have the highest disease burdens and the largest target sample populations with an array of infrastructural deficiencies.[21] There is a need to go beyond the promises in documented frameworks addressing equitable genomic and biobank research collaborations through exploring how benefit sharing goals can be achieved. African researchers fear being exploited by their partners in HICs and these fears have primarily been based on past exploitation of African researchers.[9] The fear is fuelled by a lack of resources by African researchers in comparison to HIC researchers, resulting in concerns of them being marginalized, coupled with impediments when pursuing an African research agenda . Benefit sharing is discussed in detail in chapter 3 of this Report.

1.3.1.2 Vulnerable populations in the context of genetic diversity and the potential for exploitation

As an illustrative point in this section, genomic research is referred to because much of biobank activities involve research in this context. Concerns raised on a genomic study conducted on Chinese villagers called the “genetic harvest” (Zhao et al., 2018, pg. 73) resulted in investigations that revealed violations of research ethics principles of this vulnerable group. This was due to the low economic status of the research participants, lack of capital by the research institutes and loopholes in the Chinese ethico-legal framework.[22] While the Chinese institutes of research and members of personnel gained the advantage of working with renowned international research institutes, the research participants only received a meal free of charge and an insignificant reimbursement amount that was far less (less than a tenth) of what was promised, job leave and travel allowances. The research participants were subjected to other ethical violations. These include participants not being informed that they were being enrolled into the study but were misled into believing that they were being provided with “free physical examinations” (Zhao et al., 2018, pg. 74). Other research ethics violations included differences in what was approved versus how the research was conducted, for example, recruitment of more than 8 times (16, 686) the number of approved participants which was 2,000 samples, and different apparatus being used as compared to that which was approved. It is evident from this case that it is not only ethical aspects related to re-imbursements that can result in abuse/exploitation. Cross-border transfer of biomaterials presents a challenge for low and middle income countries (LMICs) since a large number of these countries have inadequate or no regulatory frameworks in that regard.[23]

Many research participants across the African continent are considered to be vulnerable because of poverty, low research literacy and obstruction of access to healthcare.[12] Common risks of biobank research are social and dignitary harms particularly when research findings

reveal genotypes that are associated with susceptibility to certain diseases resulting in discrimination, which is widely feared resulting in stigma and discrimination.[24] Dignitary violations occur when personal and religious values are violated. In 2015, the SA health insurer, Discovery, announced that it would offer genetic testing for its members at 250USD (approximately ZAR 3400, 00) in collaboration with Craig Venter's company, Human Longevity Inc.[25] This might appear innovative and futuristic, however, there are considerable problems that require guarding against for the protection of potential donors. Moreover, there was the promise of genetic testing in the name of providing healthcare but the initiative was apparently for the purpose of creating a large research database in a different country. This was an exploitation of the deficiencies in the SA regulatory framework on the storage, use and export of biomaterials. Typically, biobank participants donate samples altruistically for the common good and what would make them vulnerable in addition to the issues mentioned would also be exposure to unsolicited findings without actionable clinical and psychological benefit.[26] As a result of an awareness of exploitation of research participants, the San leaders of SA recognized the need to partner with researchers to develop the San Code of Ethics to protect the San people from unethical research practices with particular focus on collaborations that entail an imbalance of knowledge, power and resources.[27] The code of ethics provides for the inclusion of not only the local communities and participants, but also the inclusion of local researchers throughout the research process if possible, providing for local researchers to be granted ownership of data, intellectual property and publication authorship.

1.3.1.3 Consent for biobank samples

Consent is central to the consideration of biobank ethics as it is considered by many as the most wide-ranging and significant comprehensive concept with multiple concerns of an ethical nature.[28] The concept is wide-ranging in a sense that various kinds of consent models are used. The different models of consent are;[28,5] (1) blanket consent which is non-specific regarding use of samples, (2) meta consent covers research uses throughout a life, (3) broad consent which is for a broad range of future uses, (4) tiered consent which is for the primary research with a choice to permit storage for use in the future and (5) waived consent where samples are re-used and the research cannot be conducted without the waiver with minimal harm for the participant. Dynamic consent was developed as a follow-up process of potentially an interactive nature for biobank sample participants and is an internet-based interactive type of consent.[29] The difference between broad and dynamic consent is that participants are continuously asked to re-consent as new projects arise in the former while re-consent is usually not obtained in the latter. The main ethical concern with consent is that what is required

as a minimum for adequate consent in one jurisdiction may not be sufficient for consent in another. In a number of African countries including SA, broad consent is allowed with conditions such as the need to inform the participants of storage of future use of their samples.[30] Laws and regulations from 22 African countries including SA on consent, storage (whether allowed or not & period of storage), re-use of samples, export of samples in international collaborations, biomaterial and data sharing, ownership and return of results, revealed differences and a general lack of biobank specific guidelines, but rather that they were developed for general health research.[30]

Central to the debate on biobank consent is "whether broad consent can ever truly be informed and therefore fulfil the established principles of consent" (Scott et al., 2012, pg. 145).[31] The reason for broad consent in the context of biobanking could be because at the time of consent, the information necessary to make the consent "fully informed" (Widdows et al., 2011, pg. 209) is not available due to insufficient knowledge about the specific envisaged research.[32] While some commentators argue that the broader the consent is, the less informed it becomes,[33] it is often impossible in the context of biobank research for the participants to be fully informed about the purpose, methods, risks and all the other informed consent requirements. The ethical considerations around consent that could result in challenges in international collaborations are different preferences and a lack of consensus in that regard, for example in Europe broad consent is preferred while in the United States of America and Canada multi-layered consent which requires participants to make different choices detailed on a form is favoured.[34] Broad consent is consent that entails an unspecified use of future related health research.[35] Most biobank researchers in SA prefer broad consent that would enable future sample use and regard re-consenting as resource intensive and impractical.[14] Other researchers in SA, however, particularly those working with indigenous groups, are of the view that indigenous people would not subscribe to broad consent.[14]

Some commentators have argued, for the development of robust models on open consent as a means of addressing privacy of genetic information of not only individuals but by extension through genetic material, that of families and communities when using specimens from biobanks.[36] Open consent approach is a model which was proposed in the Personal Genome Project (PGP) and entails invitation of participants to willingly share their personal information for the common good.[37] The justification for open consent in this argument is veracity by the researcher as the main moral obligation. However, the criticism with this model is that open consent is a contradiction of terms and a "moral illusion disguised to serve narrow interests of closed minded researchers" (Karlsen et al., 2011, pg. 577).[38]

Section 64 of the NHA addresses consent in that it makes provision for human samples to be used for research after consent has been granted and the National Material Transfer Agreement (NMTA) provides for protection of samples obtained by the recipient, and usage according to the protocol that was approved by the Health Research Ethics Committee (HREC). Another protection in section 68 of the NHA[4] is that of regulations relating to the import and export of human biomaterials with export permits by the Director General of Health to be obtained prior to samples being exported across the borders of SA.[39]

1.3.1.4 Ownership of biomaterials and associated data

Some of the important questions pertaining to ownership of biobank samples and data that have been debated are, "should ownership rights be assigned to the biobank?", "do those who have donated the biomaterials have a claim for ownership rights?" and "who should control the samples when there are disagreements between biobanks and sample donors?" (Elger et al., 2008, pg. 197-198).[40,41] There are different schools of thought within the theory of property law in the definition of the concept of ownership.[42] Several theorists use the term ownership as the ability to use, transfer and enjoy exclusive possession and control over a "thing" (Capron et al., 2009, pg. 107), as well as to manage its use by others and to collect benefits for such use. However, there appears to be confusion about who owns samples and data with potential ramifications in the general guiding principles that may fail to take into account the different interpretations. Many experts therefore, prefer the idea of custodianship instead of ownership because of their discomfort with the idea of anyone owning human samples and the association with "irreversibility" (Capron et al., 2009, pg. 108) of transfer. Although a participant has the autonomy to consent or refuse to their sample donation for research, such a right is usually limited legally as in a limitation of ownership, for example property rights are not extended to the selling of human organs as a matter of rights.[43] The importance of the issue of ownership is reflected in the idea that it has to do with human dignity particularly in relation to cultural identities and ownership rights potential consequences, in particular financial as in benefit sharing, which property rights (including intellectual) is a part of.

While a few drops of blood have little scientific or economic value, sample collections from a cohort have an aggregate scientific economic value. A sample alone does not possess this.[34] The value is even greater when samples are linked to data and therefore biobanking gives value to samples resulting in contested ownership rights. A discussion on ownership requires familiarity with the legal concept of property. The common perception of the majority of medical researchers is that the research ought to benefit the community as a whole rather than the individual and this is reflected by the notion that individuals do not have rights of sample

ownership that they have donated for research.[44] The National Material Transfer Agreement (NMTA) assigns ownership of biobank samples to those who have donated the samples while, custodianship is assigned to the institution collecting the samples.[45] Some reports indicate that ownership of samples belong to institutions and individual researchers and that ownership is not transferred when biomaterials and data are exchanged; thereby creating confusion in responsibility for sample management and ownership.[46] Disparities in legal frameworks of different countries are a complication to biobank collaborations. There is a view that, by granting consent to donate a sample for the purpose of biobanking, the donor has not automatically granted consent for the biobank to own the sample(s).[47] The ethico-legal aspects of ownership of biomaterials and associated data are discussed in detail in chapter 5.

1.3.1.5 The commercialization of biobank resources

It is common practice for South African biobanks and biobank researchers to seek funding from agencies that are independent of the biobank and researchers are often required to share biomaterials and data as part of the agreement, in particular, in international collaborative research. The commercialization of biobank resources presents policy challenges for research participants, scientists and funders.[48] In the context of this research, biobank resources that can be commercialized include samples and their associated data as well as research results. However, Chapter 8 section 60 of the NHA prohibits the selling of human samples as well as the donation of samples for financial gain except other than the reimbursement of reasonable expenses relating to the transfer of those samples.[4]

The debate on commercialization of biobank resources is based on whether scientific progress is best achieved by awarding of patent rights or avoiding open access of samples and data.[49] The African continent is known to have the highest level of human genetic variation in the world, attributed to a range of factors, including: variation in the environment, diet and disease exposure, among others.[50] Genetic variation makes African samples the most sought-after type of samples and this creates room for exploitation by outsiders that seek to fulfil their own interests. As articulated by Steinsbekk et al, commercialization of human organs and biological materials is perceived as a threat to human dignity, worth and personhood.[51] This violation of human dignity reduces human beings to mere objects or commodities. When legally binding ethico-regulatory frameworks are in place to protect participant dignity, trust could be built up between researchers and participants. In addition, there is clear evidence of biopiracy as a result of exploitation in international and local collaborative research activities on the African continent.[52] Biopiracy is the act of acquiring genetic material for academic and commercial purposes without fair redress to those from whom the samples and data were obtained.[53]

Some infamous cases from South Africa have been reported, such as the Hoodia case in which the San people challenged a patent registered by a SA research and development organisation, the Council for Scientific and Industrial Research (CSIR)[54] in 2001. The San claimed traditional knowledge rights of the hoodia plant due to them guiding the CSIR in the knowledge of this plant as an appetite suppressant. It was only after the dispute that an agreement for benefit sharing was signed between the two parties in 2003 that the San were provided with 6% of future royalties. Another case was that of the herb, *pelargonium sidoides,* which had been used by Xhosas in the Eastern Cape for many years, where the knowledge and access of the plant was transferred to a European pharmaceutical company. Although the company shared in the benefits of the initial patent with the primary knowledge holders (the Xhosa people), there were however a number of other patent applications in relation to the pelargonium that did not include the primary knowledge holders, and this was challenged by a number of Xhosa groups.[55]

It is not only the African continent which is faced with the dilemma of funders of research being keen on the commercial exploitation of samples and data, but also in other parts of the world such as the United Kingdom (UK) where there are questions raised as to whether scientists are trustworthy and whether research ought to be more stringently regulated.[56] In light of the preceding discussion, the notion of mandated data and sample sharing by funders and biopiracy reports prompt the need for addressing the concerns on commercialization through regulatory means.

1.3.2 Biobank networks and harmonization

In recent years, a number of initiatives aimed at developing biobank networks and harmonization for regionally and globally standardized protocols have emerged.[57] One such initiative is the Pan-European Biobanking and BioMolecular resource Research Infrastructure-European Research Infrastructure Consortium (BBMRI-ERIC). Biobank networks that have been identified include;[58] (1) storage networks, (2) “bring and share” (Shickle et al., 2010, pg. 124) networks, (3) catalogue networks, (4) partnership networks, (5) contribution networks and (6) expertise networks. Ethico-legal challenges have resulted in ineffective biobank networking. The view in support of biobank networks is that of the benefit of a wider network of samples and data.[13] In support of this argument, there have been claims that even big institutions cannot collect enough samples on their own to produce statistically significant sample sizes, hence the need for biobank networks.[59] There is, however, an acknowledgement of far reaching social and ethico-legal implications of such networks as a result of heterogeneity of existing ethico-legal frameworks among the collaborators.

Several studies illustrate variations among the legal and ethical norms governing biobanks in different jurisdictions.[7] Although harmonization of biobank Standard Operating Procedures

(SOPs), best practices and governance is an essential tool for sharing of biobank samples and data, the concept is context specific and relates to the compatibility of methods and approaches to facilitate synergy.[60,61] The major hurdle with harmonizing legislation is due to the extent of variation that exists between different government systems. In addition, the adoption of best practice guidelines that have been developed by international organizations have rarely been co-ordinated.[62] This has resulted in confusion over which practices are appropriate for biobanks and biobank networks.

1.4 Rationale for the study

Funders for biobank research are mainly from organizations outside the borders of SA. Conditions attached to funding include access to biomaterials and data by the international organisations, coupled with the transfer of these materials and data to biobanks outside SA's national borders. As yet to my knowledge, there has been no study conducted to examine whether these conditions could result in the commercialization of biomaterials and data and whether such practice is considered ethical.

1.5 Research question

The research question in this study is whether it is ethically justified to share biomaterials and data for biobank research in exchange for funding from sponsors and funders in international collaborative health research.

1.6 Research aim

The aim of this study is to critically analyse, with the use of the principles and theories of ethics and the relevant regulations and laws the practice of access and transfer of biomaterials and data in international collaborative health research, in exchange for funding.

1.7 Research objectives

The study objectives are as follows:

1. To critically discuss and normatively evaluate the major ethical issues related to biomaterial and data sharing where biobank research funding in international collaborative research is concerned.
2. To explore what benefit sharing ought to be when biomaterial and data are transferred from biobanks in SA to HICs in international collaborative health research.
3. To critically discuss and evaluate the current SA laws, regulations and guidelines specific to biomaterial and data sharing with particular focus on exchange of biomaterials for funding in international collaborative research.

1.8 Research design

This study is a normative enquiry with an ethico-legal component. A normative enquiry answers questions on ‘what ought to be done’ and ‘what ought not to be done’ in a systematic critical manner and justify the answers given. The normative component of the study will draw from the principles and theories in bioethics and ask the question: “Ought access to and transfer of biomaterials and data to biobanks outside the country be a condition to funding in international collaborative research?” The ethico-legal analysis will examine current South African laws, regulations and ethical guidelines pertaining to biobank and biobank research, biomaterial and data sharing.

1.9 Research methods

This study is based on desktop and library-based research. No research participants are involved in the study and no new data is collected or analysed. In the study, relevant literature and practice is critically analysed. Ethical principles and theories are used to answer the research question. There is an analysis and evaluation of relevant ethico-legal frameworks and literature has been retrieved from a variety of sources including but not limited to, search engines such as Google Scholar, research journal articles, books, legislation and any other academic search engines.

1.10 Outline of the Research Report

In this chapter, the literature and backdrop to the debate on sharing of biomaterials and data have been reviewed.

Chapter 2 begins with an account of the arguments for and against sharing of biomaterials and data in exchange for funding. An analysis of the regulations pertaining to the export of biomaterials as well as the transfer of donor (or research participant) data across the borders of SA is also explored. Legislation from different, but relevant countries pertaining to biomaterial export and data sharing is examined.

Chapter 3 comprises a normative analysis on commodification of the human body and its parts. The principles and values in this analysis apply just as appropriately to biomaterials being exchanged for funding in biobank and health research. The problem of the extent of commodification and its consequences are explored as a basis for an argument against commodification of biomaterials. Counter arguments to commodification are examined.

In Chapter 4, the current context with regard to resources is discussed and a possible benefit sharing model is considered.

Chapter 5 explores ownership of biomaterials.

Chapter 6 concludes the Research Report and offers recommendations.

1.11 Research outcomes

The outcomes of this research are as follows:

1. The results of the study will be published in a peer-reviewed journal and presented at conferences.
2. Recommendations for the sharing of biomaterials and data where biobank research funding is concerned will be provided to the National Health Research Ethics Council (NHREC).

1.12 Ethics

The study does not involve participation of human research participants or the use of animals. An ethics waiver for the research was granted by the Wits HREC (Medical) prior to commencement of the study (see appendix 1).

1.13 Limitations

The literature on the topic of this study is limited. The limited literature is on vulnerable population exploitation in the context of genetic diversity in SA as well as SA case law on sample ownership. The researcher's experience as a medical scientist in the laboratory has been counted on.

Chapter 2

Normative and regulatory analysis on the sharing of biomaterials and data in South Africa.

2.1 Introduction

Moral theories enhance clarity, systematic order and precision of an argument.[63] The laws pertaining to biobanks and biobank research should reflect and be consistent with protection of biobank samples and data as a means of preventing inappropriate sharing and access, thereby causing an infringement of ethical principles. Unlike morality, laws are enforceable. The health system in SA, with specific reference to health research, is regulated by a number of instruments in the form of the Bill of Rights of the Constitution of the Republic of South Africa, Act No. 108 of 1996 (hereinafter referred to as the Constitution)[64] which is the supreme law, the National Health Act No. 61 of 2003 (NHA)[4] and its relevant research-related regulations, the Health Professions Council of South Africa's policies and professional codes of ethics (general and research-related) (HPCSA Booklet 13 ref. General Ethical Guidelines for Health researchers) and the National Department of Health's Ethics in Health Research Principles Processes and Structures.[5]

Legislation is different in various countries in as much as virtues applicable in one society may not necessarily apply in another, hence the need for a more specific and adequate national regulatory framework. In this chapter, arguments against sharing of biomaterials and data in exchange for funding are discussed through exploring fundamental ethical issues that could arise as a result of such sharing. In addition, arguments that support material sharing in exchange for funding are examined. As a follow up to these ethical concerns, commodification of biobank material is explored in the following chapter. This chapter is aligned with objectives 1 and 3 of the study.

2.2 A defence on a prescriptive normative position on the major ethical issues related to biomaterial and data sharing where biobank research funding is concerned.

Arguments against and in support of material sharing specifically are presented in this chapter, while the report gives an overall ethico-legal analysis in this regard. In this research, it is argued that biomaterial and data sharing in exchange for funding is ethically wrong based on a number of premises:

1. A risk of dual loyalty: Interests of the funder could be regarded as more important than participants' dignity and rights.

2. Infringement of the ethical principles of participant autonomy, beneficence and justice: Unauthorised use of participant biomaterials and data and because of being acquired by financial means, benefit sharing is disregarded, hence beneficence and justice as in fairness, are violated.

3. Challenges to professionalism and the social contract between the participant and researcher: Issues such as financial gain can challenge professionalism.

4. Infringement of cultural beliefs: Cultural relativism

Each of the premises of the arguments is centred around the Kantian approach[65] that in order for each of the actions above to be morally acceptable, "one must act in such a way that every person is treated as an end and never as a means only" (Beauchamp and Childress, 1994, pg.58).[66] Treating research participants as a mere means to obtain funding by providing their biological materials and data to sponsors, results in a maxim or rule that cannot be made universal. This formulation underscores the significance of personal autonomy, dignity and rights. Health research participants ought to be treated with the respect and moral dignity to which everyone is entitled. In preserving human dignity, participants should never be used as a means towards fulfilling others' interests. A discussion of each of the identified premises follows next.

2.2.1 A risk of dual loyalty

The notion of dual loyalty is based on the premise that health care professionals (HCPs) have responsibilities and are accountable not only to their patients (research participants in the context of this research) but also to third parties such as employers and financial sponsors of research.[67] The HCP (or researcher) is faced with the ethical challenge of acting in the participant's best interests in the face of third-party pressures. In the specific situation of biobank and biobank research funding, the ethical dilemma would be potential violation of the research participant's dignity by researchers and biobank personnel being pressurised into trading the biomaterials and data for research funding. An additional challenge is that biobank collaborations with funders are not addressed in the legislation and national regulatory guidelines. The HPCSA holds HCPs accountable and responsible to further the participants' best interests. The best interests of participants whose biomaterials and data are involved, should extend above third party interests (funders in this case). As mentioned in section 2.4, however, none of the laws and regulations in SA provide conditions for sharing of biomaterials and data where funding is mentioned. This creates room for infringement of the ethical

principles when there are no legal and regulatory protections for research participants and those that have donated biobank samples.

2.2.2 Infringement of the ethical principles of participant autonomy, beneficence and justice.

Human beings have a right to choose to participate freely in research without coercion and have their autonomy respected.[68] In dealing with informed consent, HCPs should not exceed the authority granted by the patient[69] or research participant[6] in this context.

Biobank related activities and research ought to contribute to the benefit of society, and in particular, be in line with public health objectives.[2] The case studies on biopiracy and non-beneficent actions highlighted in this Research Report, however, prove otherwise. The Belmont report[70] formulated two general rules as reciprocal expressions of beneficent actions in the sense of (i) “do not harm and (ii) maximize possible benefits and minimize possible harms” (The Belmont Report, 1979, pg. 5). The role of Human Research Ethics Committees (HRECs) in the process of research protocol review is important as it ensures that participants of research are subjected to minimal harms and maximal benefits. Having their dignity infringed by exchanging their biomaterials and data for research funding would violate the principle of do no harm, albeit the harms not being physical. Not providing for benefit sharing because sponsors have acquired tissue in exchange for funding would infringe the principle of beneficence.

Applying the principle of justice means that people ought to be treated equally and further ties in with beneficence as it pertains to who ought to receive the benefits of research and bear its burdens. The question of justice in the sense of “fairness in distribution” or “what is deserved” is “who ought to receive the benefits of research and bear its burdens”? (The Belmont Report, 1979, pg. 5).[70] The formulations that have been accepted in the distribution of benefits and burdens are;

(1) “to each person an equal share,

(2) to each person according to individual need,

(3) to each person according to individual effort,

(4) to each person according to societal contribution, and

(5) to each person according to merit” (Belmont Report, 1979, pg. 5).[70]

The historical background is that as early as the 19th and early 20th century the burdens of research were borne by poor patients and the benefits of enhanced medical care were diverted to private patients demonstrating how conceptions of justice are relevant to human participant research. Accordingly, research participant selection should be scrutinized as a means of determining whether some groups of people are being selected simply because of being easily available, compromised position or being able to be manipulated rather than for research related reasons.[70] The opposite of such careful consideration in selecting research participants, challenges HCP professionalism and the social contract between the participant and researcher.

2.2.3 Challenged professionalism and the social contract between the participant and researcher

The social and moral contract between the healthcare profession and the public can be considered as the healthcare practice.[68] Central to this moral and social contract lies professionalism and professional integrity. These notions apply equally to health research. In SA, the HPCSA is the regulatory authority for HCPs and has developed ethical guidelines as an integral part of professional conduct for HCPs. Failure to adhere to these guidelines constitutes misconduct by HCPs. Some of the issues that challenge professionalism are economic factors, particularly financial pursuits that can undermine public trust in the practice of health research and healthcare. The integrity of the practice of biobank and biobank research could become tainted when there are inadequate ethico-regulatory safeguards for protection of participant samples and data. When research participants trust researchers, by inference, they believe what they are being told. This has the potential of predisposing the participants or sample donors to exploitation because of their vulnerability inherent in the trust relationship. The State is an important stakeholder in ensuring that the social contract between the researchers and participants is honoured through its legal and regulatory system. The main reason for the need to regulate the practice of healthcare and health research includes protecting the public from unsafe practices as well as to confer accountability to HCPs.[68]

2.2.4 Infringement of cultural beliefs: Cultural relativism

Various cultures have different moral codes, that is, what is perceived to be right within one group, may be an abomination for members of another group and vice versa. The concept of cultural relativism is of the idea that there are no universal truths in ethics but only different cultural codes and nothing more.[71] Despite the observation that cultural differences arguments

are not sound because the conclusion usually doesn't follow from the premise(s), these different moral codes still exist. Spiritual beliefs within the SA population are attributed to the reasoning behind why some of the research participants' object to their samples being shared with researchers in other countries. Moodley et al showed in their study that participants demonstrated fear and anxiety of not wanting their samples to be used in "satanic or cultural rituals by people in other African countries" (Moodley et al., 2014, pg. 4).[72] The phenomenon of differences in belief systems appears to be established in other parts of the world as well. Although African Americans are as likely as white Americans to donate their samples for research, the former group is less likely to agree to storage of their DNA samples for future research.[73] Few studies have explored an understanding of these differences in attitudes and motivation from the different racial groups, however in the population cited by Michie et al. 2011, the differences are due to a lack of trust by African Americans as a result of the historic problems between them and white Americans. A noteworthy observation which is not necessarily related to racial group differences, but that is attributed to trust issues among research participants has also been observed in a population in rural Ghana where participants, who were community members, were uncertain if their samples would either be sold or used inappropriately.[74] This finding was perceived to be as a result of weak community engagement. The same trust concerns are echoed by some researchers and specific cultural groups in South Africa as a reason to object to future use of their samples.[14] Moreover, the researchers themselves object to the transfer of samples to other countries as they have no control of those samples because of different or even absent cross-border transfer legislation among different countries.

2.3 Counter argument in support of sharing biomaterials and data within the current ethico-legal framework in international collaborative research.

Those in support of research collaborations do so mainly based on the idea that collaborations have the advantage of greater rewards in terms of increased dataset sizes,[28] in line with the utilitarian approach in that an action is right if it results in the greatest amount of "happiness for all those who will be affected" (Rachels, 2003, pg. 93).[75] Although the goal is to increase dataset sizes through collaborations, there is however some acknowledgement of a requirement for a proactive governance and legal approach to create foundational principles that guide sharing particularly of data. This is more appropriate an approach as compared to a reactive one.[28]

2.3.1 Utilitarian approach

A counter argument supporting biomaterial and data sharing in exchange for funding within the current regulatory framework could be that of a utilitarian approach based on the premise that biobank research would result in greater benefits of research in terms of enhancing evidence based medicine. Utilitarians hold the viewpoint that the right action in any circumstance is the one which holds the best consequences for the greater good.[75] The fallacy with this approach is that although one might think that one can bring about the best consequences, one can by no means be certain of it. Utilitarianism, also known as consequentialism, is not necessarily concerned about individual rights as indicated in the former argument but rather the collective benefits of research.[66] This viewpoint is a contradiction in a society where the legal system confers individual rights to all citizens. Moreover, section 36 of the Constitution, provides for the "limitation of rights to the extent that the limitation is justifiable in an open and democratic society based on human dignity, equality and freedom" (The Constitution of the Republic of South Africa, Act No.108 of 1996, section 36). The right to human dignity and life are the two rights that are entirely protected and non-derogable,[65] meaning that these rights cannot be limited under any circumstances. According to Jeremy Bentham (1748-1832), the law should not prohibit anyone from engaging in any type of activity unless that activity harms anyone.[75] Although this is similar to the SA Constitution in that exercising one's rights should not violate another person's right,[65] the problem here is that utilitarianism is not necessarily concerned with individual rights irrespective of whether derogable or not. Such challenges posed by this theory have led to some commentators concluding that the theory must be abandoned. The purpose of the law ought to be the same as that of morals, that is to promote the general wellbeing of all citizens.[75] It is evident that the disagreements in moral theories and concepts of morality necessitate intervention of the law on what ought to be done in specific circumstances such as the issue of regulating the access and transfer of human biomaterials and data to other parties, including funders of research and biobank sustainability activities.

2.4 The current ethico-legal framework for biobank research in South Africa

The human rights that are related to the collection and storage of biobank samples and data in the Constitution[64] are: the right to human dignity in section 10; the "right not to be subjected to medical or scientific experiments without informed consent" (Constitution of the Republic of South Africa Act No.108 of 1996, section 12(2)); and the "right to privacy which includes the right not to have the privacy of communications infringed" (Constitution of the Republic of South Africa Act No.108 of 1996, section 14). These rights align with the ethical principle of

respect for donor autonomy and are also incorporated in the National Health Act (NHA). The deficiency in the NHA, however, is that although it provides for medical and scientific research, it lacks provisions for specific aspects pertaining to the collection and storage of biomaterials and data for biobank purposes, as will be discussed below. Neither does it provide for this in its regulations. However, recently in 2018 the National Material Transfer Agreement (NMTA)[45] was gazetted into law to provide for the transfer, use and processing of human biological materials, and while it does include transfer of materials from biobanks, and storage into *inter alia* biobanks outside the country, it does not adequately address collection and storage. In section 60 of the NHA there is provision for protection of samples against commercialization and the requirement of an export permit for samples in ensuring unauthorized export. However, there are no provisions regulating conditions of funding. There are only research ethics specific provisions in the subsequent chapter (Chapter 9) of the NHA. The NHA regulations relating to tissue banks[76]are silent with regard to biobanks. In these regulations a tissue bank is defined in page 128 as an institution or person that deals with providing a service for cell and tissue transplantation,[76] which is clearly different from a biobank. The NHREC guidelines on the other hand use the terms “tissue bank” and “repository” interchangeably with no clear distinction and definition between the two. A repository is defined as the collection and storage of human biological materials such as blood, urine, bone marrow and other pathology samples for research purposes.[5] Accordingly, ambiguity results when interpreting these notions from a regulatory perspective. In addition, neither the NHREC nor the Health Professions Council of South Africa (HPCSA) guidelines address this crucial aspect of biobank regulations and in particular, funding constraints to sample and data exchange.

2.4.1 A discussion on Material Transfer Agreements

Institutional collaborations that involve sharing of materials require the use of agreements that are contractual such as Material Transfer Agreements (MTAs) as well as processes for sharing of samples and data. An MTA is an agreement which documents sharing of biomaterials and data between those involved with stipulated conditions under which the materials will be used.[45] The agreement directs transfer of materials between parties and defines their rights with regard materials and their derivatives.[77] MTAs should include the rights and responsibilities of the parties involved as well as terms that safeguard the rights of the participants. The purpose of the biomaterial and associated data transfer as well as restrictions for transfer ought to be defined in an MTA, for example, prohibiting specimen sale, use in other projects or redistribution to third parties. The governance structure of a biobank should include the criteria for biomaterial and data sharing.[2] The terms and conditions of material access

should be set by MTAs and the parties involved should agree on such terms and conditions in line with ethico-legal requirements. Specimen use restrictions should be provided for in MTAs with special consent indicated as required for purposes other than those previously consented for.[78] Prior to July 2018, SA biobanks did not have a National MTA and the drawback of this is that there was no standardized framework within which parties could engage in the use, transfer and processing of materials. This implication is supported by a research carried out by Moodley & Singh on sample export discussions. The study demonstrated that South African researchers raised concerns and strong opinions regarding the lack of a national MTA.[14] The concerns were around the fact that there was little to no control on monitoring of the fate of transferred samples with claims that some of the researchers from the HICs resisted MTA use. Other concerns were around lack of consistency among African countries in that some and not all have MTAs with variation on legislation around cross-border transfer of samples among the countries, challenging sample export. In South Africa, biomaterials can only be exported to other countries on condition of an export permit having being issued by the Director General of Health in line with the Regulations relating to the import and export of human tissue, blood, blood products, cultured cells, embryos, foetal tissue, embryos and zygotes.[39] These regulations mandate the amount of plasma intended for research purposes that can be exported not to exceed 5000ml.[39] There is no mention of conditions and provisions for export of other types of biomaterials used in biobanks and health research. The regulations specifically indicate that issuing of a permit for whole blood, frozen or fresh plasma, red cell concentrate and platelet concentrate may only be to a Southern African Development Community (SADC) member state, provided that the requirements of the SA market needs have been met.[39] This provision creates confusion and uncertainty because these materials are usually used for therapeutic purposes such as blood transfusions rather than biobank or general health research and also because the regulations are not explicit on whether such materials would be for research or therapeutic use. Tissue samples of less than 50 grams intended either for therapeutic or research purposes are excluded from the provision of these regulations.[39] Moreover, the wide range of biomaterials used for biobank and health research that include other forms of genetic material besides DNA (which is only mentioned in the definition section) are not mentioned and therefore not provided for in the regulations.

Regarding patentable material, MTAs are significant due to the fact that their terms may include the rights and royalties of an inventor that are not provided for by patent policy as well as provide limits on materials use where inventors have not been protected for the patent(s).[79] In the context of South African copyright law it is not clear as to the royalties that the publication author is entitled to over and above owning a copyright. Notably, there is subtle difference

between appropriate use and abuse of these rights and ethics and the law should always be prioritized, but this is not always the case. A discussion of the laws relating to the transfer of biomaterials and associated data follows next as a means of assessing the adequacy of the current ethico-legal framework in this regard.

2.4.2 Regulations relating to the export of biomaterials and associated data in South Africa: Is the current export permit sufficient in addressing the ethico- legal issues around export of samples across the borders of SA?

The regulations relating to the import and export of human tissue were established in terms of section 68 of the NHA[4] and mandate researchers to obtain permit(s) prior any imports and exports of human tissue.[39] The process for obtaining export permit(s) for human tissues is through application to the National Department of Health (NDOH) with a documented Turn Around Time (TAT) of 21 days. Some of the details that should be included on the application form (see appendix 2) is that the type of tissue(s) as well as the quantity and the purpose for which human tissues will be exported should be clearly stated, for example research purposes. The export permit is subject to the conditions as provided for by the NHA and those of the legal requirements of the country where the samples are being exported to. An anonymised draft export permit has been attached in appendix 3 of this Research Report to illustrate the provisions of the export regulations. Although there are protective measures for issued export permits that include a limited period of validity of the permit which is 12 months (renewable) with no blanket authorisations being issued, there are no limitations or conditions related to the export of samples.[80] To adequately answer the pertinent question of whether or not the current export permit is sufficient in addressing ethico-legal issues around the export of samples across SA, an analysis of the regulatory landscape in that regard follows.

The NHREC is a regulatory authority for human and animal research that was established in terms of section 72 of the NHA. One of the responsibilities of the NHREC is to "set norms and standards for health research involving humans and animals" (National Department of Health Principles, Processes and structures, 2015, pg. 9).[5] There are currently no biobank specific regulations in the SA ethico-legal framework, therefore different instruments are used to guide biobanking and biobank research. In section 60 of the NHA, there is provision for protection of samples against commercialization and the requirement of an export permit for samples in ensuring unauthorized export provided for in section 68, however, the limitations regarding these provisions is the lack of biobank regulations pertaining to conditions of funding. Moreover, the NHA does not address data sharing regulations in the context of international collaborations where funding is concerned. Furthermore, the NMTA does not refer to

conditions of funding when transferring biomaterials and data. Two separate legislations provide for the personal information protection and access to data in the form of the Protection of Personal Information Act (POPIA) No. 4 of 2013 and the Promotion of Access to Information Act (PAIA) No. 2 of 2000, respectively.[81,82] Section 72 of POPIA protects persons from whom information was collected in terms of restrictions on cross-border transfer of personal information unless there's certainty of legislative protections in the recipient country, owner's consent and when it is for the benefit of such a person. Protection from commercialization of data is however not addressed. Section 30 of PAIA provides for the access of health and "other records" of the relevant persons in terms of counselling or other arrangements if there's suspicion that such information could harm the relevant person.[82] The Act however, does not provide for health research information access particularly where access pertains to international health research collaborations. In addition, neither the NHREC nor the Health Professions Council of South Africa (HPCSA) guidelines address this crucial aspect of biobank regulations and in particular, funding constraints to sample and data exchange. The Publicly Financed Research and Development Act, No. 51 of 2008[83] applies to provisions for intellectual property arising from publicly financed research and development. Section 12 of the Act provides for commercialisation of intellectual property under 2 conditions, namely; (1) if there is sufficient capacity locally to commercialise or develop the intellectual property and also if the transaction will benefit the Republic of South Africa (RSA). Section 15 provides for private entities to become exclusive licensees of intellectual property if the entity meets the two stated conditions while co-ownership for intellectual property among research collaborators requires benefit sharing and commercialization of the intellectual property agreement among the collaborators.

As already alluded to in chapter 1 section 1.2, the sharing of samples and data by the recipients of funding is a condition for funding in a number of international collaborations. One such example is that of the University of the Witwatersrand Network for the Demographic Evaluation of Populations and their Health in Low-and Middle Income Countries (Wits-INDEPTH) Collaborative Centre, known by the abbreviation AWI-GEN (Africa Wits INDEPTH partnership for Genomic Research) established under the auspices of H3Africa.[84] On sample and data sharing, Ramsay et al. state that, "A characteristic of genomic research generally, and of our project more specifically, is that it usually involves international collaboration. In addition, funding conditions for AWI-Gen require us to make data and samples available for secondary analysis and use. It was recognised that there is a need to balance access with the interests of the participants, the ethics committees (in their capacity as protectors of participants) and the funders and that sharing needed to be a two-way process" (Ramsay et al., 2014, pg. 4).[84]

In 2012, AWI-GEN hosted a workshop in SA for the discussion of ethico-legal issues in Africa and sharing of samples where the workshop participants recognized the need for the balance between sample and data sharing and access with the interests of the research participants. Not all of the workshop participants from a number of African countries were certain that their countries had adequate policy frameworks to address this crucial aspect of research.[84] It is certainly the case with SA as indicated above that the laws and regulations do not address sharing of samples and data where funding is concerned and therefore, the current export permit is not sufficient in addressing the ethico-legal issues around export of samples across the borders of SA. In addition, considering the contextual complexities around issues of sharing of samples, the key stakeholders that should be taken into account in this regard are those from whom biomaterials and associated data have been collected. In particular, considering the vast cultural diversity of Africans, it is important to seek views from such individuals. Few empirical studies have been conducted to address this issue. There was a study, however, which was conducted in 2012 in two SA provinces that revealed that although about 78% of research participants were comfortable with their samples being stored, 12% insisted on having some knowledge on the reasons behind storage, while about 50% wanted to be re-contacted regarding consent for future use.[72] Most of the participants (75%) did not object to export of samples, however about 10% strongly objected with concerns based on certain spiritual beliefs.[72] About 39.5% of the participants objected to any profits being generated from the research and of this subgroup, 43% expressed a desire to share in the profits.[72] About 19.5% expressed that they would not mind if the profits were generated from the research, provided that the research was conducted for the common good.[72] The question of funding and transfer of materials was not discussed in this paper, presumably because the aim of the study was limited to exploring the views of research participants on sample export, storage and future use. To my knowledge, there has been no study to date aimed at assessing either the attitudes of research participants or researchers on their perceptions around funding in exchange for material transfer. Based on the inadequacy of SA laws and regulations including the current export permit in addressing the ethico-legal issues around export of samples across the borders of SA, development of regulations in that regard could draw on international regulations if these provide sufficient protection for those donating biomaterials for biobank research. An analysis of international regulations follows next in assessing whether or not these could serve as an appropriate guide.

2.4.3 International regulations and guidelines relating to sharing of biomaterials and associated data.

Although biobanks are governed by national laws and regulations in which they are physically located, international regulations also have an influence in the various ethical aspects of biobank processes. The list of the various regulatory instruments for the governance of biobanks below is by no means exhaustive, however, includes:

(1) The World Medical Association (WMA) Declaration Of Taipei On Ethical Considerations Regarding Health Databases and Biobanks;

(2) The WMA Declaration of Helsinki-Ethical Principles For Medical Research Involving Human Subjects;

(3) Council for International Organizations of Medical Sciences' (CIOMS) International Ethical Guidelines for Health-Related Research Involving Humans;

(4 Organisation For Economic Co-operation and Development (OECD) Guidelines for Human Biobanks and Genetic Research Databases;

(5) OECD Principles and Guidelines for Access to Research Data from Public Funding;

(6) International Society for Biobanks and Environmental Repositories (ISBER), Best Practices: Recommendations for Repositories.

A discussion of each of these regulatory instruments follows.

2.4.3.1 WMA Declarations

The WMA is an international organization which was created to ensure the highest possible standards of ethical behaviour by physicians.[85] The WMA has alliances and partnerships with international medical and professional organizations as well as academic centres, including the Steve Biko Centre for Bioethics of the University of the Witwatersrand, which is one of its co-operating academic centres.[86] Although the Declaration of Helsinki does not address sharing and access of samples and data in medical research, there is a recommendation for consulting national regulations in that regard. The challenge arises when there are no national regulations and or legislation to that effect. The WMA Declaration of Taipei on Ethical Considerations Regarding Health Databases and Biobanks however, mentions that biobanks should include in their governance structures procedures and criteria for sharing and access of biomaterials and data including the use of MTAs when necessary.[87]

2.4.3.2 CIOMS International Ethical Guidelines for Health Related Research Involving Humans

The CIOMS guidelines 11 &12 provide guidance for the use of an MTA for the transfer of biomaterials which should include the duration and fate of samples. Data sharing should also be covered in agreements that protect privacy protections of the participants.[78]

2.4.3.3 OECD Declarations and Guidelines

In 2004, Ministers of Science and Technology from 30 OECD countries including South Africa, developed a *Declaration on Access to Research Data from Public Funding*.[88] The nature of public funding is context specific and varies from one country to another as do data access policies. Public fund in these guidelines is defined as that which is provided by government. This definition does not include any other source of funding in collaborative research such as that from independent funders. The guidelines emphasize "systematic data sharing" within an agreed framework despite any restrictions that may have been put on research data access. The guidelines, however, recognize the national laws and policies of member countries as well as recommend consideration for explicit agreements for data access between collaborating centres. Only address data access in isolation is addressed without provision for sharing of the samples that are associated with the data. The OECD Guidelines for Human Biobanks and Genetic Research Databases do make mention that the criteria for access of samples and data should be clear and in accordance with consent granted by the participant.[89] The criteria are not prescriptive but left to the discretion of the parties involved in the collaboration.

2.4.3.4 ISBER's best practices

One of ISBER's key objectives is to share strategies, policies and procedures for providing fit-for purpose samples for research.[15] Due to the fact that on an international level, sample collection and use is regulated by differing laws and policies, biobanks should proceed carefully particularly with the sharing of samples and associated data in international collaborations. Best practice recommends that local regulations and laws regarding sharing of samples and data should be followed with emphasis placed on aspects such as sharing that is consistent with the consent granted and a presence of a policy for the terms of benefit sharing. Provisions for conditions of sample and associated data sharing in international collaborations is also lacking in these best practice recommendations.

Table 1: International regulatory documents analysed and key points on biomaterial and associated data transfer

Nature of document	Title of document	Key point on material transfer
Declaration	WMA Declaration Of Taipei On Ethical Considerations Regarding Health Databases And Biobanks	Mentions that biobanks should include in their governance structures criteria and procedures for access to and sharing of biomaterials and data including the use of MTAs when necessary.
Declaration	WMA Declaration Of Helsinki-Ethical Principles For Medical Research Involving Human Subjects	No provision on the conditions for sharing of samples and data by biobanks with the collaborating centres where funding is concerned.
Guidelines	CIOMS International Ethical Guidelines for Health Related Research Involving Humans	Provides guidance for the use of an MTA for the transfer of biomaterials which should include the duration and fate of samples. Data sharing should also be covered in agreements that protect privacy of the participants.
Declaration	OECD Declaration on Access to Research Data from Public Funding	Recommend consideration for explicit agreements for data access between collaborating centres with no provision for condition of access to and sharing of biomaterials
Guidelines	OECD Guidelines for Human Biobanks and Genetic Research Databases	Mention that the criteria (non-prescriptive) for access of samples and data should be clear and in accordance with consent granted by the participant

Notable in the preceding discussion of this Research Report is that the current regulations for transfer of human samples particularly in the context of cross border transfers neither include the wide array of biobank samples nor address human sample export for biobank samples and associated data.

2.5 What should the amendments be in the current export regulations for human samples to accommodate biobank sample export?

In order to address the deficiencies, examples of biomaterials in SA biobanks as well as the provisions for appropriate sample quantities that can be exported for each individual type or group of sample should be included in the export regulations. Although the application form for an export permit allows for inclusion of any type of sample as well as the quantities, these two aspects are not provided for in the regulations. A clear distinction should also be made in terms of provisions for export of samples that are used for general health research including biobank research, differentiating these from samples that are used for therapeutic purposes because research samples are often pathology samples that cannot be used for therapeutic purposes.

2.6 Conclusion

The sharing of biobank samples and data raises several ethico-legal concerns, particularly in the context of cross-border transfers due not only to different values, beliefs and notions of commodification of human biomaterials, but also as a result of inadequacies in national and international regulations addressing this crucial aspect of biobanking. While international regulations are often explicit with recommendations for individual countries to develop more specific regulations for participant protections where samples are shared with third parties, the onus is on the respective countries themselves to formulate and implement such regulations. Until such a time exists where these inadequacies have been addressed, the competing interests of the stakeholders involved in sharing of biomaterials and data need to be discussed at the beginning of such collaborations with mutually agreed terms as a requirement. In light of the major ethical issues related to biomaterial and data sharing where biobank research funding is concerned as has been discussed in this chapter, a detailed normative exploration of commodification when funding is contingent to transfer of biomaterials follows in the next chapter.

Chapter 3

Commodification of biomaterials and data when funding is contingent on transfer in health research: a normative analysis

3.1 Introduction

Commodification is “the practice of treating things as property that can be bought, sold or rented” (Resnik, 1998, pg. 388), that is as commodities.[90] In simple terms commodifying things amounts to a sale. In the context of this research, commodification of biomaterials and data (interchangeably referred to as materials herein) refers to the extent to which materials become commodities of trade and are transferred for cash. Based on this definition, commodification and commercialization will be used interchangeably. The arguments against and for commodification of human body parts in the context of organ donations and transplants will be used in this report as they present similar concepts to the commodification of human samples. In addition, there is a paucity of the latter arguments in the literature. One way to tackle the issue of biobank sustainability is to take advantage of the potential financial value of biobank samples and data. This however presents ethico-legal challenges most notably through an argument that places commercial value and the interests of private companies as well as governments that provide funding against the aims of the public good and values of biobanks.[91] The main ethico-legal challenges are those that have been presented in chapter 2, section 2.2 of this Research Report. The position being developed in this Research Report is that it is ethically unacceptable to exchange biomaterials and data for money (funding) because there ought to be restrictions imposed on what can be treated as commodities, not only based on social and political reasons but also due to moral reasoning as well.[90] The issue of commodification of the body and its parts, interchangeably referred to as commodification of the body, has been widely debated.[92-97]

One of the arguments against commodification of body parts is that there ought to be limits on what can be sold or bought as commodities and that some things such as body organs “are so valuable, priceless or sacred that they should never be allowed into the marketplace” (De Castro, 2003, pg. 1). This argument is based on the Kantian position which is that of the premise that kidneys, livers, brain, heart and eyes are an integral part of the functioning of human beings and should not be sold because selling of such integral body parts denies people human dignity.[93] The second argument against commodification of the body, particularly in the context of donation of organs is that which is based on dilution of altruism when organ donors are paid for their organs.[94] The third argument is based on the communitarian approach which emphasizes a social responsibility to donate organs as

something that a good person should do.[95] Arguments in support of commodification of the body and its parts include that of liberal individualism which gives individuals the liberty and freedom to decide on whether or not they would want to sell their organs;[96] and consequentialism, which is based on the reasoning that organ sales yields best consequences for all in terms of increased organs available for transplants which represents the common good of society because of perceived best consequences for all concerned, that is organ donors and recipients.[97]

In this chapter, arguments against commodification of biomaterials and data are discussed, namely the Kantian approach argument as it relates to interference of commodification with human dignity which is linked to a diminished sense of personhood, an argument against commodification that is based on a dilution of altruism and lastly the communitarian approach anti-commodification argument which emphasizes a social responsibility to the common good. Arguments in support of commodification based on liberal individualism, consequentialism and that which is based on respect for ethical principles are also discussed. This chapter, similar to chapter 2, is aligned with objective 1 of the study which is, to defend a prescriptive normative position on the major ethical issues related to biomaterial and data sharing where biobank research funding in international collaborative health research is concerned. However, the focus of this chapter is specific to commodification.

3.2 Background to the arguments

Many normative arguments depend upon factual information and such arguments with premises that are both moral and factual are essential to moral reasoning.[98] Based on this notion, and in order to answer the question of whether or not it is ethically justified to share biomaterials and data in exchange for funding, a discussion on commodification in terms of the extent of the problem of bodily commodification and its consequences as well as that on morality of commodification is required.

3.2.1 The extent of the problem of commodification of the body and its consequences: the case of organs

The main reasons for justifying organ sales are due to shortage of organs available for transplant, which is an issue of global concern, as well as for financial gratification in some of the poorest populations. In light of this, the human organ market is theorized as both a global macro-ethical and economic phenomenon because it has a large system of exchange across differences in the dynamics of both the High Income Countries (HICs) and Low and Middle

Income Countries (LMICs) and differences in wealth.[99] Hence, it can be inferred that economic issues have polluted the moral compass and people's judgement when it comes to making ethically sound decisions relating to organ transplants. An account of the extent of the problem of organ shortage is necessary as a means to demonstrate justification for people to be involved in organ sale or commodification. The detailed discussion on organs is necessary as a backdrop to illustrate the associated ethical issues that arise when biomaterials and data are commodified in health research. The values and principles in commodification arguments in the context of organs apply in a similar way in health research.

There are disparities in allocation of organs for transplant due to various factors including geographic variation among the recipients of donations.[100] In the United States of America (USA) alone in 2014 more than 23 000 patients (population size of more than 318 million)[101] were awaiting kidney transplants. The waiting periods were almost up to 4 years in this region.[100] There are also racial and education level disparities in this population where more black patients and those with a low education level wait longer for kidney transplants. Disparities in organ allocation for transplant have also been observed in other first world areas such as Europe. This is because of economic disparities and healthcare priorities being the major contributing factors to organ demand and supply.[102] The disparities in allocation of organs for transplant presents an even more serious challenge in developing countries, particularly Sub-Saharan Africa (SS Africa).[103] Part of the problem is due to the AIDS pandemic that fuels the burden of kidney disease where governments have to prioritize budget allocation to AIDS related healthcare services at the expense of other healthcare needs as a means of rationing resources.[104] A consequence of such resource rationing is that only a minority of patients with conditions such as End Stage Renal Disease (ESRD) in these countries including South Africa (SA) can have access to kidney replacement treatment, while diagnosis is a death sentence for the rest of the patients. Nearly every country in the world has a shortage of body organs that are available for transplantation and as already alluded to, the shortage and consequences are even more severe in developing countries.[104]

Organ shortage has led to the development of an international trade of organs where those who obtain organs do so through commercial means with facilitators for the transactions present in the recipients' countries of origin.[105] A study conducted in India in 2001 showed that the most common reasons for people selling their kidneys, particularly poor people in this population, were financial such as paying debts and for household expenses while wanting to help a person with kidney disease was not a major determining factor in about 95% of participating individuals.[104] In this population, selling kidneys did not help the sellers overcome poverty and about 79% reported that they would not recommend selling of kidneys to others based on their claim of not being better informed of the likely outcomes of a decline in health

status after kidney donation of which the most commonly cited was long-term back pain.[104] This is possibly because the organ harvesting was done unprofessionally and therefore illegally also because organ sale is banned in India. Organ sale has also been banned in Bangladesh but this country has been estimated to comprise of the majority of human organs being trafficked worldwide which warrants an in-depth investigation as it has been associated with violence when the organs are harvested, particularly in this part of the world. This violence has been termed "bioviolence" by Moniruzzaman in 2012 (Moniruzzaman, 2011, pg. 72) which has been "defined as an act of inflicting harm and intentional manipulation to exploit certain bodies as a means to an end" (Moniruzzaman, 2011, pg.72.[99] A study by Moniruzzaman revealed that 33 Bengali who were all poor reported bioviolence had been inflicted on them in order to procure their organs and this information was obtained through an informant who was also involved in organ sales.[99] Poverty forced these participants to sell their body parts. There are also reports of an economic market for organs on the black market (illegal) that is thriving in other areas of the world such as the USA and China where reports of unethical organ harvesting from executed prisoners that did not consent to the organ harvesting led to the ban of organ sale in China.[106] In SA, the reports of illegal organ sales reveal that selling of body kidneys on the "black market" costs up to R2 million per kidney by desperate unemployed poor South Africans keen to sell their body parts.[107] These cases not only represent ethical and legal transgressions inflicted on donors in the face of bans on organ sales in the respective countries but also demonstrate that when money is an incentive to obtain organs (or biomaterials in the context of biobank research) people can be used as a means to fulfil others' ends, and this is more pronounced in the vulnerable poor individuals and groups. Moreover, the cases demonstrate that if organ sale is allowed, a slippery slope results where ultimately everyone would want to be incentivized for organ donations, leaving the poor to suffer and ultimately die because they would not afford buying organs that are essential to their survival. The challenges presented by organ sales give rise to moral concerns about commodification of organs as is discussed in the section that follows.

3.2.2 Morality of bodily commodification

Morality is 'how we ought to live' and why.[108] Having said this, however, there are different conceptions of what it means to live morally. In order for commodification to occur, different commodities are exchanged in different quantities, for example coats cannot be exchanged for coats.[109] This means that in order for bodily materials to be rendered commodities, they ought to be transferred to recipients for cash or other similar goods, e.g., gold since these are a prerequisite for commodifying things. Commodities are alienable while market inalienability

often represents an attempt to prevent commodification or at least expresses an aspiration for non-commodification through probing limits to commodification.[110] There is no universally accepted definition for market inalienability but there is a notable definition by Radin, in which she considers inalienability to be that which means "insaleability" (Radin, 1987, pg. 1850).[111] Part of the problem of commodifying that which ought not be commodified is that commodification or alienability is the route to objectification which is treating as an object something which is more than an object. The notion of objectification links to both the Kantian approach that when we objectify humans, we are treating them as a means to fulfil certain ends and that objectification through commodification diminishes aspects of personhood through engendering inferior understanding and conceptualization of what a person is.[112,113] Diluting altruism is a third view which has been used in arguments against commodification and this concept is based on the idea that the practice of free donations is undermined by commodification.[114] This background information forms the basis for arguments against and for commodification of the body and its parts.

3.3 Arguments against commodification of the body and its parts

Some of the concepts used in the arguments against commercialization of the human body debate, which include organ sale, are mostly around donor coercion, commodification and objectification of body parts as well as donor exploitation and harm.[114] These concepts have been incorporated in the anti-commodification arguments used in this chapter with regard to biomaterials and data. Commentators against selling of organs, particularly kidneys argue that selling of organs amounts to exploitation of the poor where the poor are perceived to be coerced by circumstances to sell their organs.[104] The main views against commodification of the body and its parts are that of (1) interfering with human dignity through treating people as "a means to an end" (Rachels, 2003, pg. 130) and the relationship of this interference of human dignity with diminished personhood; (2) diluting altruism; and (3) social responsibility to donate organs without expecting monetary gain. The central idea of this research is based on an argument against commodification of the body and its parts, which includes biomaterials and data and holds that it is ethically wrong to commodify humans and their body parts.

3.3.1 The Kantian approach of interference with human dignity and diminished personhood

The Kantian approach confers "an intrinsic worth" or dignity to humans which makes them valuable "above all price" (Rachels, 2003, pg. 130).[66] By virtue of the interference of

commodification with human dignity, this argument is linked to a diminished sense of personhood that is perceived to be the result of such commodification. This is because the notion of personhood is based on the concept that for an entity to possess personhood, it ought to be human with full moral status which in turn entails a right to dignity and respect.[114] The concept of diminished personhood is based on the idea that body tissues have an intimate connection with personhood and that such commodification elicits social harm in the sense that it is abhorrent to equate personhood with property that can be commodified.[115] According to Immanuel Kant's idea of human dignity, human beings should never be treated as a "means to an end" (Rachels, 2003, pg. 130) but rather "an end in themselves" (Rachels, 2003, pg.132).[66] Human dignity confers an intrinsic worth" to humans which makes them valuable "above all price" (Rachels, 2003, pg.130). This directly translates into the idea that humans cannot be commodified because no price would be suitable for their worth. Whatever has a price, something else can be put in its place as its equivalent, while that which is above all price with no equivalent has dignity. Based on this notion, dignity is afforded something with an inner worth and an end in itself.[117] Based on the translation of commodification as referring to turning of people into objects of trade or commodities, the notion of commodification equates to slavery which strips people of their basic rights because the claim is that there is objectification of human beings in the same way that there is objectification of body parts.[118] From the Kantian perspective, human bodies can never be used as a means but should rather always be considered as an end outside all markets meaning selling or buying of any part of the body is strictly forbidden as it erodes the sanctity and dignity of human life[119] and hence cannot be seen as satisfying the requirements for Kant's categorical imperative which is that one must "act only in accordance with that maxim which one can at the same time will to become a universal law" (Rachels, 2003, pg. 131)[65]; i.e., accepting universal acceptability of a plan or action. Human beings should never be assigned market value and treated as commodities because they have absolute market value.[90] Assigning market value to human beings and any part of the body equates to a sale and is ethically unacceptable. In the context of sharing of biomaterials and data in exchange for funding, those who donate biobank samples can never be used as an end to fulfil the funders' interests but rather an end in themselves because they have an inner worth and dignity. This means that materials can only be collected from humans for the benefit of such individuals or for the benefit of society in order to fulfil the requirement of these individuals being an end in themselves rather than a means to fulfil others' (in this case funders') interests.

Diminished personhood that occurs with bodily commodification relates to human dignity or worth by virtue of its definition that incorporates a right for human beings to dignity and respect. Personhood is granted on an entity with consideration that (1) it is a human being (2) with full

moral status.[120] Full moral status entails a right to life and a right to respect and dignity.[114] Moreover, commodification insists on objectification, transforming people and their bodies from human form into objects of economic desire.[120] Objectification generally signifies dehumanization because it silences or even displaces the self from the social world.[109] In preventing such objectification through commodification, maintaining a spirit of altruistic donations is crucial.

3.3.2 Dilution of altruism by commodification

Altruistic actions are those that are performed purely for the sole benefit of the recipient without expecting anything in return.[122] In ethics literature, altruistic organ donation is widely accepted as a virtue as well as in religious practices such as Jewish law which regards saving human lives as an absolute value.[123] However, the Jewish teachings prohibit saving another person's life at the expense of sacrificing one's own life. Those who are in favour of altruistic organ donation have an expectation that family members should donate an organ and consider refusal to be a great shame. Other prominent religions such as Islam and Christianity also regard altruism as an important principle and generally do not object to organ donations particularly of an altruistic nature, however there's nuances in the latter that is compounded by the refusal of blood transfusions in the Jehovah's Witnesses doctrine.[124]

Despite the insistence of altruistic organ donations and the ban of organ sales, it is evident from the discussion above that illegal organ sales are thriving in different parts of the world. The major concern with the argument against commodification based on a dilution of altruism is that if payment is allowed, virtually all voluntary donations will cease because all donors will expect payments for their donations.[114] This could equally apply to "sale" of biomaterials and data in health research.

3.3.3 A social responsibility to donate organs that is based on communitarianism: Community-based theory

Communitarian theory considers everything that is fundamental in ethics as that having communal values, co-operative virtues and the common good.[67] Communitarians would not consider individual rights in the issue of organ donation but rather which communal values and relationships are present or absent for the common good. Some ethicists such as Stuart Mill, however, emphasized the need for a discussion on what constitutes a 'good' for the community.[67] The communitarian approach in the context of organ donation is of the idea that people should donate organs as a social responsibility and as something that a good person

should do.[95] Reference in this instance is not to altruism as critics of altruism have pointed out that altruism is an insufficient motive because despite the appeals to donate organs on this basis, the outcomes are still not desirable. The notion of communitarianism rather reflects the core elements of moral culture, which is a combination of societal pressure to do what is right with persuasion from other community members and an inner pressure to do what is right.[95]

3.4 Arguments in support of selling organs

Proponents of organ sales argue that the seller has a right to decide on the fate of his or her body parts and that taking away this option harms the seller financially.[104] This argument relates to liberty and freedom to choose what is right for oneself including the right to sell one's organs if people so wish. Such liberty has been linked to alienability in the context of human commodification which forms part of the argument that supports commodification with consequentialism (utilitarianism) as a basis which holds that it is for good reasons for people to be paid for their organs because of the best consequences for all due to more organs being made available to potential recipients. This would be a contribution to the greater good and overall well-being of society and which would be evidenced as increased life expectancies and improved quality of life for the recipients.[104] Those who support organ sales do so mainly, based on the idea of a regulated system for organ sales. The main argument in favour of a regulated system for the sale of organs is that financial incentives are likely to increase donations, resulting in fewer deaths of transplant candidates on waiting lists.[92] Such a system could work through establishing national criteria for tests and results required for donor evaluation. The distinction between a regulated and an unregulated system is important because in the latter system, the seller contracts with the buyer (often through a broker) to purchase a kidney. The implications of an unregulated system, is that, only the rich would be eligible to buy kidneys, with "little oversight of donor evaluation, with no long-term donor follow-up and no protection for either the buyer or the seller" (Matas, 2006, pg. 1130).[92] On the other hand, when it comes to biomaterials and data in the context of human research, it would be the poor that would sell at the expense of their dignity for the benefit, in the main for the rich. As already alluded to previously, the moral reasoning in support of organ sales is based on liberal individualism and consequentialism.

3.4.1 Liberal individualism: Rights based theory

One interpretation of liberal individualism is that people own themselves and as such, individuals have a right to sell their organs, donate them for any reason they may choose and

that any alternative contrary to this would equate to some form of slavery.[96] The view behind this argument is that which considers basic economic justice, which in this context is compensation of donors for their resources (biomaterials and data). In addition, the argument holds that it is within an individual's rights to sell his or her body parts if they so wish as long as this does not violate another person's rights. Although the vital role of rights in protecting individuals from societal intrusions cannot be disputed, the idea however that rights are important in ethics has been resisted by some ethical theories.[125] This is because individual rights are often in conflict with communal or institutional interests. Rights generally give us a claim based on a system of rules to affirm, demand or insist upon what is due to us. A distinction between moral and legal rights is made.

Moral versus legal rights

While legal rights are justified by legal claims, moral rights are justified by moral claims hence there's sometimes a conflict between laws and morality. Not everything that is legal is moral and vice versa.[98] Laws can also be immoral. A typical example is that of the apartheid laws in SA that were based on segregation of persons by their racial groups during the pre-democratic era prior to 1994. In the current scenario of sales of body parts, even though morality confers a right for people to sell their organs and bio-specimens through liberal individualism, this right would not be applicable legally in a society where the legal system does not confer such a right. The United Nations (UN) and European Union (EU) have instructed their member States to prohibit sales of body parts.[126] This means that sale of organs and biomaterials in the vast majority of countries in the world is illegal. So according to the law, individuals have a right to donate but not a right to sell their organs in these countries. In countries where organ trade is legal, different business models exist for organ trade ranging from high profit benefits to a remuneration model where only the donor expenses such as travel and lodging are covered during the process of organ donation.[127]

3.4.2 Consequentialism

The theory of consequentialism, also known as utilitarianism "requires that whenever we have a choice between actions, we ought to choose one which has the best overall consequences for all concerned" (Rachels, 2003, pg. 92).[75] Conveyed differently, morality requires that "in deciding what to do, we ought to ask ourselves what course of action would produce the greatest amount of happiness for all those who will be affected" (Rachels, 2003, pg. 93). Based on this idea, incentivizing donations of body parts for the donor would mean that the

consequences would be favourable not only for the recipients of those parts, e.g. kidney transplants in the form of overall well-being and increased life expectancies but also the best consequences for financial benefit for the donors. According to utilitarianism, the right conduct is the one that engenders the most good and in defining what is good, utilititarians define "good" as one and one thing only, namely happiness.[75] Moreover, those in support of this argument claim that subjecting a good such as organ donation to market exchange does not change its meaning or value.[97] However, "if economics was to serve as a guide on which markets serve the public good and where they do not belong, it should relinquish the claim to be a value-neutral science but should reconnect with its origins in moral philosophy" (Sandel, 2013, pg. 138-139). Critics of utilitarianism rebuke the theory based on the idea that consequences should not be the only thing that matters, for example, when a person lies and justifies it with the 'good' consequences. In the same breath, "good consequences" should not be the only thing that matter to a point where the means and ethical principles are violated and compromised in achieving the ends.

3.4.3 Respect for the ethical principles: Principle based approach

Principle based approach, also known as, 'the four principles approach' seems to have become more popular and accommodative for those not so much interested in theories but in need of a way of thinking through ethical dilemmas.[128] Although the 4 principles of biomedical ethics do not necessarily provide a precise action guideline for each and every circumstance and moral dilemma, they provide comprehensive norms in the ethical framework on decision making.[66] The principles (in italics) require that (1) individual *autonomy* is to be respected when individuals make decisions for themselves (2) harm is to be avoided- *non-maleficence*, (3) benefits are to be provided and benefits must be balanced against risks - *beneficence* and (4) benefits, risks and costs are to be distributed fairly - *justice*. All principles need to be taken into consideration.

Autonomy

Beauchamp maintains that even though those who sell their organs are at a risk of exploitation, for example through unfair market prices and manipulation to accept offers, it does not follow that a ban of kidney sales is the best way to resolve this problem.[125] This is perceived to be due to the reasoning that banning of kidney sales would make life difficult for many volunteers who see the selling of their organs as the best option, all things considered, they would still find the offers welcome and would remain autonomous agents. The argument further states

that banning of kidney sale to protect them would make their lives worse and make them more rather than less vulnerable and that banning sales of kidneys is paternalistic and ignores individual autonomy.[125] Paternalism is a concept, which refers to when healthcare practitioners (HCPs) act in what they consider to be in the best interests of their patients even though such actions may not be consistent with their patients' beliefs and desires.[129] The same reasoning would follow for sale of biomaterials in collaborative research.

Beneficence and non-maleficence

The main reasoning behind the argument that is pro-kidney sales is that sales would be for the benefit of all involved, that is it would not only benefit patients on ESRD by decreasing the number of those who die and on waiting lists but would also be to the benefit of the donors financially.[92] The non-maleficence aspect of kidney sales, similar to sale of biomaterials in heath research, would be protection of donors against exploitation and this can be done through a regulatory system that takes into account ethical principles and individual rights.

Justice

In terms of justice, those who support organ sales claim that a ban of kidney sales could be an excuse to cause neglect of the injustices that are a result of procurement and kidney transplant policies that affect many. Beauchamp holds that we ought not to assume that a fair and just system of incentive or payment for kidney procurement cannot be constructed.[125] Therefore, based on this premise the conclusion is that the ban of kidney sales can never be justified based on such assumptions. This notion of justice can be extended to the situation of biomaterials.

3.5 Conclusion

This chapter has considered arguments against commodification of the body and its parts which is represented by organ sale arguments to illustrate the point on arguments against and for commodification of biomaterials and data. In support of arguments against commodification, is that of interference of commodification with human dignity and the association with diminished personhood as it relates to human dignity as well as a dilution of altruism which is undermined by commodification. These moral concerns as well as consequences of commodification which include exploitation of the poor that are coerced by their financial circumstances as well as the bioviolence and unethical practices provide the

best reasons for not allowing bodily commodification. Arguments that support the sale of body parts are centred around firstly the notion that people have a right and liberty to decide what to do with their lives, including a right to decide to sell their body parts if they so wish. Secondly, allowing people to sell their body parts would result in adequate available amounts for treatments or research as relevant. Proponents of this view hold that this would result in a favourable situation where not only the recipients of treatments benefit but this would also result in financial benefit for those who donate. What stands out from the pro-commodification arguments is that the means to achieve bodily commodification do not matter in attaining financial benefits. This highlights the wrongness of commodification which objectifies humans through exploitation and exposure to unethical practices. In countering the effects of such commodification, a fundamental change in approach to the status quo where SA researchers are empowered through shared benefits in international collaborative research is necessary. In the next chapter, benefit sharing is discussed.

Chapter 4

Benefit sharing in international collaborative health research

4.1 Introduction

Benefits for biobank and health research are those arising from the use of biomaterials and what represents benefits for different stakeholders is affected by their specific needs, expectations and values.[130] Benefit sharing is defined in the National Material Transfer Agreement (NMTA) as the process of sharing in the benefits arising from a project in a fair and equitable manner.[45] The question of whether or not it is ethically justified to share biobank samples and data in exchange for funding relates to benefit sharing in a sense that the concept of benefit sharing puts emphasis on fair and equitable benefit sharing rather than the opposite scenario of exploitation which occurs when materials are commercialised. Benefit sharing is linked to the ethical principle of beneficence which places an obligation on researchers to think about ways of maximising benefits for research participants while minimizing risks[70] and also ties in with the ethical principle of justice[131] through its link between beneficence and justice in terms of who bears the burdens of research and receives its benefits as already mentioned in chapter 2, section 2.2.2. As such, benefit sharing has been emphasised in national as well as international regulatory instruments and in SA the NMTA addresses benefit sharing as part of the agreement between parties involved in the sharing of biological materials. Benefit sharing provides for the inclusion of sharing of benefits and these benefits include information sharing, research results use, royalties, provider acknowledgement as the source of biomaterials and data, technology or material transfer, publication rights and capacity building.[45] The idea is that all parties involved should agree on discussed and negotiated benefits before the materials are transferred to the recipient. The conceptual and practical challenges in the debates around benefit sharing issues in cross-border transfers of samples and data remain unsolved.[23] There may be resistance to benefit sharing when an institution from a HIC funds research in LMICs despite emphasis on benefit sharing by international guidelines such as the Nagoya Protocol, Declaration Of Helsinki, CIOMS Guidelines, The Declaration On The Human Genome And Human Rights.[132] Such resistance necessitates a benefit sharing model for biobank research that will enhance confidence and trust and ensure a sustainable research environment for participants of research as well as institutions.

H3Africa has developed an ethics and governance framework for genomic research and biobanking in Africa which not only considers the monetary and non-monetary benefits in the sense that has already been highlighted in this Research Report thus far, but is also more

specific to the African context in terms of values and cultural expectations, namely inclusion of representatives from participating communities in the benefit sharing discussions.[130]

In this chapter, the following are discussed; unresolved practical challenges pertaining to benefit sharing, the current SA scientific community landscape regarding resources (human and infrastructural capacity) for biobanking activities and research as a means of analysing the strengths and weaknesses in the resources as well as opportunities for benefit sharing. This chapter corresponds with objective number 2 of the study which is, to explore what benefit sharing ought to be when biomaterial and data are transferred from biobanks in SA to HICs in international collaborative health research.

4.2 Unresolved challenges pertaining to benefit sharing

Monetary benefit sharing has been part of a longstanding debate within global research ethics and it has been observed that research participants expect some form of compensation for participating in research and this necessitates further studies to determine the most appropriate form of compensation. The challenge with embracing all forms of benefits, including monetary benefits, relates to striking an ethical balance of competing interests in the midst of an absence of structures to guide the process.[131] Some commentators are in favour of monetary benefit sharing on the basis that it constitutes equitable and fair benefit sharing while those against monetary benefits do so based on the reasoning that monetary benefits could result in some form of exploitation as it relates to the issue of participant samples being regarded as commodities.[133] Even among those who agree on monetary benefits for the participants, there seems to be a lack of consensus in terms of the acceptable remuneration amounts. In addition, others are more in favour of collective rather than individual benefit sharing. This version of benefit sharing assumes group ownership of all of the monetary benefits such as intellectual property.[133] It is clear that the divergent views on benefit sharing and ownership are somewhat confused and in light of this finding, an exploration of biomaterial ownership follows in the next chapter. Because of the different views, it is important for companies (funders of biobank research in this context) to be regulated in accessing biobank resources and equally important is the use of MTAs where appropriate mechanisms for benefit sharing are in place.[50] In SA, when the NMTA became publicly available in 2018, the country was brought a step closer to fulfilling this requirement.

The question of allocating benefits fairly and equitably relates to the domain of distributive justice. There is controversy, however with this concept because what is considered equitable and fair benefit sharing is unclear.[134] However, the guidance provided in chapter 2 section 2.2.2 in terms of the formulations to distribute burdens and benefits as referenced from the

Belmont report provides useful guidance in that regard. Moreover, based on a claim that international treaties relating to benefit sharing generally do not cover what is fair and equitable benefit sharing for inter-state and intra-state negotiations and agreements, this necessitates legal intervention as far as benefit sharing is concerned[135] and this is therefore part of the rationale of the proposed benefit sharing model. In order to formulate how the benefits of research ought to be distributed in SA, an analysis of the current scientific landscape pertaining to resources for biobank activities is required so as to assess strengths, weaknesses as well as opportunities for growth in that regard.

4.3 The current SA scientific community landscape regarding resources for biobanking activities and research.

Biobanks are generally established to support scientific research and have evolved over the past decades in response to the development in scientific research as well as the fields of personalized and precision medicine.[3] Due to the fact that biobanks are generally established to support scientific research, a description of the scientific community landscape is provided in this section as a representation of human and infrastructural resource capacity for biobanks. An understanding of the SA scientific community landscape in terms of resources is necessary prior to discussing what benefit sharing ought to be.

4.3.1 Human capacity for biobank activities and research in SA

There are a number of human biobanks in SA that range from small to large collections within university academic hospitals that are usually associated with pathology laboratories in the form of profit and non-profit based biobanks.[12] There is however little evidence in terms of compliance of these biobanks with quality standards and regulatory adherence. In practice, biobank operations personnel include management, transport personnel, administration staff for receiving of samples and data, bioinformatics scientists for database management and medical scientists involved in the Quality Management System (QMS) of the biobank as well as biobank research activities. The Health Professions Act No. 56 of 1974 regulates HCPs registered under the Act and this includes medical scientists.[136] Just over 600 medical scientists are currently registered with the HPCSA and eligible for conducting laboratory human health research as per the scope of practice of medical scientists.[137] There is a huge disparity with other medical laboratory personnel with more than 3000 registered medical technicians and close to 5000 medical technologists[137] who are not primarily employed to conduct health research.[138] The regulations for the medical technology profession, however

do allow medical technologists to conduct research.[139] Moreover, within the SA context, the challenge is that of a large population of about 56 million and the overburden of communicable and non-communicable diseases that require increased research.[12] The guidelines for the scope of the profession of medical scientists in SA, restrict research scientists that are not registered under the Act to conduct health research independently.[140] Therefore, benefit sharing agreements and models between SA biobanks and their collaborators should address this need through human capacity building of more medical scientists. This has the potential of addressing concerns of exploitation discussed in chapter 1, section 1.3.1.1.

4.3.2 Funding available for SA biobanks and infrastructural capacity

Key infrastructural aspects of biobanks include the availability of constant power and back-up power in the form of generators, reliable transport services, the availability of liquid nitrogen and dry ice, as well as the biobank location in terms of climate conditions.[12] Biobanking is an important research resource but requires expensive infrastructure with expenses usually covered by a multi-faceted approach as a result. Charging fees to those submitting samples to the biobank is common with fees for this service often barely sufficient to cover the costs required for sustainability of the biobank in terms of personnel and equipment.[141] This necessitates funding from extramural projects to cover all the expenses of the biobank and to sustain it. To address this cost barrier in storing samples for research, there are agencies that provide funding in that regard.

Some of the prominent funding organizations for scientific research in SA include, the National Research Foundation (NRF) and the Department of Science and Technology (DST). The NRF was established through an Act of Parliament, the NRF Act No.23 of 1998 with a mandate of supporting research through funding in the fields of natural and social sciences.[142] The NRF funding database, reveals a paucity of funding for biobank specific activities or biobank research. However, one of the NRF's strategic objectives is to establish and maintain research infrastructure and platforms in partnership with the DST.[143] In 2016, the DST identified biobank infrastructural need as one of the key domains requiring financial support. DST aimed to fund a national biobank that would support biomaterials and database through a network of partners and stakeholders.[144] The idea behind the envisaged national biobank is to partner with biobanks for the acquisition, banking and distribution of samples.

H3Africa, a consortium funded by the National Institutes of Health (NIH), Wellcome Trust and the African Academy of Sciences (AAS) through its funding platform, Alliance for Accelerating Excellence in Science in Africa (AESA),[145] has established 3 regional biobanks in Africa, namely in; West Africa, East Africa and South Africa and these biobanks work together to

share knowledge and resources across large Pan-African collaborations even outside of Human Heredity and Health in Africa (H3Africa). Such collaborations include engagements with Bridging Biobanking and Biomedical Research across Europe and Africa (B3Africa) through bioinformatics collaborations and QMS engagements with the African Society for Laboratory Medicine (ASLM).[146] The Biobank Cohort Network (BCNET), an agency of the World Health Organization (WHO), provides expertise resources to LMICs in the form of resources such as protocols through international collaborations with institutions in these countries.[147] The challenge of high cost biobank infrastructure and sustainability as well as limited funding for biobank activities necessitate development of a benefit sharing model that would recognize these challenges in order to address them.

4.4 Relevant aspects of benefit sharing models

An ideal benefit sharing model within the context of SA is one which would take into consideration the capacity of the collaborating biobank coupled with being cognisant of the ethico-legal issues in SA. It would also incorporate benefits for all stakeholders including the participating communities in the form of improved disease outcomes or any other related need. The H3Africa Ethics and Governance Framework for Best Practice in Genomic Research and Biobanking in Africa emphasizes the two aspects of benefit sharing, namely capacity building and consideration of ethico-legal aspects as requirements for benefit sharing agreements between African researchers and international collaborators as well as participating communities[130] however, it is silent on benefits relating to intellectual property rights. A similar approach is seen with benefit sharing models and frameworks of other organisations where some and not all of the elements of benefits that constitute an ideal for a SA setting are included. The Human Genome Organization (HUGO) Ethics Committee's Global biobank governance *Statement on Benefit Sharing* (2000) puts emphasis on aspects such as eventual prevention or treatment and affordable medical services for participating communities, community engagement and cultural or tribal group benefits.[148] This benefit sharing model is, however, more of a participating community oriented model and does not cover the participating biobank and researcher benefits in terms of capacity building and aspects of copyright and intellectual property rights. Although the United Nations Educational, Scientific and Cultural Organization's (UNESCO) *International Declaration on Human Genetic Data* (2003) incorporates participating community benefits in the form of provision of medical care and diagnostics as well as research capacity building, it does not mention copyright and intellectual property rights as a benefit.[149] OECD's *Principles and Guidelines for Access to Research Data from Public Funding* (2007) does mention protection of intellectual property

and adherence to the laws and regulations in the collaborating biobanks' jurisdiction, but however, omits the other elements of benefit sharing mentioned above.[88] Of note, none of the entities mentioned include payment for exchange of biomaterials and data as benefit sharing. Table 2 represents a comparison of the different aspects of the benefit sharing models of various entities.

Table 2: Comparison of the different aspects of the benefit sharing models of various entities.

Benefit sharing model features	**Entity**			
	H3Africa[130]	**HUGO[148]**	**UNESCO[149]**	**OECD[88]**
Covers research or biobank capacity building (human and infrastructural)	√	X	√	X
Return of research results to participating communities covered	√	X	X	X
Intellectual property rights and copyrights included	X	X	X	√
Provision of benefits for participating communities that include medical services	√	√	√	X

√ = yes; X= no

In light of the identified limited research capacity and issues of exploitation, benefit sharing should be a requirement where funding and biobank sample exchange are concerned. It is crucial to develop a practical and equitable benefit sharing model for biobank collaborations. To address the question of unfair co-authorship, and thereby ensuring shared and equitable authorship based on contribution, authorship rights based on the recommended criteria should be included in every signed contractual agreement. Lastly, parties involved in the collaboration should state explicitly, to the extent possible, sharing of royalties for perceived patents, in every signed contractual agreement.

The proposed benefit sharing model for SA biobanks with international collaborations is one with a holistic approach that would incorporate the following aspects: (1) capacity building for human and infrastructural resources; (2) shared and equitable intellectual property rights benefits in accordance with the law and regulations and (3) benefits for participating communities.

4.4.1 Capacity building for human and infrastructural resources

The low number of registered medical scientists presents a challenge in the form of limited laboratory health research capacity, which includes biobank human research capacity as a resource. It is for this reason that benefit sharing agreements in collaborations, particularly with international collaborators from HICs that provide research capital ought to consider capacity building of SA researchers in the form of training of more medical scientists to address this challenge. Moreover, SA biobanks are mainly non-profit and self-funded, therefore, funding of existing biobanks to sustain them can be through international collaborator development as a benefit in the agreement. However, this funding must be specific to building biobank capacity as well as sustainability of the biobank and must not include conditions like the transfer of biomaterials to the collaborator for finances received. Developing capacity ought to go a long way in decreasing dependence on HICs.

4.4.2 Shared and equitable intellectual property rights benefits in accordance with the law and regulations

In the context of biobanking, original literary work and published editions protected and recognized by chapter 1 of the Copyright Act No. 98 of 1978 include co-authorship of journal articles, which are a result of the collaborative research.[16] Africans are currently under-represented in collaborative publications and local authorship can be made a requirement for benefit sharing[150] when there's evidence of sound contributions based on authorship guidelines. Criteria for authorship are based on authors meeting all 3 stipulations as recommended by the International Committee of Medical Journal Editors (ICMJE).[151,152] The criteria is as follows:[152]

(1) "substantial contribution to the conception and design or acquisition or analysis and interpretation of data,

(2) drafting or revising of the article for important intellectual content; and

(3) final approval of the version that will be published" (Ogden 2007, pg. 1).

In addition, the authors should take responsibility for their contributions to all publications in line with appropriate criteria.[153]

Relevant patentable material include; discoveries, scientific theories, literary creations and the presentation of information according to section 25 of the Patents Act No. 57 of 1978.[17] The Act prohibits granting of a patent where there's exploitation or where immoral behaviour is expected. Section 28B of the Intellectual Property Laws Amendment Act No. 28 of 2013[18]

protects and recognizes indigenous knowledge which includes copyright and patent material as intellectual property not only from the individual point of view but from the context of indigenous communities who created the work or contributed substantially. If any commercial benefit is derived from the created work, the one who derives the benefit has to pay the creator royalties as provided for by section 28G and the amount is subject to the agreement between the user and the owner of the work or the representative of the owner according to section 28H.

SA biobanks and biobank researchers can safe-guard themselves against exploitation and ensure application of equity in intellectual rights through incorporation of a legally binding agreement for incorporation of intellectual property rights according to the provisions of the law, as advised in the NMTA Template.

4.4.3 Benefits for participating communities

A 3-year trend analysis (2014-2016) in SA shows that mortality rates associated with certain communicable diseases ranged from 18.2%-21.6% with non-communicable disease associated deaths, particularly cardiovascular diseases ranging from 17.4%-18.5% of all the deaths.[154] As part of the benefits of research, sponsors and researchers could provide ancillary care which is defined as care that is provided to study participants but that which is not required for scientific validity of the study and includes treating ailments unrelated to the aims of the study.[155] Such care would assist the State in its delivery of healthcare services and this could be construed as a benefit. The concept however is an object of contention and opponents of ancillary care hold that providing clinical care to research participants would drain limited resources based on a claim that nothing is owed to them, while proponents question this position and perceive that monitoring a research participant's disease without the willingness to treat them amounts to treating them merely as a "means to an end" (Rachels, 2003, pg. 130) of research.[156] Other benefits for the community include shared and equitable intellectual property rights benefits and continued engagement of the participating communities not only as a means of enhancing the research but also as a recognition of their human dignity. Neither ethical principles, nor laws and regulations alone ought to govern how research participants are treated but rather the two should complement each other to promote the greater good and overall wellbeing.

4.5 Conclusion

Funding agencies usually either only fund biobank research projects or a single biobank infrastructure for a stipulated period of time as opposed to funding of multiple biobanks. The challenge presented is that of long-term sustainability of biobanks. This can be addressed through an all-inclusive benefit sharing model translated into an agreement. An ideal benefit sharing model is one which incorporates benefit sharing for all stakeholders of biobank research activities, in the form of addressing capacity and infrastructural needs, shared equitable intellectual property benefits as well as participating community benefits. The concerns in benefit sharing in the context of cross- border transfers have not been adequately addressed in SA. Moreover, based on the ethico-regulatory analysis performed in the previous chapter, benefit sharing cannot include funding for transfer of biomaterials hence the need for an adequate benefit sharing model to address these concerns. A discussion on ownership of biomaterial is required as it has been associated with issues of benefit sharing discussed in this chapter. Accordingly, material ownership is discussed in the next chapter.

Chapter 5

Ethico-legal aspects and cases on ownership of human samples as they relate to sharing of the materials.

5.1 Introduction

Issues of biomaterial ownership particularly in collaborative international health research have been widely debated, however there is no consensus among commentators in terms of who owns the samples. Controversies in the ownership of biomaterials particularly arise when samples that were donated for altruistic purposes have the potential to be exploited for commercial purposes.[156] Some fear that promises of profits for donating research samples by participants could lead to a decline in altruistic donations and objectification of the human body as a result of commodification. The disquiet is further amplified when the objectification is perceived not only by self but others as well.[157] Opponents of the objectification argument are in favour of incentivizing donations out of fear that not doing so would hinder biotechnological developments.[158] They further justify their standpoint based on the notion that granting property rights to human research participants as in ownership rights would guard against unauthorized use of their samples with the property rights enabling the participants to share in the benefits of research participation through monetary and non-monetary means similar to researchers benefitting in the form of professional prestige as well as any patented product arising from the research.[158] In this chapter legal aspects of human sample ownership are briefly discussed, followed by pertinent case law that demonstrate court rulings in this regard. The chapter briefly responds to objective 3.

5.2 Pertinent legal aspects of human sample ownership

In the SA legal system, the National Material Transfer Agreement (NMTA) makes provision for sample ownership by the donor where it states explicitly that the sample(s) belong to the individual from whom they were collected (donor) while the institution that collects the sample(s) is the custodian of the sample(s), however the conditions under which biomaterials and associated data can be shared with funders of research is not provided for in any of the regulations. Safeguard for protection of participants are specified in both section 60 of the NHA and Regulations relating to the use of human biological materials (HBMs).[159] The latter pertains to health research, which includes biobank research and also includes prohibition of commercialization of human samples. Reimbursement is allowed only when it is required to cover the acquisition of such biomaterials. The NMTA, makes reference to the provider of

HBMs as the custodian. Custodianship calls on those engaged in research to recognize their ethical obligations in the interests of biomedical research.[160] By inference, sharing of samples with other parties would be enabled by ownership and not custodianship and therefore taking into account this perspective on human sample ownership, those who have collected the samples, namely the researchers or biobank personnel who are custodians of materials, are in no position to either share or exchange human samples for funding because they do not own the samples but rather their interests ought to be solely for protection and safeguard of the materials.

Conventional legal construct for ownership is conferred by property law which permits others to use their property as they see fit.[161] Property law deals with the rights and duties that relate to "things" (Balganesh 2011, pg. 1890).[162] Once ownership has been recognized, responsibilities and rights related to the property can be recognized.[161] The legal fraternity finds it difficult to treat human biological material as property and this has been demonstrated by specific case law, which is discussed below. It has long been established, as far back as the 1920s, that the law does not attach property rights to natural things.[163] Feldman articulates this notion appropriately, as follows (Feldman 2011, pg. 1378):[164]

"*Through the rambling pathways of property and intellectual property law, we are fast approaching the point at which just about anyone can have property rights in your cells, except you. In addition, with some alteration, anyone can have intellectual property rights in innovations related to the information contained therein, but you do not. I should be clear at the outset that I am talking about property and intellectual property rights to cells when they are no longer in your body… When a researcher is working with a sample of human blood or tissue, the researcher, or the lab, has a property right in those cells. Similarly, if the researcher isolates a protein or a segment of DNA from that sample, the researcher or the lab has property rights in the tangible isolated elements."*

According to Dressler, from the participants' point of view, however, ownership is rarely an issue and participants assume researchers and institutions will use the samples in their best interests and that of the society at large.[165]

Different countries deal with ownership of biomaterials collected for research in various ways.[166] Moreover, some countries use the terms 'ownership' while others use 'custodianship' with no clear distinction between the two. This is unlike in SA where the distinction between the two is made. In Zambia, a decision on ownership of biomaterials is made by the Minister

of health, while in Malawi, biomaterials remain property of the Ministry of Health and in countries like Botswana, Rwanda, Uganda, Ethiopia and Ghana, biomaterial custodianship is that of the institution that collected the biomaterials. Some countries like Nigeria and Cameroon are not specific about ownership but indicate that ownership has to be agreed upon by local researchers and collaborators. The same ethico-legal issues of ownership in LMIC seem to be apparent in HICs, for example, in the US, no State laws establish individual ownership rights of human samples that are used for research. Similar to SA, however, some States regulate more stringently on aspects of confidentiality of information and informed consent.[167] Although none of the states have declared an individual to have ownership of their samples, including DNA, four of the States have declared individuals to have exclusive ownership of their genetic material. However, this ownership is defined broadly as evidenced in specific court decisions, which will now be discussed.

5.3 Case law on ownership of human samples

In an advanced society which has judicial rules and the process of interpretation of the law by judges resulting in specific rulings, exceptions and anomalies occur where legislators have not made pertinent stipulations. Judges are therefore left to refer directly to moral value and justifications for judgement(s) made.[168] SA has currently created no precedent with regard to ownership of human samples therefore international cases are considered below.

5.3.1 Moore vs The Regents of the University of California of 1976

The widely documented case of *Moore vs The Regents of the University of California* of 1976 deals with, in the main:[169]

> (1) Consent where the plaintiff alleged that the defendants used his cells in a potentially lucrative medical research without disclosure of economic interests and his consent; and
>
> (2) Ownership of the patented cell lines.

The benefit derived from the research was the profits generated from the patent, the value of the patent itself and financial benefits for the treating physician. The court recognized that a reasonable participant would want to be informed whether a physician has a financial interest that might affect his or her professional judgement. At the time of the case, California law did not give physicians the unlimited discretion to decide on what to disclose and based on this,

the Court found the treating physician to be in breach of his fiduciary duty in terms of a lack of informed consent.

Court rulings mostly suggest that participants and other human research participants do not maintain ownership of their own tissue.[170] The dilemma, however, on the issue of ownership in this specific legal system was that there was no provision for ownership of human samples and therefore it could not be said with certainty whether or not the plaintiff was entitled to compensation of his cells. Further adding to the complexity, was that the patented cell lines and their derivatives could not be regarded as Moore's property by the court.

5.3.2 Catalona vs Washington University

In the case of *Catalona vs Washington University,* Dr Catalona started collecting prostate cancer tissue samples from his participants with their informed consent since the early 1980s. This resulted in a collection of tens of thousands of tissue samples.[171] This research led to the development of the Prostate Specific Antigen (PSA) test for the diagnosis of prostate cancer. With time, Dr Catalona requested that a restricted number of samples be sent to a biotechnology company for evaluation of the test's effectiveness. His employer, Washington University resisted this request, after realizing the potential for profit from those samples. In 2003, Dr Catalona then moved to Northwestern University, notified his participants of this and gave them a choice of either continuing their care at Washington University or moving with him to Northwestern University for care. In addition, research participants could choose whether to transfer their samples from Washington University to Northwestern University. Washington University then filed a lawsuit against Dr Catalona, alleging ownership of the research participants' samples and also requesting a court order preventing him from "interfering" with the research participants and the samples they had provided because they perceived the samples to be worth more than one million dollars at the time. The research participants challenged this, saying that the consent documents which they signed granted them ownership rights of their samples-their literal "flesh and blood." Washington University, however, argued that it could use the samples as it wished, in its "sole discretion." The court ruling stated that the consent documents were immaterial and declared that Washington University owned the samples, a decision which allowed for ethically questionable research on the participants' tissue samples including selling them for profit. On appeal, the Judge nevertheless found that the university did not have to abide by its promise of withdrawal from the research at any time. The reasoning for this was that the participants gave their samples to the university as a "gift" and that the university need not return the samples.

5.3.3 Greenberg v Miami children's hospital

The parties involved in this case were engaged in detecting and finding a cure for Canavan disease, a rare genetic disorder.[172] In this case, Greenberg and others (plaintiffs) were parents of the children that provided blood and tissue samples to Dr Matalon who was affiliated with Miami Children's Hospital (MCH) and Miami Children's Hospital Research Institute (MCHRI) (defendants). The samples were provided for research on Canavan disease and this led to a breakthrough where a gene causing the disease was isolated in 1993. This discovery led to registering of a patent where Dr Matalon was listed as the inventor in 1997 and this resulted in acquisition of the defendant to restrict any disease related activity including testing, research involving the gene and its mutations, as well as gene therapy. The plaintiffs alleged breach of informed consent where they claimed that they were neither informed of the defendants' intentions to seek a patent nor intentions to commercialise the results of research and restrict Canavan disease testing. The plaintiffs alleged unjust enrichment (royalties in excess of $75,000 and a grant awarded to Dr Matalon for further research on the gene patent), breach of fiduciary duty, conversion, fraudulent concealment and misuse of trade secrets against Miami children's hospital. On conversion, the Court ruled that the samples and genetic information was voluntarily donated to the defendants and therefore the plaintiffs did not have property interest in their donated samples.[172]

An extensive search of the literature has revealed little information on evidence monitoring use of the material by the transferring institutions. This, coupled with the controversies in human sample ownership as well as the fact that SA has created no precedent with respect to human sample ownership, ethico-legal norms and standards for transferring of biomaterial and data in international collaborative health research are requisite and are discussed in the section that follows.

5.4 Ethico-legal norms and standards for transferring biomaterials and data in international collaborative health research as it relates to custodianship of materials.

The SA legal system is made up of (1) legislation (statutes or laws or Acts), (2) precedent (courts' decisions) and (3) common law (Roman-Dutch law principles).[173] Overarching the legal framework is the Constitution, which every law must be measured against. The Constitution lays out judicial authority as vested in the courts. SA statutory laws are enacted through a process of engagement and discussions with members of parliament and the

relevant committees.[174] Common law is applicable when a particular matter is not governed by legislation, and is precedent law in that judgements serve as setting precedents with regard to determining matters. While the NMTA confers ownership and custodianship to research participants and institutions, respectively, there is no legislation or legal precedent that determines the legal status or propriety rights regarding biomaterials and data that are transferred as a condition for funding or whether such sharing and resultant custodianship are legitimate.

Complexities around ownership and custodianship of samples, particularly in the context of international collaborations often pose challenges of confusing contracts and exclusive ownership and custodianship claims by outside funders even though the samples were collected by local providing institutes. Difficulties with settling disputes further add to the challenges and complexities.[175] Norms and standards for biomaterial and data custodianship must consider participant's rights to protection of human dignity, and prevention of unintended use of samples and data, as well as consideration of participant privacy and confidentiality in accordance with SA laws. Funding being contingent to transfer of biomaterials is a clear affront to the dignity of the participant.

The National Department of Health's (DOHs) ethics guidelines do mandate that conditions under which samples and data can be shared with other researchers have to be stipulated, however the guidelines do not provide for these conditions and leave discretion to the parties involved in the agreement. This has the potential of lack of standardization and inconsistency among different biobanks, hence there is a need for incorporation of such conditions when developing national norms and standards.

The conditions for receiving of biomaterials and data by funders (recipient institution) that ought to be fulfilled, consolidated in the SA legal framework and incorporated in agreements to ensure compliance will need to factor in the following: It is the responsibility of the funder to uphold the initial consent granted by the participant as a means of avoiding dignitary and social harm to the participant through unintended use, other than that which has been consented for. Consent is explained in the NMTA as the donor (research participant) agreeing to participate after being informed about the process and determining how their materials will be used subject to approval by a HREC.[44]

1. The research conducted by the funder should be to the benefit of society and local communities at the providing sites and this benefit must be substantiated by clear aims and objectives for the use of materials to be transferred. These should be in line with particular public health objectives of RSA.

2. It is the responsibility of the funder to demonstrate that security measures are in place to protect the samples and data against unauthorized access.
3. Benefit sharing provisions must be made to include acknowledgement in publications and royalties for patentable inventions until termination of the agreement.
4. As the custodians, the local institutions that transfer the materials ought to honour the responsibilities for safe-guarding of the materials.

The following restrictions on the transfer of materials should be considered: Funding agreements are prohibited from including biomaterials and data transfer from the local research site or biobank to the sponsor, as a condition of funding to the local site.

1. The funder is prohibited from using the materials for commercialization.
2. The funder is prohibited from transferring the materials to another party, unless such transfer is part of the agreement. The other party should also be a part of the agreement in compliance with the conditions and restrictions proposed herein.

5.5 Conclusion

Some countries are not prescriptive on matters of biomaterial ownership while others confer ownership to researchers and institutions rather than the participants. In legal terms, HBMs are generally not regarded as an individual's property. This has been reflected in a number of legal cases abroad with implications for commercialization of materials, resulting in exploitation of participants in some instances. In all of the cases discussed in this chapter, sample ownership is not granted to those from whom samples have been collected and this is inconsistent with the SA context of human sample ownership whereby those that have donated the samples are referred to as the owners of the samples according to the NMTA. Controversies in the courts' decisions and lack of clarifying legislation relating to specific aspects of human biological material ownership, mandates the formulation of adequate ethico-legal frameworks in this regard.

Chapter 6

Recommendations and conclusion.

6.1 Introduction

This Research Report considered the practice of access and transfer of biomaterials and data in international collaborative health research, in exchange for funding. The objectives of the study were as follows; (1) to critically discuss and normatively evaluate the major ethical issues related to biomaterial and data sharing where biobank research funding in international collaborative research is concerned, (2) to explore what benefit sharing ought to be when biomaterial and data are transferred from biobanks in SA to HICs in international collaborative health research, (3) to critically discuss and evaluate the current SA laws, regulations and guidelines specific to biomaterial and data sharing with particular focus on exchange of biomaterials for funding in international collaborative research. Each of the study objectives have been achieved.

Objective 1 was achieved through a demonstration that the sharing of biobank samples and data particularly in the context of cross border transfers where funding is considered raises ethico-legal concerns as a result of different values, beliefs and notions of commodification of human biomaterials and also as a result of the inadequacies in national and international regulations in that regard. The wrongness of commodification as a result of transferring biomaterials and associated data in exchange for funding objectifies humans through exploitation and exposure to unethical practices.

Objective 2 was achieved based on the finding that benefit sharing in the context of cross-border transfers have not been adequately addressed in SA. However, benefit sharing for the funder cannot include transfer of biomaterials and data in exchange for funding because of the ethico-legal challenges highlighted in this Research Report.

Objective 3 was achieved by showing that the controversies in the courts' decisions and lack of clarifying legislation relating to specific aspects of human biological material ownership, particularly as it pertains to biomaterial and data sharing in international collaborative health research mandate the formulation of ethico-legal frameworks in that regard.

In light of the findings of the study, recommendations are offered in the next section.

6.2 Recommendations

The recommendations of the study are in line with the initial argument that is based on the Kantian approach that persons should never be used as a "means to an end" (Rachels, 2003, pg. 130) but rather as "ends in themselves" (Rachels, 2003, pg. 132.). Based on this approach, the recommendations are rooted in the principle of respect for moral dignity for everyone and that biobank sample participants should never be used as a means for fulfilling others' interests as in being used as a means to obtain funding by biobanks or as a means to have access to biobank samples and data by funders.

The recommendations are as follows:

1. There ought to be amendments in the current ethico-regulatory structure to provide for conditions under which biomaterials and data can be shared with funders in order to protect participants' rights. This includes stipulations prohibiting sharing of biomaterials and data as a condition of funding, coupled with a comprehensive regulatory framework that covers protections of the material when it is in the hands of the recipient institution, which is the funder in the context of this research.
2. A benefit sharing model ought to be one which incorporates benefit sharing for all stakeholders of biobank research activities in the form of addressing capacity and infrastructural needs, shared equitable intellectual property benefits as well as participating community benefits while avoiding commodification of biobank materials.
3. Based on the inadequacies in the current export regulations for biobank cross border transfer, the study recommends an inclusion of biobank sample export in the current regulations to cover the wide array of biobank samples as well as a clear distinction between pathology samples and those that are for therapeutic use.
4. A recommendation to address the ethico-legal framework that provides for the conditions and restrictions for sharing of biomaterials and data with the funder proposed in this study would either be the development of a separate MTA for collaborations where funding is concerned or an amendment of the current National MTA to include these aspects.
5. A recommendation for future studies aimed at monitoring the fate of exported samples in light of little information in that regard.

6.3 Conclusion

There is a need for the development of a national ethico-legal framework that addresses sharing of biomaterials and data where funding is concerned as a means of protecting against biobank sample exploitation as well as exploitation of the researchers themselves. While

international guidelines provide a platform that allows for collaborators from different legal systems to work together, legally binding frameworks are useful and hence inadequacies in national regulations must be addressed. It is unethical to share biomaterials and data in exchange for funding because this has the potential for exploitation of the participants due to a lack of respect for their dignity and rights. In addition, it results in inequitable benefit sharing for all stakeholders as well as an exploitation of the inadequacies of the current SA ethico-legal framework with regard to the transfer of materials during international collaborative health research. The regulations would also need to address conditions under which biomaterials and data can be shared with funders as well as restrictions prohibiting such sharing as a condition for funding.

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