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An ethico-legal analysis of broad consent for biobank research in South Africa: Towards an enabling framework

Mantombi Rebecca Maseme

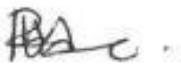
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April 2024

Declaration

I, Mantombi Rebecca Maseme, declare that this Thesis is my own, unaided work. It is being submitted for the Degree of Doctor of Philosophy in Bioethics and Health Law at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



Signature _____

Signed on the ___26th____ day of __April___ 2024_____in _Johannesburg___

Dedication

I dedicate this thesis to my parents, Mbali Wilson Maseme and Kelebogile Martha Maseme for your support, endless love and for the countless sacrifices you have made in ensuring that all of your children have opportunities for education.

Acknowledgements

My sincere gratitude goes to:

God for the opportunity to pursue this qualification and the grace to see it through;

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Abstract

Biobanks preserve collections of human biological material and data for the benefit of medical research. Using and transferring human biological data and materials both inside and outside of South Africa is often a requirement of biobank research. Broad consent is allowed by the South African National Department of Health Ethics Guidelines but appears to be prohibited by section 13(1) of the Protection of Personal Information Act 4 of 2013. Additionally, the Act mandates that all personal data (including biobank sample data) be collected for legitimate, definite, and clearly stated purposes. There is room for several interpretations of the Act because of this discord between the two instruments. Given the connection between the transfer of samples and data, the long-term nature of biobanking, which makes it impractical to provide too much or adequate information because it is simply not available at the time of sample collection, and the various ways that the Protection of Personal Information Act 4 of 2013 have been interpreted, I aim to respond to the following question: How should South Africa's current regulatory framework appropriately permit broad consent use for biobank research where the transfer of samples and their associated data are contemplated?

The research question is addressed by applying ethical principles and theories, as well as analysing and evaluating relevant ethico-legal frameworks and literature. The study involves no research participants and no collection or analysis of any new data. Arguments for and against using broad consent for biobank research are discussed by demonstrating the potential for biobank research to do a great deal of good for humanity; the ambiguity in the current regulatory framework regarding whether broad consent is permissible for personal information/data; and the ethical justifiability of

broad consent. In summary, the proposed regulatory framework amendments are those that would be required to allow for ethically justifiable biobank research broad consent use. These include removing regulatory ambiguity regarding broad consent use, ensuring adequate safeguards for research participants by specifying rules for data access and personal information processing, and incorporating consent form information requirements into the national Consent Template as specified in the National Department of Health Ethics Guidelines.

Acronyms

ABGC	American Board of Genetic Counselling
ASSAF	Academy of Science of South Africa
ASU	Arizona State University
BAC	Blood Alcohol Consumption
BECs	Biobank Ethics Committees
BIMS	Biobank Information Management System
CAB	Community Advisory Board
CAGC	Canadian Association of Genetic Counsellors
CAI	Central American Integration
CDC	Centres for Disease Control and Prevention
CIOMS	Council for International Organization of Medical Sciences
COC	Code of Conduct
COFEPRIS	*Comisión Federal para la Protección de Riesgos Sanitarios*
CT	Computed Tomography
DNA	Deoxyribonucleic acid
DTA	Data Transfer Agreement
DNOSP	Draft National Open Science Policy

DSI	Department of Science and Innovation
EU	European Union
EUA	European University Association
FAIR	Findable Accessible Interoperable Reusable
FDA	Food and Drug Administration
GDPR	General Data Protection Regulation
HBMs	Human Biological Materials
HICs	High Income Countries
HREC	Human Research Ethics Committee
ID	Identification
IFs	Incidental Findings
IT	Information Technology
IP	Intellectual Property
IR	Information Regulator
IRB	Institutional Review Board
ISO	International Organization for Standardization
MRI	Magnetic Resonance Imaging
MTA	Material Transfer Agreement
NHREC	National Health Research Ethics Council
NCB	National Commission of Bioethics

NCI	National Cancer Institute
NDoH	National Department of Health
NHA	National Health Act 61 of 2003
NHS	National Health Service
NIH	National Institutes of Health
PAIA	Promotion of Access to Information Act No. 2 of 2000
PDCA	Plan-Do-Check-Act
PIPEDA	Personal Information Protection and Electronic Documents S.C. 2000, c. 5 (Canadian federal law)
POPIA	Protection of Personal Information Act No. 4 of 2013
QMS	Quality Management System
RSA	Republic of South Africa
SA	South Africa
SNPs	Single Nucleotide Polymorphisms
SOPs	Standard Operating Procedures
SU	Stellenbosch University
TCPS	Tri-Council Policy Statement
UIHC	University of Iowa Hospitals and Clinics
UK EAC	United Kingdom Ethics Advisory Committee

UNESCO	United Nations Educational, Scientific and Cultural Organization
UNC	University of North Carolina
UNESCO ROS	Recommendation on Open Science
US	United States
USPHS	United States Public Health Service
US DHHS	United States Department of Health and Human Services
WHO	World Health Organization
WMA	World Medical Association

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Chapter 1

Introduction

1.1 Introduction

According to the South African National Department of Health's (NDoH), Ethics in Health Research: Principles, Processes, and Structures (hereinafter NDoH 2015), broad consent is an informed consent model granted for future research use of human samples, subject to Human Research Ethics Committee (HREC) oversight. The distinction between broad and narrow (specific) consent is that the latter only permits single use of samples with no option for sample storage and no sample or data sharing (NDoH 2015). Although broad consent is less specific for each use, it is more restrictive than blanket consent, which is unrestricted (Grady et al. 2015). Due to the long-term nature of biobanking, it is impossible to provide too much or sufficient information because it is simply not available at the time of sample collection.

As a result, broad consent has been suggested as a suitable consent model for biobank research (Mikkelsen et al. 2019). In the current study, biobank research entails health research using human samples (biological materials/biomaterials) of any kind and their associated data previously stored in a biobank (Annaratone et al. 2021; WMA 2016). Following literature review and the challenges associated with different definitions of biobank research, I use this as a working definition. The analysis in this study is limited to biobanks, which typically store samples for research purposes, and does not include tissue banks, which store human samples for therapeutic purposes

under the *Regulations Relating To Tissue Banks of the National Health Act* (No. 61 of 2003). A biobank, also known as a repository, is a system for collecting and distributing human biological material for research purposes (NDoH 2015).

The main point of contention in the debate over the reliability of broad consent is the concept of providing adequate information to research participants, with an emphasis on "relevant information" rather than "more information" (Steinsbekk et al. 2013:899). In light of the ethical concerns and debates surrounding broad consent, a discussion of the risks specific to biobank research is provided, along with a discussion of risk-benefit ratio assessment in health research. Broad consent is frequently justified by the potential benefits of future research, provided that adequate safeguards for the privacy and confidentiality of those who donate the samples (donors) are in place (Sheehan 2011). Healthcare professionals have a legal and ethical obligation to protect their patients' personal information. Patients, in turn, have the right to autonomy, privacy, and confidentiality, as well as the ability to control the use of their personal information (WMA 2016). Biobanks, in turn, must safeguard not only collections of human biological material but also the data associated with them. As a result, the discussion of the protection of sample associated data or personal information is relevant.

The Protection of Personal Information Act No. 4 of 2013 (POPIA) came into effect in July 2020 and provides for personal information protection, prompting the research community to plan ahead of time for its implementation. Institutions were given a one-year grace period before POPIA came into effect in July 2021, and compliance with the Act has been a legal requirement since then. The impact of POPIA on the health research sector, as well as the lack of specific rules for personal information processing for research purposes, is a major challenge in its implementation,

particularly in the context of biobank research. This is because the Act is a broad framework that governs the processing of all types of personal information (Staunton et al. 2019). This is a challenge for research in South Africa (SA) because none of the regulatory instruments address this issue, leaving room for the processing of personal information that does not correspond to consent granted.

"Processing" is defined by POPIA as any activity concerning personal information that includes the collection, receipt, storage, updating, retrieval, distribution, or degradation of personal information. Personal information, according to Section 1 of POPIA, is information pertaining to an identified, active, natural person who is still alive, and, if appropriate, an identifiable, active, legal individual. As a result, POPIA does not apply to de-identified or deceased individuals' personal information. Demographic information, medical history, and biometric information are examples of personal information covered by the POPIA definition. POPIA defines "biometrics" as a method of identifying people using their physical, physiological, or behavioural characteristics, such as voice recognition, blood typing, fingerprinting, deoxyribonucleic acid (DNA) analysis and retinal scanning. Personal information in the context of biobank and health research includes research findings or results of analysis of other sample types, not just DNA. Although "medical history" is included in POPIA's definition, it is not the same as research findings. This is because the former is concerned with patient treatment or healthcare, whereas the latter is concerned with the processing of biomaterials in order to respond to a specific research question.

To protect participants' autonomy and personal information, as well as to address the main concern about the legitimacy of broad consent in terms of providing adequate, relevant information, a discussion on the criteria for valid consent in the context of future research use of samples and associated data is required. As a result, this topic

is covered in Chapter 4. Personal information protection is discussed in relation to the concept of open science, which is defined by The United Nations Educational, Scientific, and Cultural Organization Recommendation on Open Science (UNESCO ROS 2021) as a construct aimed at facilitating access to scientific knowledge, available, and reusable for all as a means of increasing scientific information sharing and collaborations for societal and scientific benefits (UNESCO ROS 2021). It is believed that open data sharing through open science enables technological advances through open data access for any purpose without restrictions (Ramachandran et al. 2021).

Given that open science promotes unrestricted data access, this concept is related to personal information protection, regulated by POPIA in SA, in that POPIA ensures lawful processing, thereby avoiding misuse of such information, such as processing that does not align with consent granted. As previously stated, personal information in the context of biobank research relates to sample associated data, which necessitates seeking consent (e.g. broad consent) as a condition for processing. As a result, before discussing broad consent ethical concerns and debates, this chapter discusses open science as it relates to biobank research and consent; data stewardship; and researcher incentives. Given that research involving human participants (including biobank research) is regulated, determining whether the South African regulatory framework allows for broad consent use for biobank research is an important consideration. As a result, the following section provides an overview in this regard and emphasizes the importance of the current study.

1.2 Why is the study relevant?

The NDoH Ethics Guidelines do not prohibit the use of broad consent, whereas section 13(1) of POPIA appears to prohibit its use. Additionally, the latter stipulates that the reason for collecting personal information must be "specific, explicitly defined, and lawful." Due to the notion that an individual's samples and the associated data, which equates to personal information, are linked, there is room for differing interpretations of the Act. Staunton et al. (2019) argue that POPIA allows for broad consent use for personal information. They maintain that this is because a purposive interpretation of POPIA would allow the processing of personal information for the purpose of research when broad consent is used, despite the fact that the Act does not explicitly address the use of broad consent. Staunton et al. (2019) go on to argue that under POPIA, privacy is not absolute, but rather subject to limitations designed to protect the interests and rights of others. With regards to the purposive interpretation of section 13(1), they further point out that according to section 2, the purpose of POPIA is to protect personal information in order to uphold the constitutional right to privacy. Moreover, that it is it is plausible to argue that the public interest of promoting genomic research in SA is significant, and that any research study that requires a specific consent model would be detrimental to that interest. My contention is that the law should be clear in that regard rather than being subject to various interpretations specifically when it is intended for medical scientists/researchers who do not necessarily have legal training. Hence the overarching intention of the current study. I elaborate on the rationale of the study further in section 1.6. On recommendations of what should be done to ensure that broad consent is not abused, Staunton et al. (2019) refer researchers to the various instruments that regulate biobank research in SA and

these include the *National Health Act (No. 61 of 2003)* and its regulations as well as the NDoH Ethics Guidelines. All these are analysed in chapter 3 of the current study. Contrary to Staunton et al.'s argument, Thaldar and Townsend (2020) contend that there is nothing in the entire context of POPIA that implies that section 13(1) can refer to anything other than a specific research study. According to Thaldar and Townsend (2020), a purposive interpretation of section 13(1) of POPIA undermines the meaning of the words used in that section ("specific, explicitly defined purpose") and maintain that the South African regulatory framework does not allow for the use of biobank research broad consent. In line with my view that POPIA does not allow broad consent, a study panel (a group of experts) on a consensus study on ethical, legal and social implications (ELSI) of human genetics and genomics in SA also acknowledges that there is disagreement over how POPIA affects broad consent, and that if the Information Regulator provides clarification, this could change (Academy of Science of South Africa (ASSAf) 2018). The panel also notes that since the POPIA mandates that individuals be provided with specific information about how their personal information is used, that specific consent most closely complies with the Act's requirements. In addressing the matter of a purposive interpretation of POPIA's section 13(1), Swales (2022) states that section 13 of POPIA is very clear because it deals with the collection of personal information and makes it clear that such information must be collected for a specific and explicitly defined purpose. This understanding of the background and purpose of POPIA, along with an awareness of the mischief it seeks to address, help to clarify section 13. Another clear definition of consent is that it must be specific and voluntary according to this section. Therefore, specific consent is the unavoidable conclusion that one must reach based on a plain reading of sections 13 and 27(1)(a) along with the definition of consent and the

previously mentioned purposive interpretation tools (protection of personal information to protect privacy and in the context of further usage of personal information). Furthermore, according to Swales (2022), one cannot say that broad consent will always be prohibited, especially if one is depending on the NDoH Ethics Guidelines' provisions. Therefore, it is necessary to examine the nature of the consent in order to ascertain whether, despite the fact that it is typically described as broad in nature, an initial consent was made on a specific and well-defined purpose. In closing, Swales (2022) poses the following question: Does POPIA need to adhere to the NDoH Ethics Guidelines? In a nutshell, no. It is implausible to argue that POPIA is subject to NDoH Ethics Guidelines. POPIA governs personal information, and while it is not more powerful than the NHA, it also does not have the same authority as published guidelines issued in compliance with the NHA. Every act is independent of the others, and adherence to one does not always imply adherence to the others. Though they are separate, they should be read together. There is no legal justification for POPIA to follow the NDoH Ethics Guidelines. POPIA presents novel dynamics that research teams should take into account.

POPIA is referred to as "the disruptor" by Thaldar et al. (2021) due to its alleged potential to disrupt health research due to its restriction on broad consent. They propose a sector-wide exemption from specific consent for all health research projects to allow for broad or tiered consent. Given the future-oriented nature of biobanking, an exemption from specific consent for biobank research would benefit this type of research. An exception, immunity or freedom from liability, or other requirements are examples of such exemptions (Cornell Law School n.d.). For a variety of reasons, a sector-wide exemption from specific consent for all health research projects as proposed by Thaldar and Townsend (2021) from specific consent may not be a rational

approach. For starters, research exceptions already exist in the Act, and a Code of Conduct for Research is under development by the Academy of Science of South Africa (ASSAF). Second, management of a sector-wide exemption from specific consent may weaken data subject protections in the sense that blanket application of broad consent for research that has specific aims and methods is unnecessary, as this may result in data subjects not being provided with the relevant information required for autonomous decision-making. Third, if a sector is exempt from the Act, how will it self-regulate, and how will this self-regulation be standardised? Finally, how would the application process for exemption be regulated?

Based on the notion that the South African regulatory framework, specifically POPIA, does not allow biobank research broad consent use, as demonstrated in the preceding discussion, the current study, which seeks to develop a more enabling framework for broad consent through an ethico-legal analysis, is relevant. Moreover, based on the divergent interpretations of section 13(1) of POPIA, the relevance of the study is based on the notion that the current regulatory framework, specifically POPIA, is ambiguous and unclear about whether broad consent is permissible in terms of data/personal information use. This aspect is discussed in detail in chapter 3. The following section contextualizes biobank research in terms of its scope and implications.

1.3 Scope of biobank research

Population-based and disease-specific biobanks have been identified as types of biobanks (Budimir et al. 2011). In this study, I cover discussions on both categories of biobanks. The purpose of population biobanks is to aid research concerning the effects of environmental factors on genetic susceptibility to the development of specific diseases (Coppola et al. 2019). Thus, genomic or genetic research is only a subset of

biobank research and does not encompass all forms of biobank research, despite what appears to be a common assumption in the literature regarding biobank research. Disease-oriented (specific) biobanks, on the other hand, are established to support human disease research in order to identify potential therapeutic strategies (Coppola et al. 2019). Human health biobanks' research scope includes genomics, cancer, and drug research (Doucet et al. 2017). More than half of biobanks share samples and data as part of research collaborations (Kiehntopf and Krawczak 2011). As previously stated, open science promotes unrestricted data access for any purpose. This concept pertains to the protection of personal information in terms of data associated with samples in the context of biobank research. In the next section, open science and biobank research are discussed in terms of three factors: 1) biobank consent; 2) data stewardship; and 3) researcher incentives as a means of promoting open science.

1.4 Open science and biobank research

The South African Department of Science and Innovation (DSI) developed a Draft National Open Science Policy (DNOSP) in January 2022 in response to the global shift towards open science. The policy aims to promote socioeconomic development for current and future generations by expanding the benefits of science (DNOSP 2022). Chapter 3 examines the DNOSP. A major ethical concern with data sharing is when consent forms do not explicitly state that participant data will be shared and the data is then shared (Lochman 2021). This violates data subjects' autonomy because they may not have agreed to participate if they were aware that their data would be shared. On the other hand, there is increasing pressure on researchers to commercialize their research, share data through collaborations, and disseminate knowledge quickly in order to encourage scientific developments and maximize

research impact (Harmon et al. 2012). Open science collaborations that involve the commercialization of research have received strong support from research funders (Harmon et al. 2012). Given that the main ethical concern with open data sharing is when it is not specified on consent forms, the following section discusses open science and biobank consent.

1.4.1 Open science and biobank consent

Consent that is compatible with open science is essential for data access, sharing, and use (Ali-Khan et al. 2018). Similarly, managing the sharing of old data sets collected using consent forms that did not anticipate open science sharing is a major concern (Ali-Khan et al. 2018). The disadvantage of open science in terms of providing information for usage of participants' data for future research during the consent process is that researchers cannot be aware of the full extent of future research use of participant data at the time of participant recruitment, particularly in the context of biobanking (Allen et al. 2013). Joly et al. (2015) argue in favor of open science for biobank broad consent, claiming that it relieves biobanks of the administrative burden of constantly re-contacting participants. In Canada, between 2013 and 2014, Joly et al. (2015) performed a survey of the public's opinions on open science in relation to biobanking. The majority of respondents to the survey stated that they would be open to taking part in a project where their data and samples would be distributed to a global audience (without their names or other personally identifying information attached) (54%, n = 61). Of the 48 respondents who selected the one-time general consent option, 67% (n = 32) selected the option to share their data and samples overseas. Although that subgroup shows signs of interest in widespread sharing methods, it only accounts for 28% of the cohort as a whole and does not imply that the public is in

general agreement on all facets of open science. Given that it is used to define consent for future sample sharing, the term "general consent" in this context appears to indicate broad consent.

Various open science models have been developed. The Montreal Neurological Institute-C-Big Hospital's repository, in particular, was designed with an opt-in system for principal investigators (PIs) to prevent the institute from forcibly mandating data sharing as a way of respecting autonomy (Das et al. 2021). Due to the notion that open science is still in the early stages of determining how to regulate large amounts of personal data, it is unclear how participants' rights should be aligned with informed consent without imposing an undue burden on researchers (Sklar and Crescioni 2019). Informing a data subject about third-party data use entails not only knowing how the data will be used, but also knowing the nature of the data shared (Wolf 2019).

To ensure that the benefits of participating in open science outweigh the risks, stewardship is required (Beauvais et al. 2021). Given that open science promotes data access for any purpose without restrictions, the risks in the context of biobank research would be those related to misuse or inappropriate access and use of sample associated data that does not align with participant consent. If the consent form did not indicate secondary use of data, data cannot be shared with third parties for any reason (Birch 2016). Similarly, data stewardship is required to prevent data sharing that is not in accordance with participant consent.

1.4.2 Open science and data stewardship

Data stewardship is required for scientific research integrity as well as compliance with legal requirements (Jansen et al. 2019). As a result, data stewardship models are

proposed as a means of encouraging responsible and equitable use of health (or disease) data (Bernier 2020). Global data sharing poses significant challenges for the responsible stewardship of large and complex datasets. Accountability, data management, and oversight are all part of this (Rubinstein et al. 2020). For data stewardship, UNESCO ROS (2021) recommends Findable, Accessible, Interoperable, and Reusable (FAIR) principles. These principles were developed in 2014 as fundamental guidelines for managing research data in the life sciences (Boeckhout et al. 2018). FAIR data stewardship must involve the research community, research teams, and individual researchers in order to lead to better science and data in the life sciences (Boeckhout et al. 2018). The goal of a data steward is to bear a certain level of trust (fiduciary) responsibility for the data (Rosenbaum 2010). The ability to demonstrate mechanisms for responsible data acquisition, use, and storage is an important consideration when laws are evolving (Rosenbaum 2010).

Stewardship (steward) and custodianship (custodian) are used interchangeably (O'Brien 2009). The South African Material Transfer Agreement (SA MTA) defines custodianship as an entity or person entrusted by the donor with the protection and safeguarding of materials (samples and associated data) in accordance with the *NHA Material Transfer Agreement of Human Biological Materials* (SA MTA herein after). According to the SA MTA, the provider is the custodian of the materials, while the material donor owns the materials until they are destroyed (SA MTA 2018). Commercialization of African sample-associated data has previously occurred. For instance, in the Sanger case, Stellenbosch University researchers (SU) entered into a legally binding collaboration with the Sanger Institute in the United States (US) to transfer African samples to Sanger (Moodley and Kleinsmidt 2020). Sanger allegedly then entered into an agreement with Thermo Fisher Scientific to create gene chips

based on genomic data from these samples (Moodley and Kleinsmidt 2020). Gene chips (microarrays), are microscopic glass slides with DNA from different genes which cost less than whole genome sequencing and are used for quick genetic testing (Moodley and Kleinsmidt 2020). According to reports, SU researchers did not agree to such commercialization in the MTA, and their research participants did not consent to the commercialization of their data (Moodley and Kleinsmidt 2020). Peng et al. (2018) propose a Plan-Do-Check-Act (PDCA) model for efficiently overseeing data stewardship efforts for scientific research. In summary, their approach is to define integrated requirements (plan/define), create guidelines and procedures (do), assess the current maturity of practices and processes (assess/check), and take steps to institutionalize or improve procedures and processes for meeting the requirements (improve/act) based on this model (Peng et al. 2018). The model's "check" feature allows for the evaluation of results, such as the implementation of procedures and processes, using evaluation models based on best practices (Peng et al. 2018). PDCA is a quality improvement concept first introduced by Shewhartz (1931) and later reintroduced by Deming (1986). The concept emphasizes the importance of top-level management involvement and consistency of purpose in quality improvement (Fonseca 2015).

Some of the barriers to data sharing identified include privacy and proprietary barriers, differences in the nature of research and data handling practices, and incentive structures that are counter-productive to open science (Committee on Toward an Open Science Enterprise; Board on Research Data and Information; Policy and Global Affairs; National Academies of Sciences, Engineering, and Medicine 2018).

1.4.3 Researcher incentives as a way of promoting open science

One of the challenges that European Union (EU) member state universities face in transitioning to open science is a lack of incentives for conducting research, with over 25% of institutions surveyed having limited awareness of the benefits of open science (European University Association (EUA) 2021). According to the EUA survey, approximately half of the surveyed university respondents have mandatory or optional data provision policies with incentives (EUA 2021). Data sharing, data management, and FAIR data plans were optional or alternatively incentives in the policies of 39-45% of the institutions surveyed (EUA 2021).

UNESCO ROS (2021) recommends policies to encourage researcher participation in open science. According to Bartling and Friesike (2014), due to a lack of incentives, 17th century researchers were secretive about their discoveries. They also mention the pursuit for the most journal article publications as one of the perverse incentives for research participation, along with the pursuit for the most research funding (Bartling and Friesike 2014). The disadvantage of incentivizing researchers by granting them access to publish their work is that it puts pressure on the research team to publish results in a timely manner. As a result, such incentives necessitate careful consideration because they influence how science is conducted in terms of data generation speed and teamwork (Kaye et al. 2009). Many concepts for incentivizing open science, according to Friesike et al. (2014), lack clear incentives for individual researchers. Examples of incentives for open science participation include improved research quality, maximum value and potential impact of research, and stimulating scientific cooperation and collaborative research (DNOSP 2022).

This section, in summary, discussed open science in the context of biobank research. Furthermore, it highlighted the primary ethical concern surrounding open science and biobank research, which is data sharing without consent. The following section discusses the ethical concerns and debates surrounding broad consent, followed by the risks associated with biobank research.

1.5 Ethical concerns around the use of broad consent

The main ethical concern with broad consent use for biobank research, as discussed in the previous section, is the need to provide appropriate or adequate information to research participants in order to obtain informed consent (Hansson et al. 2006; Steinsbekk et al. 2013). This concern is related to participant autonomy and trust in the biobanker or health researcher that their samples and associated data (hereinafter referred to interchangeably as "materials") will be used in accordance with their consent. Broad consent opponents question the ability of this model to predict risks for future research. The concern is based on the idea that biobank research is "open ended" (Hofmann 2008:128). Hofmann (2008) does not define open ended research, but describes biobank research as such. Due to the notion that broad consent is used in biobank research, this implies that samples and data can be used in novel and unexpected ways. To address this concern, the current South African regulatory framework should include a statement stating that when requesting broad consent, participants should be provided with the relevant information on proposed research. This should not necessarily include specific research details, as these are unlikely to be known at the time biobank research material is collected. Another disquiet related to broad consent is the alleged breach of confidentiality, in which materials are said to be more likely to be abused or subjected to unauthorized use (Karlsen et al. 2011).

This argument is flawed because, in the absence of sufficient safeguards, privacy and confidentiality violations may occur in general health research and not only in biobank research. One of the concerns related to biobank research is a claim of breach of confidentiality, which is covered in detail in Section 1.6. Providing enough and pertinent information to study participants in relation to autonomy, being able to anticipate risks for future research, and a claim of confidentiality breach are all examples of ethical difficulties that relate to the use of broad consent. The issue over the ethical acceptability of broad consent centres on the capacity to inform participants about the research in which they would be taking part in (Steinsbekk et al. 2013).

1.6 Debates around broad consent

Based on national laws and cultural norms, biobanks have adopted various models of informed consent (Mikkelsen et al. 2019). As a result, broad consent debates frequently revolve around the extent to which the various models provide the same level of safeguards as traditional informed consent in clinical research. Mikkelsen et al. (2019) argue that this "limited" type of comparison is inappropriate because the context of broad consent differs from the context "for which study-specific consent was originally designed" (Mikkelsen et al.:2). This viewpoint is based on the idea that biobank research poses risks that are "more general" (Mikkelsen et al. 2019:2) and distinct from those of study-specific research. As a result, a different consent model, such as broad consent, is required.

Grady et al. (2015) argue in favour of broad consent, claiming that, when compared to specific consent or tiered consent, broad consent reduces the cost of additional (fresh) consent required for sample re-use. Broad consent is deemed ethically justified based on this premise and a proposal that includes initial consent granted, future research

oversight, and mechanisms for providing more information to participants where feasible (Grady et al. 2015). Another point of view on the cost of future research in biobanks contends that the costs of protecting the confidentiality and privacy of large datasets are higher than those of smaller studies (Fisher and Layman 2018). This argument ignores sample anonymisation, which is used in all research involving human participants to protect participant privacy and confidentiality.

There is a gap in the literature on discussions as well as empirical research on the use of broad consent in SA. A few literature sources focusing on this topic, however, have been identified in the current study. Some researchers in SA are opposed to using broad consent, citing concerns that it is incompatible with respect for autonomy and building trust (Moodley 2017). This argument is further elaborated on in chapter 5, section 5.2. About 66% of researchers in a study by Mwaka and Horn (2019) support broad consent use for biobank research. The NDoH Ethics Guidelines do not prohibit broad consent. The debates on broad consent use in SA also cover the use of this consent model in relation to section 13(1) of POPIA (Staunton et al. 2019; Thaldar and Townsend 2020; Thaldar and Townsend 2021). The problem of divergent interpretations of POPIA as regards permissibility of broad consent use, to my knowledge, has been debated but no consensus around the issue reached in the literature. Thus addressing and providing a way forward demonstrates the novelty of the current study.

Another criticism is that broad consent violates participants' rights to ongoing control over their samples, because a biobank participant does not have the authority to direct the biobank to act on her behalf (Manson 2019). According to this argument, broad consent is morally deficient and cannot be interpreted as informed consent (Manson 2019). Manson supports this claim in two ways: 1) broad consent does not provide

participants with specific information about the use of their materials, and 2) participants who give broad consent are unable to withdraw from the study at any time. The first claim of the argument is addressed in Chapters 4 and 5 (sections 4.4.2 and 5.3.2, respectively), while the second claim is discussed in Chapter 5. (section 5.3.4). In the same manner that withdrawal of consent applies to any other type of research involving human participants, biobank research participants have a choice to discontinue their participation at any time. Furthermore, a counter-argument to the claim that broad consent violates participants' rights to ongoing control over their samples is that even with study-specific consent, participants' ability to control the use of their samples and data is limited. Assessing the risks involved with research involvement and thinking about ways to lower those risks is one of the duties of funders, researchers, and ethics committees. The risks of research in a study must be considered appropriate, taking into account the individual benefits to participants as well as the research's scientific and social value (CIOMS 2016). The practice of assessing research benefits and risks is applicable not only to biobank research but also to other human-participant research. However, the current study's focus is on biobank research risks, which will be discussed further below.

1.7 Biobank research risks

The Nuremberg Code recommends that the level of risk in human research not exceed the significance of the research problem to be solved (University of North Carolina 2021). The World Medical Association(WMA) Declaration of Helsinki (2013) reiterates that human research may only be conducted if the research objectives outweigh the risks and burdens. Furthermore, it recommends minimizing risks for those who lack the capacity to consent. Research participants’ risk exposure is ethically justified if the

research has social and scientific value. Such value has the potential to generate new knowledge while also promoting people's health (CIOMS 2016). Caulfield and Weijer (2009) define minimal risks as "daily life risks" (Caulfield and Weijer, 2009:53). One of the identified risks for biobank research samples is that they may be used by third parties outside the scope of consent granted if researchers have unrestricted access and use (Eriksson and Helgesson 2005). As a result, restrictions based on a specific scope of biobank research should be the solution to avoiding participant harm. The risks associated with biobank research involving personal information linked to an individual are of a social and dignitary nature. Social risks do not only affect individuals but can also affect entire populations (Dhai and Mahomed 2013). Discrimination and stigmatisation, for example, particularly genetic stigmatisation because it is frequently group-based (Dhai et al. 2015). However, genetic research is not only conducted in the context of biobank research, but also in general biomedical research. The most serious risks associated with genetic research are potential confidentiality violations (Wendler and Rid 2015). Violations of personal or religious beliefs are associated with dignity risks (Dhai and Mahomed 2013). The risks associated with using biobanks for research that involves personally identifiable information are of a social and dignitary nature (Dhai and Mahomed 2013; Eriksson et al. 2005). Although it is possible to re-identify and link anonymised DNA sequences to matching participant information (Schmidt and Callier 2021), sample coding and anonymisation are thought to provide reasonable participant confidentiality and privacy due to the overall reduced potential for participant identification.

Biobank materials commercialisation has also been identified as a risk for biobank research (Moodley and Singh 2016). It is an offense to sell or trade in gametes, tissue, blood, or blood products, according to Section 60(4)(b) of the National Health Act

No.61 of 2003 (NHA). Samples, data, research results, or derivatives of these materials, as well as the acquisition of private funding, are examples of biobank resources or materials that can be used in commercial activities (Caulfield et al. 2014). The term commercialisation is open to various interpretations, resulting in differing perspectives on how the concept is understood (Marshall et al. 2022). In some contexts, commercialisation may be synonymous with exchanging samples for money (making profits or financial gain), and may thus be associated with exploitation and is illegal (Marshall et al. 2022). Commercialisation and misappropriation of human samples are not limited to biobank research and have been reported in general health research as well (Moodley and Kleinsmidt 2020, Steinbekk et al. 2013, Petersen 2005, Eriksson and Helgesson 2005). In another context, this concept could be viewed as a means to an end. Capital investment in drug and vaccine research and clinical trials, for example (Marshall et al. 2022). The former example of commercialisation refers to negative commercialisation in the context of the current study, whereas the latter example refers to positive commercialisation.

Hofmann et al. (2009) contend that disclosing medical or biobank research information in the form of incidental findings (IFs) is a risk for research participants and constitutes "informational harm". This claim, however, is unsubstantiated. Mikkelsen et al. (2019) mention informational harm or risk in the context of long-term storage of biobank material as an increased likelihood of informational risk. As part of biobank governance, biobanks are required to safeguard samples and associated data while in their custody by implementing security measures to prevent unauthorized access and sharing (WMA 2016).

Rhodes et al. (2011) propose "de minimis risk" (Rhodes et al. 2011:4) as another risk category for research risk. They argue that the physical risks of taking a sample from

a donor or participant in biobank research are minor in comparison to the risks of everyday life. These are regarded as *de minimis* (Rhodes et al. 2011). According to Rhodes et al. (2011), research involving de minimis risk would be exempt from Institutional Review Board (IRB) (or REC)[1] waiver and informed consent requirements. This recommendation is consistent with CIOMS guidelines, which state that RECs may waive informed consent if the research poses minimal risks to participants, would be impractical without the waiver, or has social value (CIOMS 2016).

It is clear from the preceding discussion that the risks identified as biobank research risks also apply to general health research. These include those involving personal information and the risk of confidentiality breaches, human sample misuse, and commercialisation. The Nuremberg Code (1947) defines unacceptable risk in human research as when there is a priori reason to believe that disability or death will occur (UNC 2022.). A priori justification is one that is not based on experience (Russel 2020). For example, a person is justified in believing that 2+2=4 because they understand the concepts involved (what the terms in the sum mean) (i.e., the knowledge is independent of experience) (Wayne State University, 2018). To avoid an unacceptable level of risk in human research, in order to support their conclusion that an investigational agent has a favorable risk-benefit ratio and that its risk-benefit profile is at least as good as any existing alternatives, researchers should present a trustworthy interpretation of the available information (CIOMS 2016).

1.8 Risk-benefit ratio assessment in health research

A mathematical algorithm or formula cannot express the risk-benefit ratio in human research. Instead, it is the outcome of a choice made after considering the potential

[1] RECs or HRECs will be used throughout this thesis in keeping with the SA context.

benefits and risks of the proposed research (CIOMS 2016). The level of acceptable risk in biomedical research is determined by legally binding regulations and professional norms (Simonsen 2012). The difficulty in assessing risk in human research is the wide range of "acceptable risks" judgments. This raises the possibility that research protections will differ from one research site to the next and from one REC to the next (Wendler and Rid 2015). According to the World Health Organization (WHO) (2011), acceptable research is one that poses minimal risk to participants. The NDoH Ethics Guidelines define minimal risk in research as when the magnitude and probability of potential harms for participation "are no greater than those posed by daily life" (NDoH 2015:54). In the context of this study, I submit that acceptable risk is synonymous with minimal risk. According to Wendler and Rid (2015), genetic research falls within the scope of research with minimal risk of harm because it does not exceed daily life risks (i.e., the rule of thumb is 1 in 10,000 risk of mild harm, 1 in 1,000,000 danger of death), which is the standard for daily life risk (Wendler and Rid 2015).

Coleman (2014:20) claims that RECs approach research proposal reviews with a "jury" mentality, especially when it comes to participant risk assessment. Coleman (2014) adds that one limitation in this regard is that such unstructured group deliberations leave individuals with a great deal of discretion in making decisions. This is exacerbated by their failure to apply standards or provide justification for their decisions. As a result, Coleman (2014) suggests using analogical reasoning to balance the risk-benefit ratio. Applying this concept to the context of REC reviews would imply evaluating prior minimal risk determinations by identifying any shared characteristics of interventions that have already been determined to meet (or not meet) the definition of minimal risk (Coleman 2014).

Biobank Ethics Committees (BECs) review biobank research to avoid participant non-maleficence in accordance with the regulatory framework. The regulatory framework, specifically the NDoH Ethics Guidelines, also allow for the use of biobank research broad consent, whereas POPIA allows for the use of data associated with samples (personal information), with specific consent required for data use (section 13). In order to address the discrepancy between NDoH Ethics Guidelines and section 13(1) of the POPIA in allowing broad consent use, the current regulatory framework should be clarified within the context of health research.

Given the differing interpretations of Section 13(1) of POPIA and the long-term nature of biobanking, the research question is: How should SA's current regulatory framework enable the use of broad consent for biobank research involving the use and transfer of samples and their associated data? An ethico-legal analysis of the literature will be conducted to answer the research question. This includes using theoretical frameworks, SA laws, and policies to develop arguments and counterarguments on the use of broad consent for biobank research, as well as identifying areas for improvement in SA's regulatory framework that would allow the use of broad consent. A principlist approach is used to support the use of broad consent for biobank research. In the current study, the basis of this approach is on beneficence, which is based on the concepts of altruism, solidarity, and reciprocity; autonomy, which is not limited to the scope of choices; and avoiding non-maleficence of biobank research participants in terms of seeking ethics committee review for proposed research, as with other types of human research.

1.9 Research question

The current study answers the following research question:

1. How should the current regulatory framework in South Africa enable the use of broad consent for biobank research where the use and transfers of samples and their associated data are contemplated?

1.10 Rationale for the study

As previously stated, the NDoH Ethics Guidelines do not prohibit broad consent, whereas section 13(1) of POPIA appears to prohibit the use of this consent model, with conflicting opinions over how to interpret the latter. Furthermore, given the future-oriented nature of biobanking, broad consent for future research use is a consent model that is frequently used by researchers in South Africa (SA). The study's rationale is to address divergent interpretations of POPIA and to fill a gap in the literature regarding whether the South African regulatory framework limits the use of broad consent in the context of biobank research. A detailed account of the relevance of the study has been presented in section 1.2. Briefly, based on the divergent views as to whether or not section 13(1) of POPIA allows broad consent, the relevance of the current study is demonstrated by highlighting the need to address this problem through developing a clarified and more enabling framework for broad consent that is unambiguous, through an ethico-legal analysis. As previously mentioned in section 1.2, Staunton et al. (2019) argue that a purposive interpretation of POPIA would allow the processing of personal information for the purpose of research when broad consent is used, despite the fact that the Act does not explicitly address the use of broad consent. A purposivist approach to statutory interpretation decides the law by reconciling the language of a statute to its intended purpose (Colinvaux 1997).

Legislative history is a popular option for the task of determining such a purpose. Another approach to statutory interpretation is textualism, which emphasizes semantic context (word usage) (Manning 2006). According to Manning (2006), it becomes incredibly difficult for legislative actors to consistently agree upon terms fully when interpreters disregard obvious contextual cues concerning semantic detail. In Staunton et al.'s purposive interpretation of section 13(1) of POPIA, the semantic detail that is disregarded are the words: "specific and explicitly defined." I agree with Manning (2006) that because textualism prioritises semantic context when it is obvious, it provides a more compelling defence of legislative supremacy than purposivism. This is because legislators can determine the boundaries and extent of the policies they wish to enact mostly, if not exclusively, with the help of semantic meaning.

1.11 Thesis statement

In the current study, I argue that because the use and transfer of samples and data/personal information are linked in the context of biobank research, SA's regulatory framework should allow the use of broad consent for biobank research, and that specific consent for personal information would not be ethically justified considering the future oriented nature of biobanking.

1.12 Aim of the study

The study aims to identify areas for improvement in SA's regulatory framework that would allow the use of broad consent for both samples and data/ personal information.

1.13 Study objectives

The objectives of the study are as follows:

1. To defend the claim that biobank research is a common good on consequentialist/utilitarian grounds and for reasons based on solidarity and altruism thereby demonstrating that restricting the use of broad consent in biobank research potentially limits the utility of biobank research (as per Chapter 2).
2. To defend the claim that the current regulatory framework in SA is ambiguous and unclear about whether broad consent is permissible (as per Chapter 3).
3. To provide an account of informed consent in research involving humans with an intention to demonstrate that the standard study-specific model of informed consent in human research is inadequate for biobank research (as per Chapter 4).
4. To defend the claim that broad consent for biobank research is ethically justifiable using ethical principles and providing counter-arguments to objections to this position (as per Chapters 4 & 5).
5. To propose and argue for what amendments would be necessary to allow for ethically justifiable broad consent (as per Chapter 6).

1.14 Research design

Normative analysis seeks to identify and clarify actions that should be taken in response to a specific issue (Robert and Zeckhauser 2011). In other words, a normative ethical inquiry attempts to evaluate and guide morally acceptable behaviour, with justification for the reasons given (Beauchamp and Childress 1994a:4). This research is normative (ethico-legal). It is desktop and library research, and no new data will be analysed. The study includes no human participants. It employs standard philosophical research methods and standards. The study also discusses and ethically

analyses relevant literature. This entails primarily interpreting and critically analysing significant literature.

It also entails a critical examination of laws, government policies, and guidelines. The review of relevant literature includes descriptions and clarification of concepts. It also entails identifying and criticizing inferences. The study also entails the examination and exploration of theoretical frameworks. The significant concepts discovered are correctly interpreted and articulated. Books, Google Scholar, PubMed, research articles, SA laws, policies, and guidelines, and other relevant academic search engines are examples of literature sources included. Biobanking, biobank research, informed consent, broad consent, personal information/data, and privacy are keywords used.

1.15 Argumentative strategy: Overall argument in standard form

The argumentative strategy is consistent with each of the study's objectives, as stated briefly below and in detail in the respective chapters. The study defends the claim that biobank research has the potential to benefit humanity greatly and thus can be considered a common good (Chapter 2), provided that broad consent use is not restricted. Based on the principlist approach, the study also defends the claim that broad consent for biobank research is ethically justifiable (Chapter 5): (1) broad consent promotes beneficence; (2) because autonomy is not specific to the scope of choices, this principle does not need to be restricted to specific (narrow) consent, but that broad consent, by virtue of participants being able to consent, dissent, or withdraw from research, fulfills the requirement for respect for autonomy; (3) broad consent use is permitted as long as participant maleficence is avoided through BEC. BECs function as a subcommittee of the registered REC with the National Health Research Ethics

Council (NHREC); (4) the use of broad consent provided that participants are informed of the use of their samples and data/personal information through ongoing communication. This maintains participant autonomy because they can choose whether or not their materials can be used for further research. Finally, the study takes into account virtue ethics as a defence for broad consent based on participants' trust in biobank personnel.

Counter-arguments to broad consent use include: (1) interference with autonomy; (2) the challenge of understanding consent information; (3) concerns about ethical participant protection; (4) the challenge of broad consent withdrawal; and (5) limitations of sample anonymisation as a criticism of broad consent. Counterarguments are addressed by emphasizing the view that autonomy is not limited to the scope of choice and that, as a result, consent does not need to limit participants if they are given the right to autonomy to grant broad consent; simplifying consent text in a language that participants can understand to improve clarity; ethical review of the research and ongoing communication with participants; participants should be able to withdraw their consent if there is no coercion or deception. Finally, as mandated by BECs and the WMA Declaration of Taipei, biosecurity of materials within a biobank should be a requirement for biobanks.

The study also argues that the current regulatory framework, specifically POPIA, is ambiguous and unclear about whether broad consent is permissible in terms of data/personal information use (Chapter 3). Given how much good biobank research can do for humanity, SA's regulatory framework that is ambiguous on whether broad consent is permissible or not is unethical.

1.16 Outline of the thesis

The literature and background to the debate on broad consent for biobank research were presented in this chapter. Chapter 2 defends the concept of biobank research as a common good, demonstrating that limiting the use of broad consent in biobank research may limit its utility. Chapter 3 examines South African laws, regulations, and ethics guidelines pertaining to the provision of broad consent for biobank research. The fourth chapter discusses informed consent in human research. The use of broad consent for biobank research is defended in Chapter 5. The chapter also includes a discussion of the arguments for and against broad consent. Chapter 6 discusses a proposal and argument for what changes to the SA regulatory framework would be required to allow for ethically justifiable broad consent. The conclusion and recommendations are presented in Chapter 7.

1.17 Ethics

Due to the fact that this is ethico-legal research, no ethics clearance from the Wits HREC is required.

1.18 Research outcomes

The following is the research's expected contribution:

1. To clarify POPIA ambiguity and the resulting divergent interpretations of section 13(1) regarding the collection of personal information for a "specific, explicitly defined, lawful purpose" for health research. This clarification (which I propose should be included in the Code of Conduct for Research) will also resolve the

conflict between POPIA and the NDoH Ethics Guidelines on broad consent for biobank research.

2. To make recommendations for improving the current regulatory framework in order to accommodate and enable broad consent for biobank research while ensuring adequate safeguards for research participants through the specification of rules for data access and personal information processing.
3. The study's findings will be published and presented at conferences for distribution to relevant stakeholders, including government departments.

1.19 Limitations

Since the current study is limited to the South African context, its findings are not generalizable.

Chapter 2

An ethical defence for biobank research as a common good

2.1 Introduction

The goal of this chapter is to demonstrate how a regulatory framework that prohibits the use of broad consent in biobank research may limit the utility of biobank research. Such a framework hinders the development of health research. As a result, disease diagnosis, management, and prevention are jeopardized. The chapter provides an ethical justification for biobank research as a common good. The consequentialist approach is used to defend biobank research as a common good. Consequentialism (also known as utilitarianism) holds that actions are morally right if they result in the best outcomes for all parties involved (Rachels 2003). In this chapter, I argue that biobank research has the best overall consequences for everyone involved.

In defence of biobank research as a common good, concepts from the solidarity-based approach are invoked. The principle of solidarity is central to communitarianism, emphasizing the importance of the community over the individual (Ogunrin et al. 2018). In turn, communitarianism considers ethics to be derived from the common good and communal values, with a positive impact on communities (Sutrop 2011). The solidarity model proposed by Ogunrin et al. (2018) allows for the expression of individual rights and preferences in furthering the common good. It is compatible with communitarianism that is responsive rather than authoritative. Authoritarian communitarianism, according to Ogunrin et al. (2018), imposes communal values on people without democratic debate or careful consideration of what is good and bad about traditional practices, resulting in severe restrictions on personal freedom, civil

and political rights. Responsive communitarianism promotes the common good while taking individual preferences into account. Solidarity in biobank research participation is critical for promoting the common good through communal research benefits. It respects the autonomy of participants and their right to withdraw from research (i.e., solidarity that is based on responsive communitarianism with an acknowledgement of a liberal understanding of the common good). As a result, communitarianism is being debated in support of biobank research as a common good. Ubuntu is an African ethical theory that promotes values such as solidarity and service to others (Ewuoso et al. 2021). As a result, in terms of solidarity, this chapter invokes Ubuntu in order to defend biobank research as a common good. The concept of a common good has also been linked to the Norwegian concept of dugnad in medical research. Dugnad is associated with volunteering for the greater good, both altruistically and in solidarity with society as a whole (Ursin and Solberg 2009).

Altruistic actions are those performed solely for the benefit of the recipient, with no expectation of recompense. For example, actions that are highly regarded and praised, as well as those that are beyond the scope of duty (Mihaela et al. 2010). As a result, biobank research is discussed in the context of altruism as a common good. Finally, Forsberg et al. (2013) propose a social contract-based duty to participate in biobank research. This chapter considers empirical studies in developing these arguments because of their role in medical ethics. Sulmasy and Sugarman (2001) note several ways in which empirical studies can be useful in medical ethics. One method is to conduct purely descriptive studies, which may introduce facts that were not previously considered in reaching normative conclusions. As a result, such discoveries help to inform future work. Another example is the description of facts pertinent to normative arguments. Many normative arguments rely on factual information. Thus,

empirical studies contribute to ethics when they can demonstrate the truth of a proposition. Furthermore, empirical studies using slippery slope arguments can uncover facts relevant to normative arguments. Empirical studies can thus help us understand the likelihood of a slippery slope occurring. Slippery slope arguments contend that changing a moral rule will result in unfavourable moral consequences. Although empirical studies cannot predict whether a slippery slope will occur, they do contribute indirectly to slippery slope arguments by increasing understanding of the likelihood of a slippery slope occurring. Empirical studies can also help moral decision makers assess the likely consequences of actions. Empirical testing of normative claims in the sense that demonstrating empirically that what has been proposed as a normative requirement is impossible renders the normative claim invalid. Descriptive empirical studies can be used to demonstrate the implementation of a normative idea. For example, survey data on a program's acceptability, as well as its perceived value and importance. Empirical study on why biobank research is perceived to be a common good are therefore also considered in this chapter.

This chapter also discusses a number of counter-arguments to the notion of biobank research as a common good. These include critiques of the social contract (Forsberg et al. 2013), the claim that policymakers should define a common good and the scope of any benefits to society (Van Beers et al. 2018), the therapeutic misconceptions as in brief medical examinations and disclosure of results to research participants (Forsberg 2012), and a purported loss of participant autonomy in genomic research (Hoedemaekers et al. 2006). In addressing the argument about determining the societal benefits of biobank research, guidance from national research priorities framework and institutional policies in determining biobank research priorities should be sought. This, in turn, would determine the extent of societal benefits in addressing

disease burden, thereby contributing to improved health and advancing the common good. Researchers have a responsibility to protect study participants while assessing the risks and benefits of using biobanks for research. To make the case for biobank research as a common good, it is necessary to first define what exactly a common good is. As a result, this idea is examined in relation to biobank research before making additional points.

2.2 Biobank research as a common good

According to Etzioni (2015), the "common good or public interest or public goods" are goods that benefit all members of a community (Etzioni 2015:1). In the literature, the terms "common good" and "public good" are frequently used interchangeably. However, Bialobrzeski et al. (2012) argue that using these terms synonymously is incorrect because they have different definitions. Bialobrzeski et al. (2012) define "public goods" as "that which is commonly used in an economic context and whose use neither diminishes nor excludes people from using them" (e.g. clean air). They define "common goods" as goods that are relevant to the community based on certain normative considerations and are used in non-economic settings (Bialobrzeski et al. 2012). Public interest is linked to a liberal perspective of society, although people have varied life plans based on various ideas of "the good" (Hoedemaekers et al. 2006:418). It is probable to cause confusion when the terms "common good," "public good," and "public interest" are misused. As a result, I base my concept of the common good as defined by Ornstein (2013). The term "common good" in the context of this study refers to shared welfare as a result of cooperation to advance biobank research. It is explained later in this section how biobank research advances shared welfare (i.e., a common good). Based on the notion that the context of biobank research is non-

economical, the distinction between "a common good, public good, and public interest" is important. Biobank research is concerned with human samples that are donated voluntarily. These, as previously stated, cannot be commercialised. This is because as mentioned in chapter 1, section 1.7, in some contexts, commercialisation may be synonymous with exchanging samples for money (making profits or financial gain), and may thus be associated with exploitation and is illegal (Marshall et al. 2022). Biobank research is therefore not referred to as a "public good(s)" because the term refers to what is commonly used in an economic context, as defined by Bialobrzeski et al. (2012).

Hoedemaekers et al.'s (2006) definition of public interest is likewise inapplicable to biobank research because it is linked to a liberal understanding of society in which people have various life goals based on various notions of "the good." Thaldar (2022) criticizes the Information Regulator's (IR) Guidance Note on the Processing of Special Personal Information as misaligned with the South African courts' interpretation of public interest and suggests that it be revised. The Guidance Note defines public interest as something that varies across jurisdictions, benefits the public in general, and should not be limited in application and scope (Information Regulator 2021). Considering the differences between the three ideas described above, the idea of "a common good" is most appropriate for biobank research in my view. The phrase "the common good" and "a common good" are frequently used interchangeably in literature. However, because it is in singular form, biobank research is considered "a common good" in the context of this study. In fact, the World Medical Association (WMA) considers biobank research to be a common good in its Declaration of Taipei (WMA 2016). Different perspectives are considered in demonstrating how biobank research is a common good, as outlined below.

Christensen (2009) asserts that the advantages of taking part in biobank research are a contribution to the common good. To begin, biobank research contributes to balancing social differences in health because the diseases studied in biobank research are related to socioeconomic conditions. Furthermore, new knowledge acquired from biobank research is one of the most important tools for combating health-related social differences. However, health benefits must be distributed in such a way that the disparities are balanced, allowing everyone equal access. This suggests that person(s) should participate in biobank research because it is essential for the development of new knowledge required to treat diseases brought on by social problems. Second, biobank research benefits those who are susceptible to hereditary illnesses. Those who are not predisposed to developing certain diseases should not use this as an excuse to avoid participating in biobank research because doing so would imply that they used their advantage to increase rather than decrease the differences in disease risk development. This contradicts the concept of treating everyone equally because it would only benefit some groups while neglecting others. Despite variations in the genetic propensity for acquiring diseases, participating in biobank research improves the condition of individuals who are the most vulnerable, assuming that the risks are distributed equally among different groups (or that the worst off gain the most).

According to Caenazzo et al. (2013), there are a number of factors that make providing samples for biobank research advantageous for society as a whole from a common good perspective. The choice to donate samples for research may also be influenced by an altruistic desire to benefit society. Solidarity is cited by Caenazzo et al. (2013) as a driving force for donating research samples to the common good. According to the authors, patients should be helped to see sample donation as a means to benefit

society. In the interest of a single donor who is regarded as a part of society, the aim of biobank research is to increase medical and scientific understanding about disease prevention and treatment. This means that when potential biobank research participants are asked whether or not to participate, they will have a better understanding of the significance of what is being asked of them, as well as a realization of their solidarity for society's common good. Widdows et al. (2011) consider biobank research to be beneficial to society if, for example, it has contributed to the development and discovery of a disease cure, with the relevant information subsequently documented, published, archived, and made available to the scientific community. The cure provides societal benefits in a variety of ways. For starters, it is available to all individuals both now and in the future. Second, there are benefits associated with future research (as a result of the developed cure) that go beyond the benefits of the cure to individuals and benefit society as a whole. Finally, cured individuals' improved health and increased life expectancy will generate other goods and social capital in the form of shared economic and social goods, as well as individuals who are rendered healthy by it. Thus, this good affects not only individuals but also the population (communal), who will live longer due to the development of the cure and the health of future generations who may not suffer from the disease at all. As a result, it provides additional economic, social, and health benefits.

The discussion on why biobank research is considered a common good emphasizes that this is due to the consequences of biobank research. Moreover, the shared well-being of individuals as a result of collaboration, contribution, and involvement in biobank research to fulfil a shared objective, such as the acquisition of new knowledge in disease diagnostics and therapies for societal benefit. The results of biobank research include the balancing of social differences through disease research, the

acquisition of knowledge for those at risk of developing certain diseases through genomic research, the improvement of medical and scientific knowledge regarding disease prevention and treatment, and the improvement of current and future generations' health through advancements in biobank research. Consequentialist logic therefore backs up the case for biobank research as a common good.

2.2.1 Consequentialist approach to biobank research as a common good

The appropriate course of action in any given situation is one which produces the best overall result when viewed from an impartial perspective that equally evaluates the interests of all parties concerned (Beauchamp and Childress 1994b:47). The theory of utilitarianism, which asserts that we should constantly achieve the greatest feasible balance of positive value over disvalue, is the most well-known consequentialist theory (Beauchamp and Childress 1994b:47). Utilitarianism was first presented by David Hume (1711-1776), and later expanded by Jeremy Bentham (1748-1832) and John Stuart Mill (1806-1873) (Rachels 2003). The approach accepts that the only basic ethical principle is utility (Beauchamp and Childress 1994b:47). Bentham (1781) defined utility as a property in any object that tends to produce advantage, benefit, good, pleasure, or happiness, all of which in this case amount to the same thing, or (also all of what also amounts to the same thing) to prevent mischief, pain, evil, or unhappiness from occurring to the party whose interest is being considered.

According to the utility principle, we should always choose the course of action that will have the best overall results for all parties concerned whenever we have an option between two choices (Rachels 2003). There are two different types of utilitarianism: act utilitarianism and rule utilitarianism (Childress 2009). The utility principle is applied

to numerous potential actions in act utilitarianism to evaluate which action has the highest likelihood of resulting in the greatest good. Act utilitarians contend that performing this action is both morally justified and required. When assessing whether a certain action is lawful or wrong, rule utilitarianism shapes other principles and rules in accordance with the utility principle (Childress 2009).

Resnik (2015) asserts that certain paternalistic practices can be justified on utilitarian grounds in order to save human participants from harm. According to Dworkin (1972), paternalism is an infringement on someone's liberty that is justifiable due to the person's good, interests, happiness, needs, welfare, and values. According to Resnik (2015), research policy should be grounded on the utilitarian principle, and while putting this principle into practice, societal consequences should be taken into account. For example, research policies should maximize the positive consequences while minimizing the negative ones. According to this viewpoint, rule utilitarians could argue that research above a certain risk level should be prohibited, but lower risk level research should be permitted if there is a possibility of societal benefit as a result of the acquisition of new knowledge. For example, if this concept is applied to research involving the administration of antiretrovirals to healthy volunteers in order to determine drug levels from the volunteers' samples in order to develop a diagnostic method for determining concentration levels in patients on treatment. This intervention has no benefit for the participants, and there is a risk that they will experience side effects such as nausea and vomiting. Nonetheless, the newly acquired information will benefit society by enabling the development of a cutting-edge technique for the therapeutic drug monitoring of HIV patients in that particular community or society. If remnants from these samples are kept in a biobank for future research (with consent), this research (biobank), as described in section 2.2, may serve the common good by

advancing scientific knowledge. Reverting to Resnik's perspective, a utilitarian evaluation of the benefits and risks of study involvement should establish if the advantages, including the risk of death, outweigh the risks. The limits of the risks to which healthy volunteers are exposed in research should be determined in light of these kinds of utilitarian considerations. In view of utilitarianism's critique that it disregards the rights of human participants, Resnik (2015) also promotes transparency and openness in the dissemination of knowledge about research involving human participants to the public in terms of the unfavourable consequences of research. A consideration for individual rights/welfare, distributive justice, and policy development should also be made in favour of utilitarianism-based research policies, along with an assessment of the effects of various laws. The right to withdraw one's samples from research is provided by biobanks, and research participation in general (including biobank research) is voluntary, therefore government cannot compel persons to take part in research by making it legally binding (Tamburrini 2011). As a result, a paternalistic regulatory framework that mandates research involvement would go against informed consent and the freedom to withdraw participating in studies at any time. Paternalist regulatory frameworks are discussed in the next section, along with the reasons why they are not ideal.

The prevalent paternalism theory claims that when paternalism interferes with a person's autonomy, it is wrong (Birks 2018). According to Birks (2018), paternalism is "all things considered wrong" since it interferes with a person's autonomy (Birks 2018:138). According to Birks (2018), one way to analyse whether paternalism is bad is to view the opposing arguments as normative justifications. Birks contends that a non-interference-based explanation based on autonomy could clarify the autonomy perspective on the impropriety of paternalism. If there are more reasons to refrain from

executing the action than to do so, it is assumed that the person is acting incorrectly all things considered. In order to make this point, Birks employs the term "ABRONI," which he defines as a normative justification for not interfering with a person's free will decisions and actions (Birks 2018). Therefore, in order for something to be universally regarded as wrong, the ABRONI must either be among the set of reasons that collectively defeat all of the reasons that count in favour of acting contrary to it or it must defeat all of the reasons that count in favour of acting contrary to it. Concern for one's well-being can be used as a defence for defying the ABRONI.

Paternalistic regulatory frameworks imposing a duty for biobank research participation would be wrong under all circumstances given this conceptualization of paternalism's autonomy-based wrongness because it infringes on the rights to voluntary research participation and the right to withdraw from such research. In the situation of forced (paternalistic) biobank research participation disguised as a common good, the two rights can be viewed as an ABRONI. They so disprove any justifications for acting in opposition to them. In the context of biobank research, the most likely candidate to oppose the ABRONI would be for conducting research that seeks greater societal benefit through a utilitarian approach and the wellbeing reason. As an example, in some cases, a Research Ethics Committee (REC) will grant a consent waiver for human research, including genetic research (which could be part of biobank research) (Almarzooqi and Campbell 2018). As previously stated, consent waivers are appropriate for research that poses minimal risks to participants, would be impractical without the waiver, or has social value. As a result, these considerations trump an ABRONI (right to autonomy in this instance). By seeking greater benefit for society, the consequentialist approach to biobank research as a common good is linked to the principle of beneficence.

Biobanks play a crucial part in storing research biomaterial and the associated data, which aids in understanding of disease and improve the efficacy and safety of prophylactic, diagnostic, and therapeutic interventions (WMA 2016). Therefore, restricting the use of biobank research will hinder the development of health research and jeopardize disease diagnosis, management, and prevention. Genomic research (part of biobank research), according to Hoedemaekers et al. (2006), contributes to the common good because it affects a large number of people. According to Dhai et al. (2015), because biobank research involves the contributions of a larger number of people, the ethical emphasis for biobank research should be based on the utilitarian common good, such as the greatest good for the greatest number. Tamburrini (2011) contends that, based on the positive outcomes for biobank research, individuals who are hesitant to donate their samples or withdraw from research act in a way that negatively affects others, albeit indirectly. Tamburrini (2011) goes on to say that those who question the relevance of this submission may argue that "harm to others" does not have to be the only criterion to consider when deciding which policy to implement. Another claim in this argument is that if we fail to recruit an adequate number of biobank research participants for whatever reason, we should not hesitate to use law enforcement to compel people to participate. The justification for this claim is that, should they get sick, making involvement legally enforceable will help both the participants and those who declined or withdrew as a consequence of new medical procedures and therapies developed as a result of biobank research. If, as explained above, there is no justification for consent waiver by a REC, the argument for enforceable participation contradicts the principle of autonomy in terms of the rights to voluntary research participation and withdrawal from research. It thus causes harm to research participants by violating the principle of non-maleficence, albeit not

physically. According to Mill (1859), who refers to the "harm to others" principle, the only justification for any member of a civilized community to be subjected to force against his will is to prevent injury to others. His own wellbeing, whether it be physical or moral, is insufficient justification. He cannot be legally compelled to do anything or stop doing something just because it will make him happier, be advantageous to him, be wise, or even be right in the eyes of other people. There are strong justifications for disputing, convincing, appealing with, etc., but not for forcing him to do something. His independence is, by definition, limitless to the extent that it solely impacts him. The person is in charge of himself, his own body, and his own thoughts.

Regarding the principle of "harm to others," Mill (1859) contends that the only reason a person can be compelled to do anything against their will is to prevent harm to others, and that not even his own good justifies exercising such power over any person against their will. In this case, one example is the criminal justice system, which imposes (exercises power) on citizens in order to prevent crime and enforce law and order. Mill (1859) also mentions the concept of human liberty, which includes a number of requirements. The freedom of thought, conscience, opinion, and sentiment on all topics, including moral and scientific ones, is a prerequisite for consciousness. The second requirement of the concept of human liberty is that we must be free to pursue our interests and pursue our preferences in making our own life plans, regardless of the possible outcomes, without interference from others as long as we do not harm them, even if they may find our actions to be immoral or perverse. Thirdly, after each person has the right to act as an individual, others have the freedom to unite within the same parameters, to come together for whatever reason without harming others, and without being forced or deceived. Regarding these liberties, Mill also makes reference to the principle of liberty, which maintains that it is about supporting people

rather than limiting their acts. Whether the government should take action for the benefit of its people, as opposed to leaving it up to them to take individual or voluntary action, is the question at hand (Mill 1859). According to Tamburrini (2011), a consequent application of the principle of human liberty would be self-defeating from a utilitarian standpoint, presumably because Mill does not propose a prima facie application of the principle of liberty. Government-enforced happiness, such as forced research participation, is incapable of producing the trust and stability in authorities that social and human flourishing (happiness) requires in broad consequentialist terms (Tamburrini 2011).

Rule utilitarian paternalistic regulatory frameworks would be ethically wrong in light of the preceding account of utilitarianism as an ethical theory and application to biobank research, as well as the "autonomy view of the wrongness of paternalism" presented above. The justification for biobank research as a common good should thus be based on act utilitarianism rather than rule utilitarianism. Participants are also harmed when coerced participation violates the principle of non-maleficence. Individuals are obligated by solidarity not to obstruct potentially beneficial research if it poses no risk of harm to individuals (Forsberg et al. 2009).

2.2.2 Solidarity-based approach to biobank research as a common good

In addition to helping others, contributing to biobanks' solidarity system by donating samples highlights the value of the human body and encourages a giving mind-set (Onisto et al. 2011). According to Munung et al. (2021), one of the guiding concepts for the governance of genomics research in Africa, particularly Sub-Saharan Africa, is solidarity. The advancement of precision medicine is one of the objectives of genomics research. As a result, considering genomics variations across different population

groups is critical, because if genomics research is limited to a single population group, the research results may not be applicable to other populations (Munung et al. 2021). Precision medicine is defined as a multidisciplinary combination of new knowledge and approaches aimed at promoting a better understanding of health and disease in terms of cure and prevention (Kinkorová 2016). Precision medicine such as genomic research improves disease diagnosis by directing clinicians toward more personalized patient care (Strianese et al. 2020). Biobanks have been identified as one of the pillars of precision medicine due to their role in providing high-quality research samples (Andry et al. 2017). Monitoring disease natural history and enriching sample-associated data is another example of how biobank research contributes to precision medicine other than through genomic research (Annaratone 2021).

Solidarity requires African populations to participate in genomics research so that they can benefit from precision medicine and other outcomes of such research (Munung et al. 2021). The term "solidarity" is derived from the Latin concept obligatio in solidum, which was used in Roman Law, and denotes joint debtors' group liability (Laitinen and Pessi 2014). Around the 1840s, the term was adopted in English and German, was also politicized by the international labour movement, and later adopted in social science. According to sociological theory, the current concept of solidarity is the linking of individuals into a close-knit collectivity based on normative responsibilities (Hechter 2015). Individual self-interest is secondary to the concept of solidarity, which facilitates collective action (Hechter 2015). Solidarity arose from three theoretical perspectives or points of view (Hechter 2015). The normatist viewpoint holds that those who share core values, such as those indoctrinated in ethnic or religious organizations, are most inclined to come together in solidarity. The sharing of similar material interests, such as those seen in social classes, according to structuralists, is the basis for the

development of solidarity. According to the rational choice theory, dependencies and control mechanisms lead to the emergence of solidarity. Solidarity is central to communitarianism and is based on valuing the community over the individual (Ogunrin et al. 2018). As previously stated, communitarianism considers ethics to be derived from the common good and communal values, with a positive impact on communities (Sutrop 2011). The idea of solidarity proposed by communitarians is founded on a shared good and is focused on having a common understanding of society, its objectives, and what the good life entails (Prainsack and Buyx 2011).

Praisack and Buyx (2011) suggest a solidarity-based governance of research biobanks based on their interpretation of solidarity as a collective commitment to bear "costs," whether financial, emotional or otherwise, to help others in the hopes that biobank research findings will contribute to advancements that will benefit them or fellow research participants. The emphasis should therefore be on helping others rather than expecting something in return (Prainsack and Buyx 2011). Such an approach recognizes the potential for future benefit from research results through clinical developments that result from biobank research participation. Ogunrin (2018) suggests a theory of "relative solidarity" based on respecting people's rationality and interests while keeping in mind shared values. People would be able to integrate their preferences and viewpoints into the larger context of shared ideals, embracing togetherness. This solidarity is relative in that it respects individual decisions and choices while still taking into account the welfare of others. Responsive communitarianism, as opposed to authoritative communitarianism ethical framework served as the foundation for the development of the relative solidarity model. Authoritative communitarianism rigidly compels communal values on people without democratic dialogue. The differences between communal and relative solidarity are

based on the common good's goals: (1) with the former's execution based on shared values (an awareness of society and its goals) and personal judgements in the latter. (2) Responsibility in the sense that in the former there is a strong sense of obligation to communal principles, whereas in the later there is only a limited sense of obligation to communal values that go against personal beliefs. (3) Expense, as in the readiness to incur expenses on behalf of others to advance the common good in the former and in the latter, when such expenses are consistent with one's personal convictions.

Relative solidarity is seen to be a modification of fundamental communal values, hence it falls under the ambit of communitarian ethics. Relative solidarity allows individuals to pursue their own autonomous aspirations, whereas relative autonomy allows individuals to advance their own autonomous wishes, allowing autonomy to flourish. Individual judgements made under the context of relative solidarity frequently align with achieving the common good, which benefits everyone in the community, as opposed to taking an individualistic approach. The relative solidarity model is likely to encourage people to accept research risks (costs) in order to advance the common good based on individual assessments of the research's benefits to society as a whole. The relative solidarity model is likely to encourage people to accept research risks (costs) in order to advance the common good based on individual assessments of the research's benefits to the community, which is why there is a proposal to implement relative solidarity in genomic research (a component of biobank research). According to the African ethical philosophy of ubuntu, people should show their support for one another by encouraging behaviours that seek to increase the wellbeing (quality of life) of others (Ewuoso et al. 2021).

The Nguni people simply say, "umuntu ngumuntu ngabantu," and in Sesotho and Setswana languages, botho; "motho ke motho ka batho ba bang," which translates as

"I am, because you are." This basically means that our survival and happiness are dependent on others (Metz 2011). Ubuntu promotes not only the value of solidarity, but also the common good (Ewuoso et al. 2021). By virtue of the notion that volunteers provide samples for research that will benefit the entire population, biobank research might be considered as complementary to ubuntu (Staunton and Moodley 2016). Solidarity is a core value of the ubuntu-based governance proposed for African genomes research (Munung et al. (2021). This perspective contends that solidarity exemplified by ubuntu necessitates that in order for African populations to benefit from the outcomes of genomics research, including precision medicine and other health improvements, and to be exemplified by ubuntu, they must be included in such research. Given the concerns about global health disparities in African genomics research, one strategy to avoid such a divide would be to: (1) prioritize diseases that significantly increase the disease burden in Africa; (2) support genomics research to create an environment that is conducive to the implementation of genomic medicine on the continent; and (3) increase capacity for genomics research and medicine in Africa. Other research stakeholders, particularly funders, should promote genomics research in Africa as a sign of solidarity, and communities should be eager to take part in research for the common good. Specifically, participants should be informed of how their samples were used to advance the common good in order to create trust. In order to advance the common good, all research stakeholders should share their experience, knowledge and resources.

According to Moodley (2016), improvements in public health brought about by medical research, particularly the preservation of materials in biobanks for future study, ought to be viewed as a common good. Movements toward moving away from approaches like as solidarity and reciprocity in favour of the common good and toward a shift

toward the individual good are crucial, but they depend on researchers and research participants re-establishing trust. In an African setting where ubuntu is practiced, these principles reflect the communitarian ethic of the common good, which is particularly significant. Moreover, Moodley (2016) advises that South Africa's bioethics must be "decolonized" because it is not in line with African philosophy and also given that the common good perspective aligns with African philosophy. She uses recent student demonstrations in South African higher education as proof of a "thirst" (Moodley 2016:10) for alternative philosophical schools of thought. More African philosophy sessions, as opposed to solely Western ethics, which were requests by students at Stellenbosch University's (SU) faculty of medicine and health sciences.

The African Academy of Science (ASSAF) (2018) also advocates for the promotion of ubuntu in genetics and genomic research, arguing that the concepts of autonomy and ubuntu are mutually exclusive rather than complementary. Furthermore, a community's context is necessary to understand fundamental rights. Relative solidarity is a key aspect of ubuntu, claims Ogunrin (2018). According to this perspective, research ethics influenced by the principles of ubuntu should take place within the framework of a mutually beneficial partnership that enhances the welfare of individuals and communities (i.e., the common good). This has an impact on benefit sharing in research and prevents vulnerable communities from being exploited. Community benefits include ancillary care and educational opportunities. Ubuntu's central reciprocity influences how research is conducted and how it affects communities and participants by emphasizing the importance of improving the lives and well-being of the community. To improve community healthcare and well-being, for instance, health policy could be influenced by research findings. Owing to the idea that human samples are not considered to be property under SA law, materials (such as genomic samples

and associated data) should be viewed as a common good. Property in this context refers to public property that does not exist for commercial purposes and cannot be owned privately; ASSAF 2018).

The implication of the claim that human samples are not considered to be property under SA law is that the State would be responsible for providing resources (presumably through the regulatory framework) for material governance, which includes access to and use of such materials. If genomics research contributes to the common good, a framework for benefit sharing that benefits society as a whole is required. The nature and scope of intellectual property (IP) rights, as well as the scope for commercialisation, determine whether or not genomics resources are to be considered a common good; otherwise, they would fall under the domain of private property. By virtue of the influence of communitarianism, participants are expected to participate in research based on altruism and solidarity (Ogunrin et al. 2018). The communitarian perspective on research participation uses notions of solidarity and altruism to justify participation (Caulfield 2009). Furthermore, the concepts of solidarity and altruism emphasize a shared interest in promoting a common good (Petersen 2005). The following section discusses biobank research as an altruistic common good.

2.2.3 Altruism approach as a common good to biobank research

Genuine altruism is motivated by concern for the wellbeing of others, and in clinical research, genuine altruism entails participation for the benefit of future patients (Jansen 2009). Based on empirical studies that show that participants may have more than one motivation for participating in research, two types of altruistic motivation have been identified (Jansen 2009). (1) Primary altruistic motivation, which necessitates the

presence of a sufficiently strong altruistic motive in order to motivate the individual to participate. (2) Subsidiary altruistic motivation, in which the person's altruistic motivation alone is insufficient to motivate the person to participate (i.e., there are other motives as to why the person makes the decision that they make). For example, a person may participate in research because he or she believes it will benefit them (primary altruistic motivation), but they may also be motivated by the hope that future patients will benefit as well (subsidiary altruistic motivation). Jansen (2009) explains how altruistic drive can be utilized to assess the benefits of taking part in research. When participation is not in the participants' best medical interest, either because there is no reasonable expectation of direct therapeutic benefits or because the benefit is insufficient to outweigh the risk(s), it may be necessary to make an appeal to altruism to help make sense of the choice to participate. Clinical trial participants who are in good health do so out of sheer altruism; there is no therapeutic benefit to them, just to potential patients. Additionally, as previously mentioned, if samples from these participants are kept in a biobank for future research, this work will advance the common good through acquisition of new scientific knowledge.

In the United Kingdom (UK), discussions about sample donation for genetic research, particularly proposals for a national biobank, re-established the notion of altruistic blood donations as a "gift to strangers" (Busby 2006). According to Busby (2006), the gift metaphor for donor altruism used in the development of the UK Biobank is not imposed on an unwilling public. Instead, the effectiveness of particular public representations of donated blood is measured by the degree to which these associations concerning the National Health Service (NHS) and welfare state are mobilized (Busby 2006). The (NHS) is government-funded medical and healthcare services available to citizens of the United Kingdom (UK) (NHS 2019). Participation in

biobank research should be accompanied by a moral obligation to use the resource for the common good, at least in part (Williams and Schroeder 2004). Participants in a study on biobank research acknowledged the value of donating for "our collective social good" (Locock and Boylan 2015:813). The concept of altruism (actions performed solely for the benefit of others with no expectation of recompense) is related to the concept of biobank research participation as a common good because the latter is also typically characterised by sample donations by participants with no expectation of recompense. In the context of biobank research, altruistic donations could be viewed as a common good on the grounds that research results benefit society as a whole and future generations.

Altruism (identified as a theme for motivation) was the most frequently cited motivation for genetic research participation among US participants in a study conducted by Madrid et al. (2022) from November 2017 to February 2018. One of the subthemes identified for altruistic research participation was the benefit of learning about one's genetics as it affects family members, most often children and grandchildren. One participant described their participation as a "future gift" to their family. Other subthemes that emerged during the analysis included human advancement and scientific and medical advancement. One participant stated that he or she would be willing to participate in genetic research for the greater good even if the research would not benefit them personally.

Altruistic sample donations should be accompanied by a moral obligation to use the donated samples for the common good, at least in part (Williams and Schroeder 2004). The argument over informed consent for medical research or mandatory research participation should be considered in the context of the idea of a common good given that health research has been designated as a common good (Ursin and Solberg

2009). Biobanks depend on government support and the generosity of donors to survive. Hence, exploitation in the form of commercial research interests should be viewed as unfair and undesirable even though there may be some benefits (Williams and Schroeder 2004).

Ursin and Solberg's (2009) *dugnad* model for biobank research recruitment incorporates elements of non-economic interest or gain for research participation, reciprocity, to invoke communal solidarity and civic duties, and the pursuit of communal good and prosperity (Ursin and Solberg 2009). The concept of *dugnad* is associated with doing unpaid work for the common good, and participating in a *dugnad* makes the activity admirable (Ursin and Solberg 2009). Thus, the concept of *dugnad* is related to Mihaela et al.'s (2010) conceptualization of altruism, which states that altruistic actions are performed without expecting anything in return and are highly respected and praised. On this basis, I include an account of *dugnad* in the current study in defence of biobank research as an altruistic common good. In relation to participating in a biobank and pursuing the common good, Ursin and Solberg (2009) expand on *dugnad*. The pursuit of a common goal, equality of participants, and participation for non-economic personal benefit or interest are distinctive traits of a *dugnad*. *Dugnad* tasks do not have to be risky in a way that burdens the participants excessively. Rather than simply pointing out altruism and gift donation, as well as ethical and legal obligations, the model invites justification and motivation for biobank research participation. The *dugnad* promotes the common good as conceived by the community in question through highlighting specific conditions relating to the research design in terms of participant involvement as it relates to non-maleficence and beneficence, and a research design with a clear contribution to the common good. Due to the overwhelming influence of communitarianism, African potential research

participants are expected to participate in biobank research based on altruism and solidarity (Ogunrin et al. 2018). In addition to the communitarian viewpoint, there is a liberal viewpoint that regards biobank research as a common good (Christensen 2009). After discussing solidarity and altruism in terms of the common good, communitarianism and the liberal viewpoint will be discussed in defence of biobank research as a common good. Although individual rights and the common good appear incompatible, it is important to remember that the common good can and frequently coincides with the individual good. As a result, the two do not clash in the sense that certain individual benefits (concomittantly public benefits/common good) can only be acquired through cooperation, which requires people to give up their individual liberties (Forsberg 2012). This is why I think Christensen's (2009) view of justifying the common based on communitarianism and the liberal view is valid.

2.2.4 Biobank research as a common good based on a communitarian view

Communitarianism is based on communal normative criteria (Etzioni 2011) and, as previously stated, sees ethics as deriving from the common good and communal values, with a positive impact on communities (Sutrop 2011). Etzioni (2011) distinguishes two types of communitarianism: (1) responsive communitarianism, which recognizes that the tense interaction between the common good and autonomy should be resolved rather than assuming a priori that one of these values trumps the other and that neither autonomy nor the common good should be privileged, and (2) authoritarian communitarianism, which prioritizes communal values over individual autonomy. Within an African context, African communitarianism, in particular, has been identified and is expressed as ubuntu (Ogubanjo et al. 2005). Communitarianism has been criticized for replacing respect for autonomy and is frequently seen as the

polar opposite of liberalism. As a result, responsive communitarianism seeks to strike a balance between autonomy and concern for the common good without favouring one over the other (Etzioni 2011). The fundamental tenet of responsive communitarianism is that there are two opposing core values, autonomy and the common good, neither of which should be given precedence from the outset (Etzioni 2011). Although the foundation of responsive communitarianism is the understanding that the delicate balance between autonomy and the common good needs to be resolved rather than presuming that one of these fundamental principles is more important than the other, it anticipates that how these principles are applied will vary across societies and historical phases. Thus, for societies to reach the same end balance, they frequently need to move in different directions from one another. In line with this view, responsive communitarianism advocates should emphasise more attention to the common good in societies where individualism is prevalent, as was the case in the US in the 1980s, while those who support the balance it advocates must support autonomy in totalitarian and theocratic environments, such as those found in Singapore and Iran (Etzioni 2011). Etzioni (2011) does not elaborate on how responsive communitarianism could be applied in an African context, i.e. in line with ubuntu, however, Ogunrin's relative solidarity model for a Sub-Saharan African setting could be ideal. To recap, as mentioned in section 2.2.2, the relative solidarity model is based on respecting people's interests and rational thought while keeping in mind common values. Individuals would be able to embrace unity by integrating their preferences and points of view into the greater framework of shared ideals. This solidarity is relative because it recognises personal autonomy while simultaneously considering the well-being of others. Moreover, as also mentioned in section 2.2.2, responsive communitarianism, as opposed to an authoritative communitarianism

ethical framework served as the foundation for the development of the relative solidarity model (Ogunrin et al. 2018). Thus applying this model to responsive communitarianism as in the context of ubuntu is justifiable in this manner. In theory, because of the dominance of communitarianism, we can anticipate that African potential research participants will consent to biobanking of their samples and take part in genomic research out of altruism and solidarity. According to Ogunrin et al. (2018), their relative solidarity model, in addition to being in line with responsive communitarianism, encourages respect for communal values while upholding individual convictions in the interest of the community as a whole. Moreover, that relative solidarity may help to reduce conflicting ethical issues in genomic research participation early on, promote productive conversation at town hall meetings, and ease tension resulting from divergent opinions within the community. In addressing the ethical questions brought up by genomics, it can also provide a forum for the kind of collective solidarity that characterises liberal individualism and responsive communitarianism in African ethics. They further maintain that relative solidarity may help to reduce conflicting ethical issues in genomic research participation early on, promote productive conversation at town hall meetings, and ease tension resulting from divergent opinions within the community. In addressing the ethical questions brought up by genomics, it can also provide a forum for the kind of collective solidarity that characterises liberal individualism and responsive communitarianism in African ethics (Ogunrin et al. 2018). In exploring the notion that many people agree to participate in communitarianism, which is thought to be typical of African communities, on the grounds of solidarity and advancing the common good, Ogunrin et al. (2018) investigated willingness to participate in genomics research by a sub-Saharan African Nigerian community specifically in relation to consent to for genomic research and

what influences their beliefs regarding the donation of biological samples. In this study, the majority of adults were willing to participate in genomic research based on communal values such as respect for the decisions made by community leaders and family members, especially the heads of the family. They connected adhering to customs and traditions, or "doing it the way we have always done it in the community," with their consideration of family members' opinions and the approval of the community's leaders. Two adult participants conveyed this in their words. One discussed replacing his own choice with the collective choice based on decisions made by the community leader, who is seen as the father of the community, suggesting that individual autonomy becomes inappropriate in the face of communitarianism. The adult women believed that approval from their spouses, who were the heads of the family, was necessary in order to participate. The adult men mentioned talking to their wives about their choices before making a decision. The adult participants put emphasis on community leaders' approval of the research and expressed the opinion that doing so would shield the community from harm and exploitation.

Individual obligations should not be compromised for the good of the public (common good) in the communitarian view, whereas in the liberal view, individual rights should not be compromised for the good of the public (common good) (Forsberg 2012). According to the communitarian viewpoint, our connection and identity with the community means that we cannot be separated from it. This perspective asserts that "the individual's right to make decisions for himself cannot be isolated from society goals" (Christensen 2009:104). If we view biobank research as a common good from which we cannot disassociate ourselves, then any fulfilment of this shared good will mean that we fulfil our own concept of the good life, which is founded in part on

pursuing the common good (Christensen 2009). Christensen continues by saying that we cannot invoke communal ideals without also taking into account the type of society we would like to live in. Therefore, whether communitarian values should be a point of contention in medical research in general and biobank research in particular depends on whether we uphold the communitarian conception of individuals and communities on which these values are formed.

2.2.5 Biobank research as a common good based on a liberal view

Liberal individualism (sometimes referred to as liberalism, individualism, or liberal view in the context of this section) is a rights-based theory that maintains that an individual should be protected and permitted to pursue personal goals in a democratic society (Beauchamp and Childress 1994c:70-71). According to liberal individualism, each person has their own rights that come before and independently of any notions of what is right and wrong (Holowchack 2006). The theory is unique in that it places a strong focus on the idea of neutrality, holding that the State should not penalize or reward differing conceptions of the good but instead provide a neutral framework for pursuing such conceptions (Kymlicka 1989).

The liberal interpretation of the term "common good" is based on the unique preferences of each person. This point of view contends that the pursuit of the common good enables a person to evaluate his or her conception of the "good life" in light of other people's opportunities to achieve the same ends. According to the liberal viewpoint, the common good serves as the standard by which each person's perception of the good life is judged (Christensen 2009). The individual's perception of the good life will be assessed in light of the biobank research's portrayal of a societal good. Preferences that are in line with the common good will be given precedence

over those that are not because society understands the common good to involve ranking of objectives and values. In accordance with the concept of the common good, Rosseau (1762) proposed a social contract based on the idea that the duties and responsibilities of citizenship outweigh individual freedoms and rights (i.e., a communitarian view of society).

2.2.6 Biobank research as a common good based on a social contract

The idea of a social contract theory was developed by Hobbes, Kant (Korošec 2016), Rawls (1971), and Rosseau (1761) and can be traced back to early medieval philosophy. According to Rosseau (1761), the terms of a social contract can be summed up as an associate withdrawing all of his or her rights from society. As everyone completely gives themselves up entirely, the situation is equal for everyone. Since everyone is subject to the same conditions, nobody is motivated to make them burdensome for others. According to Rosseau (1761:164), a social contract is essentially comprised of the following clauses. Each of us submits his or her entire being to the supreme control of the collective will, and in exchange, each individual becomes an integral part of the whole.

Instead of each associate's (contracting party's) unique individuality, the association (contract) results in a moral and collective endeavour comprised of as many members of the assembly as having voices with unity, commonality, and will. John Rawls (1971) refers to a theory of justice that is based on the concept of fairness. This kind of theory generalizes and considers the accepted notion of a social contract (Rawls 1971). According to Rawls, a social contract is governed by just principles with the initial agreement's aim being the foundation of society. The fact that these principles are those that free and rational persons who seek to advance their own interests would

accept in an equal position as establishing their terms of association, is one of a number of features that these principles possess. These principles include a variety of characteristics, including the fact that free and reasonable people with an interest in pursuing their own interests would accept in an equality-based setting as the basis of their association. Rawls believed that this approach to justice principles was just. He continues by stating that those who engage in social cooperation choose the rules that govern rights, obligations, and the allocation of social benefits.

In order to account for individual rights and obligations in the context of medical research, Forsberg (2012) suggests a concept for a social contract that takes a person's self-interest into account. This makes it mandatory for everyone to take part in biobank research under the presumption that the risks are negligible and outweighed by the benefits. Collaboration is the only way to gain these benefits. Everyone has an interest in medical advancements that can only be attained through research, according to a social contract-based duty for biobank research participation. This is because there are many diseases for which there are no effective treatments and we do not know what kind of medical care we (or those we care about) will need in the future. Furthermore, according to this viewpoint, a social contract arguably provides a relevant picture of the involved conflicting interests. It is also consistent with the idea that individuals should not obstruct sample usage that does not pose risks when it could benefit not only them but others as well. Accepting a hypothetical contract that imposes a duty for research participation is thus rational. Accepting a contract implies a moral obligation to follow through on it and this is justified by a prior duty to maintain one's word and uphold one's commitments. The proposed contract's goal is not to maximize public benefit, but rather to maximize the outcome for each individual, in the sense that everyone would be pursuing their own interests

independently (i.e., future benefit that they or their loved ones might need). A proposal for implementing such a contract would be to base legislation and regulations on a contract view, implying the need for public education and debate to enable policy understanding and acceptance. Due to the idea that there is no actual contract that people can sign if there is a hypothetical social contract outlining regulations that must be followed, allowing individuals to opt out may be appropriate as a means of avoiding coercion. Individuals who choose not to contribute should arguably be willing to forego the benefits that could result from such cooperation from a moral standpoint (i.e., healthcare advances that are achieved). In light of a social contract as a duty to participate in biobank research, biobank research offers a way to reconcile individual rights with the benefit of the public (i.e., shared wellbeing of people as a result of working together towards a common goal/common good). Forsberg et al. (2013) note in a separate publication that there should be limits to the duty to participate in biobank research because the benefits of accepting the contract should outweigh the risks involved for each individual. As a result, they agree that the contract does not have to apply to specific research.

The defence of biobank research as a common good generally emphasizes the idea that participation should not be an absolute duty, with emphasis placed on the idea that the outcomes (acquisition of new knowledge for disease prevention and treatment) should not be all that matters. Rather, the interests of potential participants in terms of their risk of harm as well as their interest in furthering this common good should be considered. This finding demonstrates that participation in biobank research should be a prima facie duty rather than an absolute requirement. A prima facie duty is one that would be a proper duty if no other morally significant duty existed (Ross 2002). Ross sees the duty of non-maleficence as more binding than the duty of

beneficence. As an example, it is not justifiable to kill one person in order to keep another alive. In the context of the current study, this concept relates to human research in the sense that participants should not be subjected to lethal experiments for the sake of society.

As stated in section 1.5.1, an unacceptable risk in human research is when there is a priori reason to believe that disability or death will occur (UNC 2022). Ross admits that, while it may be argued that when prima facie duties conflict, determining an actual duty will be difficult. He goes on to argue that it is a prima facie duty to create things that are intrinsically good rather than not. Knowledge, virtue, and, with certain limitations, pleasure (hedonism), are three intrinsically good things. According to Ross (2002), while there is a prima facie duty to produce some things that are good, there is no such duty to produce pleasure that we will enjoy. Based on Ross's definition of intrinsically good things, biobank research can be considered intrinsically good in the context of the current study because it results in the acquisition of new knowledge (medical advances). According to Ross, the duty of non-maleficence is based on the idea that if there are things that are intrinsically bad, we should not do them to others.

2.3 Counter-argument for biobank research as a common good

Forsberg et al. (2013) raise a number of concerns about the social contract as a duty to participate in biobank research in relation to the common good. For starters, because the contract is hypothetical, individuals cannot be held liable for a contract to which they have not consented. Second, the proposed contract is based on false premises because we are not all benefit-maximizing, self-interested creatures. Third, more rational contracts to accept are those that impose a duty on everyone else to participate except oneself. Finally, a general objection to a duty to participate in medical research is that it does not guarantee advances in clinical care.

One criticism levelled at the notion of medical research as a common good is that it is unclear how policymakers should define the concept and the scope of any societal benefits (Van Beers et al. 2018). Beneficence is a set of norms for providing benefits while balancing those benefits against risks. This is one of the principles of biomedical ethics (Beauchamp and Childress 1994d:259). As a result, in the context of this study, beneficence and research benefits will be used interchangeably. By virtue of the definition of beneficence, this argument appears to be based on beneficence (quantification thereof) for participating communities. According to the viewpoint that research risks should be weighed against benefits, when resources such as funding are allocated, the potential of different studies to improve health and healthcare should be compared (Forsberg 2012). Furthermore, regulatory requirements for conducting research should be optimized so that the risks assumed by participants and the funding used for the research results in the best possible outcome for current and future patients.

Overestimation of the benefit of research participation or underestimation of the risk of harm from such participation has been labelled as misconception (Forsberg 2012). Therapeutic misconception may be promoted in the context of biobank research, according to Forsberg (2012), by offering brief medical examinations or disclosing individual results to participants, thereby conflating the goals of research and clinical care in this manner may induce people to donate tissue samples to biobanks, deceiving them and giving them a false sense of security (Forsberg 2012). This viewpoint also holds that for research to have any impact on medical advances, it must be applicable to clinical needs. As a result, it must be within healthcare, identifying problems and determining (testing) potential solutions. The criticism levelled at

biobank research is that, while it can lead to new medical knowledge with only minor risks, the good that it may lead to cannot be predicted in advance.

A recommendation is made for collaborative research between local and international researchers in order to maximize the good that can be obtained from biobank research. Such collaboration is justified by the argument that it would result in sufficient sample sizes to make the results valid. The calculation of sample size or determining a representative sample size is applicable to health research in general (Fox et al. 2009), and is not limited to biobank research. A study's representativeness, such as an appropriate sample size, allows the findings to be generalizable to a larger population (Fox et al. 2009). As a result, unrepresentative or biased sample sizes are also applicable to general health research, not just biobank research.

Hoedemaekers et al. (2006) contend that not all genetic research has the potential to be beneficial to society and question if the common good warrants "individual sacrifices" for genomic research (Hoedemaekers et al. 2009:415). They argue that the only genetic research that will contribute to the common good is that which develops effective or novel cures for conditions that substantially hinder social interaction and human autonomy (Hoedemaekers et al. 2006). One example is the study of pharmacogenomics for psychiatric diseases that lack a cure (such as "really" disabling diseases like cancer or Alzheimer's disease). The authors point out that when evaluating whether disorders will result in severe impairment of autonomous and social functioning and thereby satisfy the requirement for being considered a contribution to the common good, the term "serious" refers to the burden of the condition. This pertains to the notion that a patient's essential physical and mental health must be considered when evaluating the patient's remaining quality of life.

Additionally, they argue that a general appeal to the common good is insufficient to justify giving up something for someone's autonomy (Hoedemaekers et al. 2006).

According to Hoedemaekers et al. (2006), an individual's limited interpretation of the common good will allow researchers and ethics committees to determine when "some loss of autonomy" is morally justifiable. As a result, according to this argument, viewing all genomic research as contributing to the common good sacrifices individual autonomy. Additionally, according to this perspective, genomic research results in a loss of control over how samples and related data are used (i.e. loss of autonomy). The purported loss of autonomy linked to genomic research is not clearly articulated in this argument. In order to ensure that people impacted have the freedom to make their own decisions, such as whether or not to participate in research, efforts to advance the common good should be bound by liberty and informed consent (Sutrop 2011).

2.4 Response to the counter-arguments for biobank research as a common good

Although it is impossible to predict whether the proposed research will result in improved healthcare, the prospect of making medical advances is arguably compelling enough to justify, at the very least, research with minimal harm as a means of increasing medical knowledge (Forsberg 2012). To adequately address the argument of defining a common good in the context of biobank research, consideration of Ross's (2002) conceptual account of a good as it relates to a common good is required, in addition to an account of how biobank research contributes to the common good provided in section 2.1. The relevant discussion of what constitutes biobank research benefit(s) in a specific setting or population is also taken into account. According to the definition of a common good presented in section 2.2 (shared welfare of people as

a result of working together toward a common goal), the definition of a common good in the context of biobank research would be shared cooperation of biobank research participants with researchers toward a common goal of advancing acquisition of new knowledge for disease prevention and treatment through research. As previously stated, knowledge is a good, according to Ross (2002). Ross believes that one of the most important factors in determining whether actions are right, is whether they promote general good, which he uses synonymously with maximum good and appears to use the two terms interchangeably to refer to a common good. The general good is that which ensures that whatever produces general welfare while also increasing general welfare on its own. As a result, right acts include the production of welfare as a component of their rightness. In alignment with Ross's view, biobank research is beneficial because it results in the acquisition of (new) knowledge. Furthermore, it can be deduced that biobank research is appropriate based on the benefits it provides to future patients. Given Van Beers et al.'s (2018) concern that it is unclear how policymakers should define a common good, a discussion of a common good from a policymaking perspective is appropriate. In general, the importance of a common good is viewed as both a rationale for policy decisions and an ideal against which policy, rights, and procedures should be evaluated (Diggs 1973).

Such an ideal is most visible in its negative application when it is clear that a policy is unreasonable in the eyes of citizens and that more equitable solutions are needed. Insofar as benefiting from common goods constitutes human wellbeing, public policy that disregards common goods may hinder rather than contribute to human wellbeing (Deneulin and Townsend 2007). The concept of a common good governs not only individual behaviour but also government decisions and public policy (Mastromatteo and Solari 2014). According to Mastromatteo and Solari (2014), when providing public

services, public authorities must refer to the concept of a common good. According to this viewpoint, policymaking inspired by the common good(s) entails a consideration of the consequences of actions that are expected to have practical effects in accordance with ethical principles. The practical reason approach suggests that politicians have a duty to uphold the common good when developing legislation. The correct answer to the question of which policies contribute to achieving a common good is context dependent. Policies aimed at the common good are context-dependent, as communities should be able to discuss and define them in light of current interests and problems. Applying this concept to the current study's context in terms of defining or determining a common good within a specific community or population is dependent on the population's prevailing health problems. To improve healthcare and the general well-being of South Africans, the South African Health Research Policy (2001) was established. In terms of an objective for public policy, wellbeing is replacing welfare more and more (Taylor 2011). Yet, the phrase seems to suggest population well-being in the framework of the Health Research Policy. According to the Policy, the research agenda should include priorities for health research. Research priorities can be established using both the technique of focusing on country-specific health issues and the approach of global health research aiming to address health issues of general significance.

In responding to the latter part of the argument, Beauchamp and Childress's (1994d:259) account of beneficence serves as a point of departure. This is consistent with the definition of beneficence as a set of norms that provide benefits while balancing those benefits against risks. Beneficent actions that contribute to people's well-being fall under the umbrella of the beneficence principle. Beneficence requires more than the principle of non-maleficence in that agents must actively help others

rather than simply refraining from harming them. By virtue of the idea that participants must take positive steps to participate in research, this criterion fits the endeavour of human research (of which biobank research is a part). Thus, future patients are helped by contributing to their welfare (synonymously wellbeing), for example, by funding research that leads to disease prevention, diagnosis, and cure. The manifestations of welfare would be lower disease rates, better disease outcomes, and longer life expectancies. Prevention and removal of harm, according to Beauchamp and Childress (1994d:259), require positive acts to benefit others and fall under the principle of beneficence rather than non-maleficence. Taking this interpretation of beneficence a step further from passive non-maleficence to more active intervention, beneficence entails a duty to protect others from harm (Pellegrino and Thomasma 1987).

Positive beneficence and utility, according to Beauchamp and Childress (1994d:259), are two principles of beneficence. Positive beneficence necessitates benefits, while utility necessitates a balance between benefits and drawbacks. The argument for biobank research involvement as a benefit for the common good would be described by the principle of utility as a beneficent principle given the backdrop provided thus far and the need for all human research to balance risks and benefits. In order to control disease burden efficiently, according to this perspective on beneficence, the scope of societal benefits in the context of biobank research ought to be in line with disease priority areas. The framework for establishing research priorities should not be viewed as static, but rather as adaptable and responsive to changing health-related needs and circumstances in SA (NDoH 2021). The National Research Strategy has established broad priority areas and recommends that more specific research areas be established at the institutional level following stakeholder workshops. One of the

National Research Strategy's considerations is lowering the disease burden in SA. The NDoH of SA identified disease research objectives in the National Health Research Strategy: Research Priorities for South Africa 2021–2024 (NDoH 2021). The strategy includes research priorities related to biobank research. Examples of communicable diseases include the human immunodeficiency virus (HIV), coronavirus disease 2019 (COVID-19), and tuberculosis (TB). Furthermore, covered in the strategy are non-communicable diseases like diabetes, cancer, and cardiovascular disease.

A framework for establishing priority research areas considers ethical principles (respect for persons, beneficence, non-maleficence, and justice), as well as consequentialist and deontological approaches, to ensure that health research has the potential to benefit those in greatest need while not excluding any group, thereby contributing to improved health (benefit). Research directed at a specific population in order to address research priorities or disease burdens, ensuring that those in greatest need benefit. As a result, aligning biobank research with such a framework would ensure that the disease burden in SA is addressed, thereby contributing to the common good through improved health.

The ethical principle that claims a duty not to purposefully cause harm is non-maleficence. This ethical principle responds to the notion that research risks should be evaluated against benefits (Beauchamp and Childress 1994e:192). Understanding a duty of beneficence is equivalent to understanding a duty of non-maleficence (Ross 2002). Non-maleficence, or the need to avoid doing harm to another directly, is the lowest level of interpretation of the concept of beneficence (Pellegrino and Thomasma 1987). The duty not to harm is therefore implied by the non-maleficence principle. When applied to biobank research, researchers not only have a duty of non-maleficence, but also a duty to protect research participants from harm. When non-

maleficence and beneficence conflict, the overriding principle, according to Beauchamp and Childress, is non-maleficence (Beauchamp and Childress 1994f:191). However, the weights of ethical principles vary depending on the situation. As a result, there can be no priori rule that favours one over the other (Beauchamp and Childress 1994f:191). Notably, the NDoH Ethics Guidelines specify that participants in research should not be put at unacceptably high risk of harm only because they are anticipated to benefit anything from the research. Risk assessments should consider the magnitude and likelihood of harm (NDoH 2015).

It is crucial to ascertain whether therapeutic misconception is common in human research generally or only in biobank research in order to evaluate the therapeutic misconception claim. In some study contexts, therapeutic misperception happens when participants' expectations brought on by clinical standards cause them to misunderstand the research (Lidz and Appelbaum 2002). Research and clinical standards influence expectations in two different ways. To begin with, clinical treatment concentrates on a single patient's issues. Second, the goal of research is often to generate generalizable knowledge. Clinical care benefits an individual patient in this way, whereas research benefits future patients collectively. When a participant is unable to distinguish between the imperatives of clinical care (routine treatment) and clinical research, he or she inadvertently attributes the intention of patient therapy (treatment) to research procedures. Despite being widespread in clinical studies, therapeutic misconception can also occur in non-clinical settings (Lidz and Appelbaum 2002). A case of therapeutic misconception occurred in a clinical trial setting where FDA-approved drugs were tested for efficacy in participants. The study's findings revealed a high prevalence of therapeutic misconception among the participants (Appelbaum et al. 2004). The therapeutic misconceptions in this study ranged from

participants' incorrect beliefs about the individualisation of their treatment (31.1%) to unreasonable beliefs about the likelihood of benefit (51.1%). On one (n=93) or both (n=46) of these bases, 61.8% (n=139) had therapeutic misconception. There is more evidence of therapeutic misconception in clinical trials, which is in research that is not always conducted in the context of biobanks.

Horng and Grady (2003) use the following analogy to explain the phenomenon of therapeutic misconception. Mark has a therapeutic misconception that contradicts a phase I cancer clinical trial. His interpretation of the trial is that the chemotherapeutic agent's goal is to shrink his tumour, when in fact the goal is to test for safety. Therapeutic misconception is a barrier to informed consent (Lidz and Appelbaum 2002). The phenomenon thus points to a lack of comprehension of the research, which is meant to be addressed during the consent procedure. The above examples of therapeutic misconception are unrelated to biobank research. On this basis, the claim that therapeutic misconception is only prevalent in biobank research (Van Beers et al. 2018) is misguided and thus implausible because it is not factual. Additionally, the claim is unsupported by anything other than the argument that participants in the experiment should be made aware that, while therapeutic benefit is hoped for and feasible, it is improbable and that they could become worse off as a result of taking part. Another reason this claim is implausible is that informed consent and its process are not only a feature of biobank research but also of all research involving humans. Any therapeutic misconception should be addressed. This is because failure to do so may foster mistrust in researchers and the healthcare system as a whole if participants believe they were deceived (Appelbaum et al. 1987). Casati et al. (2022) propose a risk assessment tool for managing uncertainties and ensuring active informed participation in order to address therapeutic misconception. The assumption that

biobank research is not applicable to clinical needs is also part of the argument. This premise is also false, rendering Van Beers et al.'s argument invalid. This is due to the fact that biobanks, in practice, store samples for future research of communicable and non-communicable diseases, the results of which are applicable to clinical needs.

The discussion that follows responds to the alleged loss of autonomy associated with future genomic research. According to Hoedemaekers et al. (2006), genomic research results in a loss of control and, as a result, autonomy over samples and data. The authors do not elaborate on this claim, but it appears that, according to them, the consent procedures used in genomic research do not meet the ideal standard of informed consent. Chapter 4 discusses the validity of informed consent and the standard of biobank research consent. It is unreasonable to claim that genomic research, and not all research involving human samples and data, results in participants losing control of materials. This is because all of the materials would be in the researcher's custody and thus subject to the same types of risks, if any, throughout the duration of the research. According to Hoedemaekers et al. (2006), only genomic research that contributes to individual autonomy and/or social function contributes to the common good. Attempts have been made to strike a balance between beneficence or rights and autonomy and the common good, which most ethicists believe are in conflict (Sutrop 2011). Strand claims that the rights of dissidents (those who hold the minority view that research will not serve the common good) within a common good context may be influenced by two factors. These include the significance of what the minority claims or recognizes to be at stake, as well as the legitimacy, plausibility, or reasonableness of the dissidents' point of view (Strand 2011). Without respect for an individual's autonomy, beneficence may result in non-beneficial actions because such actions would have been done against that person's will in order to promote the

person's well-being (Sutrop 2011). This means that striking a balance between autonomy and beneficent actions is critical.

Principles that need to be balanced are not absolute, but are considered prima facie. As a result, they must be fulfilled unless they conflict with a stronger or equal obligation (Beauchamp and Childress 1994a:33). Balancing prima facie obligations necessitates providing good reasons for such a decision (Beauchamp and Childress 1994e:189). One point of view on balancing autonomy and beneficence holds that if the research benefits society sufficiently, research without the participants' consent is justified (Veatch 1995). As previously stated, one of the CIOMS guidelines recommended reasons for informed consent waiver by RECs is if the potential research has social and scientific value. Research's social and scientific value is based on three factors: (1) the quality of the data it produces, (2) its applicability to major health issues, and (3) its contribution to the development and assessment of interventions, practices, or policies that advance health, whether it be individual or public health (CIOMS 2016).

2.5 Conclusion

Biobank research is important for advancing health research, which improves disease diagnosis, management, and prevention. As a result, biobank research and research participants could be viewed as serving the common good. The notion of biobank research as a common good was defended in this chapter using the following justifications: (1) the notion that restricting the utility of biobank research will harm the development of health research and, consequently, disease diagnosis, management, and prevention would be jeopardized, (2) solidarity for biobank research due to its beneficial role in precision medicine and other research outcomes, and (3) such solidarity is linked to the philosophy of ubuntu and the concepts of dugnad,

communitarianism, and altruism, which are linked to the idea of the common good and use biobank research to advance the wellbeing of others. One counter-argument to the idea that biobank research should be considered a common good is that it violates individuals' right to autonomy. A counter-argument to this counter-argument is that researchers have a duty not only to be non-maleficent, but also to safeguard research participants from harm. Following this analysis in support of biobank research as a common good, the following chapter examines the current regulatory framework applicable to biobanks, particularly how broad consent is applied.

Chapter 3

The South African regulatory framework relevant to broad consent for biobank research

3.1 Introduction

The current regulatory framework for biobank research consent in South Africa is examined in this chapter. A special emphasis is placed on broad consent as a means of identifying any gaps in determining what the framework should be in that regard. The use of personal data and samples for research purposes is influenced by a variety of laws and guidelines. Personal information and personal data are used interchangeably. First, an overview of the relevant national legislation and guidelines is provided, with a focus on POPIA and the uncertainties it creates around broad consent. As a result, this chapter discusses the implications of these instruments for biobank research consent. The POPIA debate serves as a backdrop for the defence of the claim that POPIA, as part of the current regulatory framework, is ambiguous and unclear about whether broad consent is permissible in terms of personal information. This defence meets the current study's Objective 2. Subsequent to that, as a follow-up discussion on the various interpretations of POPIA, the diverging views on legal interpretations are considered.

By virtue of the notion that sample transfers and personal information are frequently linked, this chapter also discusses the law's implications for limiting biobank research. Following that, open science is considered in terms of personal data access and use, as well as data commercialisation. In addition to national regulatory instruments, relevant international instruments are being examined in order to improve SA's current

framework for broad consent for biobank research. Furthermore, a comparison of the NDoH Ethics Guidelines, the SA MTA, and the WMA Declaration of Taipei regarding consent for storage and future uses of human samples is provided in order to improve the NDoH Consent Form Template. The first edition of the NDoH Ethics Guidelines was published in 2004, the second edition in 2015 and it is currently under revision towards a third edition. The NDoH Consent Form Template has been removed from the 2023 draft version of the NDoH Ethics Guidelines and seems to have been replaced with a Template for genetic and genomic informed consent documentation. The latter Template does not cover storage and future research use of samples and data that is typical of biobank research but is more specific for genetic and genomic research which is characteristic of not only biobank research but general health research as well. As mentioned in chapter 1, section 1.3, genomic or genetic research is only a subset of biobank research and does not encompass all forms of biobank research, despite what appears to be a common assumption in the literature regarding biobank research. Guidance in the latter Template mentions the responsibilities of researchers to inform participants on research-associated risks of harm such as: a feeling of faintness, risk of infection and a bruise caused by the drawing of blood as well as the risk of confidentiality breaches. Other information considerations to the participants that the Template recommends include: disclosure of research results and incidental findings to participants in the context of genetic and genomic research; considerations for informing participants on limiting disclosure of their personal information to researchers as well as information on participants' rights to withdraw from the research. Section 4.1.2.3 of the 2023 version Template does mention that broad consent could outline the kinds of secondary research that could be carried out, the kinds of personal data or biological materials that might be used in the secondary

research, whether the materials and data will be shared, as well as the names of the organisations or researchers that will use the materials or the information, how long the samples and materials might be kept, maintained, and used, whether participants will be notified when any follow-up research is carried out, whether participants will be given access to the results of follow-up research, and how participants can contact researchers with questions regarding the storage or use of their materials and information. It is imperative to describe the nature of future usage "as fully as possible" NDOH 2023:67) and to specify that an additional ethical review of the new research is required beforehand. In addition, if the intended future usage falls outside the scope of the existing consent, permission may be requested to get in touch with the individual again and obtain fresh consent. These information disclosures are not provided for in the form of a consent template in the 2023 version. I therefore propose that a consent template for sample and data storage in the context of future research similar to the Consent Form Template presented in the 2015 edition be included in the 2023 version of the NDoH Ethics Guidelines. An analysis of this Template is provided in Table 2 and Appendix 1 of this thesis.

3.2 Analysis of the regulatory framework for broad consent in biobank research

In SA, there is no single regulatory framework that is dedicated to biobank research. As a result, several instruments are employed as guidance.

3.2.1 The Constitution, 1996

Parliament has national legislative authority in SA, with the Constitution of the Republic of South Africa (RSA) Act 108 of 1996 (hereinafter the Constitution) serving as the supreme law of the Republic. To the extent of the divergence, every act or law that violates the Constitution shall be deemed illegal (The Constitution 1996). Participation in research consent is governed by South African legislation as part of the broader requirement for consent to medical intervention (Nienaber 2010). The Bill of Rights' section 12(2)(c) provides the right to informed consent by prohibiting unconsented medical or scientific research. Significantly, the right to refuse participation in medical or scientific studies without participants' informed consent is absolute, according to section 12c of the South African Constitution. This means that even though the Bill of Rights restricts some fundamental rights, the right to informed consent specifically may not be restricted, violated, or suspended in any way. Before Castell v. de Greef 1994 (4) SA 408 (C), which defined the principles for informed consent and material risks in health practice, the principle of informed consent received little consideration in South African law (Juta 2018).

In Castell v. de Greef 1994 (4) SA 408 (C), the plaintiff accused the defendant (a plastic surgeon) of negligence for allegedly failing to disclose the risks associated with a surgical procedure on the plaintiff's breasts for the removal of a lump (Juta 2018). The jury found that the defendant had a responsibility to warn the plaintiff of significant risks and offer an alternate procedure. It was also determined that if the defendant had not neglected these duties, the plaintiff would not have undergone the surgical procedure or would have considered an alternative, and the plaintiff would not have suffered damages (negligent scarring and damage to breast tissue, failure to prevent infection

post-surgery etc.). Castell v de Greef 1994 (4) SA 408 (C) resulted in the development of the doctrine of informed consent in SA in terms of medical information disclosure (Njotini 2018).

In McDonald v Wroe 2006 (3) All SA 656 (C), the plaintiff sought treatment from a dentist for an infection close to where her wisdom teeth were. Following that, the dentist surgically extracted three of the affected teeth (Carstens 2017). This allegedly caused the plaintiff to have permanent numbness and "pins and needles" sensations in the area. She then subsequently sued the defendant for this. The defendant failed to refer the plaintiff to a specialist surgeon for the surgical treatment, and failed to warn the plaintiff of any potential risks or complications, both of which were grounds for the court to find the defendant negligent (Carstens 2017).

The appellant (Venter) sued Roche (first respondent) and Dr Gouws Incorporated (second respondent) in Venter v Roche (A11/2014) [2014] ZAWCHC 157 for damages resulting from bowel perforation following clinical trial medication administration (SAFLII 2014). The respondent asserted that as part of obtaining informed consent, the respondent agreed to abide by the terms and conditions of both the SA guidelines and the Association of the British Pharmaceutical Industry (ABPI) guidelines for calculating compensation for injuries sustained during clinical trials. Compensation for patient injuries resulting from trials is one of these terms. Such compensation would be comparable to the damages typically awarded by South African courts in the event of an injury, assuming legal liability is acknowledged. The recruiting clinician, Dr. van der Merwe, and the appellant had different interpretations of the consent document. This was in relation to medical injury compensation. The latter was under the impression that full compensation would be provided, whereas the former testified that he would have made it clear to the appellant that he (the respondent) would only pay

for any growths caused by trial medication. The appellant, however, would not be entitled to compensation for any inconvenience caused by the growths. The court determined that the sponsor's compensation fell short of a legal requirement. The appeal was also dismissed after speaking with the defendant's attorney, who disclosed that the defendant was prepared to forego the claim for appeal expenses.

The preceding cases highlight the significance of the doctrine of informed consent, which binds health practitioners. Furthermore, Venter v Roche emphasizes the significance of research participants' comprehension of the consent document. As a result, the model of consent used should be clear to researchers, understood by participants, and thoroughly reviewed by RECs (Strode and Singh 2014). Parliament, as the legislative authority, is responsible for passing legislation on any matter, in addition to Constitutional amendments (The Constitution 1996). Acts of Parliament, for example, the NHA, are relevant to the discussion of informed consent for health research, including biobank research.

3.2.2The National Health Act, 61 of 2003 (NHA)

The NHA regulates the South African health system and takes into account the requirements set forth by the Constitution and other laws governing health services. The use of human samples, including their use for scientific purposes, is governed in particular under Chapter 8 of the Act. The NHA's Section 71(1)(b) permits consent if the participant is made aware of the study's goals and any possible health concerns. There is no other discussion of informed consent for human research except in section 71. On the other hand, Section 72 of the Act outlines the formation of a National Health Research Ethics Council (NHREC), which is tasked, among other things, with setting standards and norms for conducting research in animals and humans, as well as

providing additional guidance on consent (NDoH 2015). Before delving into the relevant aspects of the national ethics guidelines, a discussion of the relevant NHA Regulations in terms of consent is provided below.

3.2.3 Regulations relating to Research with Human Participants, 2014

Regulation 2 of the 2014 Regulations states that health research involving human participants must follow appropriate consent procedures. It establishes the 2015 NDoH Ethics Guidelines as the mandatory minimum standard for health research, recognizing the Ethics Guidelines' legal force. Regulation 5 of the 2014 Regulations outlines what participants should be informed of, which includes providing them with research-related information on the purpose, methods, and procedures, potential risks, benefits, the freedom of choice as to whether or not they should participate or withdraw, how privacy and confidentiality will be maintained, reimbursement for participation, researcher contact details, information about the research sponsor, insurance in cases of research-related injury, and the accessibility of products or beneficial interventions following research, together with any potential conflicts of interest, details about authorized authorities' approval (e.g. RECs). Broad consent for future research uses of human samples is not mentioned in the 2014 Regulations, likely because such instructions should be included in the Regulations relating to the use of Human Biological Material.

3.2.4 Regulations relating to the use of Human Biological Material, 2012

These Regulations, which aim to regulate the collection and use of material obtained from humans, include a broad definition of human biological materials (HBMs), commonly known as samples or biomaterials. The consent for the storage and control

of human biological materials is less clear, even though Regulation 3 mandates consent for their removal. In accordance with Regulation 13 of the 2012 Regulations, consent is required before genetic material, stem cells, and research findings are retained for an extended period of time, but nothing about long-term storage, control, and handling of other sample types or information from other types of samples is mentioned. The Regulations are also silent on future human sample research, which is typical of the broad consent model.

The preceding discussion emphasizes that the national regulatory instruments discussed thus far do not sufficiently cover sample storage and broad consent for future research use of samples and associated data. Notably, the NDoH Ethics Guidelines, which have quasi-legal standing and serve as a benchmark for ethical guidance in human research, include guidance on these two issues, as discussed below.

3.2.5 Department of Health, National Ethics Guidelines: Ethics in Health Research - Principles, Structures and Processes, 2015 (NDoH Ethics Guidelines)

The NHREC developed the NDoH Ethics Guidelines in order to guide researchers on ethical and responsible research practices (NDoH 2015). Informed consent is one of the key norms and standards for guiding ethical research, according to the NDoH Ethics Guidelines. Section 3.3 specifically addresses the use of samples and data for research purposes. The NDoH Ethics Guidelines include recommendations and restrictions for the purpose of human sample collection in relation to the type of informed consent sought and granted by healthcare professionals and research participants or patients, respectively (NDoH 2015). The NDoH Ethics Guidelines define three purposes for biomaterial collection: (1) specific research purposes, (2)

therapeutic or diagnostic purposes, and (3) a combination of purposes including future research use (NDoH 2015: Section 3.3.4). These Guidelines do not advocate the use of blanket consent based on the idea that it would make it difficult to uphold the principle of respect for persons (section 3.3.6).

As mentioned in section 3.1 of this thesis, section 4.1.2.3 of the Guidelines permits broad consent use provided that (1) the type of additional usage is "described as fully as possible" (NDoH 2023:67) and (2) prior HREC review for the new research is obtained (NDoH 2015). The rationale for informing participants of third-party use of their materials is based on a history of mishandling of human samples and associated data that does not align with consent granted, resulting in material commercialisation in some cases (Moodley and Kleinsmidt 2020; Steinbekk et al. 2013; Petersen 2005; Eriksson and Helgesson 2005). Overall, the NDoH Ethics Guidelines provide guidance on what is meant by consent information for future use of samples in that researchers should: (1) inform participants that their samples will be used in future research; (2) give them the option of sample anonymization (with an explanation of risks and benefits); (3) inform them of their right to dissent or withdraw participation; and (4) inform them of measures that they (researchers) will take to maintain confidentiality (Section 3.5.2.3). The draft version 3 of the NDoH Ethics Guidelines (2023) additionally mention restrictions on sample collections with regards to broad consent use to protect certain persons, namely that: samples cannot be collected from mentally ill or incapacitated people without Ministerial approval; minors cannot have their naturally replaceable samples taken from them; no gametes can be taken from a minor; and no fetal sample can be collected from anyone other than umbilical cord progenitor cells. When applicable, HRECs must ensure that the required special permission has been secured. The 2023 Guidelines further mention that if security and

confidentiality safeguards are insufficient, coded materials might reveal the identity of a participant or donor. Moreover, that HRECs should ensure that the researcher has sufficiently addressed this component. On protection of confidentiality, the Guidelines recommend that the person in charge of the coded data must retain the code key and that an explicit written agreement not to disclose the sample identifiers to the study team should be signed by the one who holds the code or link to the samples. Moreover, that the submission to the HREC must be accompanied by this agreement. I provide further recommendations on practical considerations for ensuring unauthorised access to biobank materials and thereby ensuring sample associated data confidentiality in chapter 6, section 6.5.1.

Although the NDoH Ethics Guidelines state that research proposals should specify whether or not incidental findings (IFs) will be communicated to research participants, this aspect is not addressed in the 2015 guidelines' consent template for storage and future use of unused samples. IFs are unexpected discoveries that arise during research but are not intended to be part of that research (NDoH 2015). An IF of chromosomal or genetic variant with potential clinical significance, an IF of misattributed paternity, unexpected detection of mass (aneurism) during magnetic resonance imaging (MRI) of the brain, and an unexpected mass in the lung detected during computed tomography (CT) are examples of IFs with the potential for health and reproductive significance (Wolf et al. 2008). It is suggested that the possibility of IFs be mentioned in consent documents as part of the information provided to participants (Wolf et al. 2008). Several laws and policies governing the return of research findings are being gradually influenced by professional societies that advocate for the reporting of findings and stipulate that researchers should, must, or may return results (Thorogood et al. 2019). The return of IFs should be a mandatory

requirement for researchers, based on the notion that research involving humans represents a common good and thus should be for the benefit of individuals and the population at large (WMA 2016). Furthermore, the WMA Declaration of Taipei recommends that participants be informed of research findings, including IFs, in order to ensure the validity of biobank consent (WMA 2016). Although an analysis of the return of IFs is not one of the current study's objectives, it is important to consider as a factor that should be built into the information that participants should be made aware of, under a broad consent model, subject to REC oversight, and the sensitivity of the information relayed to participants must be properly evaluated. The next section addresses further recommendations on material transfer as outlined in the 2018 NHA Material Transfer Agreement Template for Biological Materials (SA MTA).

3.2.6 South African Material Transfer Agreement, 2018 (SA MTA)

Concerns regarding the lack of a national MTA in RSA were expressed in 2012 by Sathar and Dhai as well as by Moodley and Singh in 2016. The SA MTA, which was published in 2018, is the first national model to establish a framework for the Parties (Providing Institute, Recipient Institute, and HREC) to engage in the usage, transfer, and other processing of materials (SA MTA 2018). The SA MTA instructs that the supplier of human materials submit completed participant consent forms to the HREC for approval and informed consent for secondary material use, if necessary, along with the research methodology (SA MTA 2018).

Thaldar and Townsend (2021) criticize the SA MTA specifically in terms of consent, claiming that the MTA introduces dynamic consent. According to the authors, the SA MTA introduces this consent model by stating that consent for new material uses must be sought on an ongoing basis. Furthermore, they claim that the SA MTA's concept

deviates from NDoH Ethics Guidelines, which recommend broad consent for future research use of samples (Thaldar and Townsend 2021). Furthermore, they point out that the SA MTA's "dynamic consent provisions" supersede those of the NDoH Ethics Guidelines because it is a more recent piece of secondary legislation, particularly when research involves the movement of samples across institutions. One could contest the assertion that the SA MTA introduces dynamic consent.

The MTA is in agreement with the principles of the NDoH Ethics Guidelines that informed consent should be obtained for secondary use of material if such use is necessary but does not support any specific model of consent (i.e., for future uses of material). In this sense, it is evident that the present NDoH Ethics Guidelines have influenced the regulation of secondary material uses in the SA MTA when the it is read in conjunction with the NDoH Ethics Guidelines. The SA MTA defines material as samples or human biological material (including personal data) and any associated data. The Protection of Personal Information Act 4 of 2013 (POPIA), which is referenced in Chapter 1, section 1.1, defines standards for the processing and protection of personal information in South Africa. One of the requirements under the Act for processing personal information is consent. As a result, the following section presents POPIA consent provisions as they pertain to broad consent.

3.2.7 Protection of Personal Information Act 4 of 2013 (POPIA)

Although the NDoH Ethics Guidelines address and allow broad consent for sample collection, there is a discord between the NDOH Ethics Guidelines and POPIA, which requires data collection to be for a specific purpose (POPIA 2013, section 13(1)). This, by implication, precludes future research use of sample-related data, which is typical of broad consent. However, research-specific exceptions under POPIA imply that

future uses of personal information are permissible under certain conditions (POPIA 2013), implying that broad consent is permissible. The NDOH Ethics Guidelines is silent on the protection of personal information derived from samples collected for future use. It does, however, refer researchers to POPIA without referring to a specific section.

POPIA governs the protection of personal information in accordance with Section 14 of the Constitutional right to privacy. The Act establishes duties and rights for the protection of personal information and applies to the activity of personal information processing. According to the Act, processing is a broad concept. Section 1 of POPIA defines "processing" as any activity that includes "collection, receipt, storage, updating, retrieval, dissemination, or degradation," as mentioned in Chapter 1 section 1.1. While human samples and their associated data are covered by the NHA, its Regulations, and the NDoH Ethics Guidelines, they are not covered by POPIA. Data associated with a biological sample, on the other hand, would be considered "personal information" and thus subject to POPIA (Mahomed and Staunton 2021). POPIA establishes minimum standards for personal information processing, including genetic and health information. According to POPIA, there are eight requirements that must be fulfilled when processing personal information: (1) accountability; (2) processing limitation; (3) purpose specification; (4) further processing limitation; (5) information quality; (6) openness; (7) security safeguards; and (8) data subject participation. The accountable party (the research institution or researcher in the context of research) is accountable for ensuring that personal data is processed lawfully, in compliance with the eight POPIA requirements, and in a way that does not infringe on people's constitutional rights to privacy (Adams et al. 2021). The Act will have an impact on all

research activities involving the collection, processing, and storing of personal data, including biobank research activities.

According to Section 11 of the POPIA, consent is one of the requirements for the authorized processing of personal information. In addition, Section 13 (1) of the Act mandates that the reason for collecting personal information be “specific, explicitly defined” purpose in relation to the activity to be undertaken. On the surface, it appears that specific consent is required by POPIA. According to Thaldar and Townsend (2021), the POPIA-required consent model is specific consent, and such specific consent should be sought for any processing of research participants' health information, including the sharing and storage of health research information. Using broad consent, which is typically unspecified consent, may thus be a violation of the Act. Master et al. (2012) correctly assert that limitations of this type hamper the importance of biobank research given the long-term nature of biobanking. This makes obtaining specific consent for each and every future study impossible. As a result, biobanks' broad consent is justified. The implications of legal limitations on biobank research are discussed further in section 3.2.5.2.2 of this chapter.

While POPIA is not industry-specific, it provides for the development of Codes of Conduct (COC), which direct how the Act should be interpreted in relation to a certain class of information or industry. The ASSAF is currently in charge of the procedure for developing a Code of Conduct for research under POPIA (Adams et al. 2021). The field of health research is covered by the COC for research. Despite the requirement in Section 13 of POPIA that personal information be collected for a "specific, explicitly defined" purpose, the Act contains exceptions that permit the processing of additional personal information for research purposes when the data is not published in an

identifiable form (section 15(e)) (POPIA 2013). As a result, POPIA contains exceptions for the processing of personal information for research. Sections 27(1) and 35(1) of POPIA also provide for the processing of children's information and special personal information for research serving a public interest, provided that processing does not adversely impact the privacy of the data subject or research participant in the case of health research (Adams et al. 2021). Table 1 (Adams et al., 2021) below lists the exceptions to POPIA that particularly relate to research.

Table 1: POPIA research exceptions

Research specific exception	**POPIA section related to the exception**
1. Records containing personal information may be retained longer than necessary for research purposes if sufficient protections are in place.	Purpose specification: Condition 3, s.14.
2. Personal information should not be processed further unless it is going to be utilized for research and will not be published in an identifiable manner.	Further processing limitation: Condition 4, s. 15(3).
3. If the information is collected for research purposes, it is not necessary for openness to prevail when informing participants about the collection of their personal information as required by s. 18(1).	Openness: condition 6, s. 18(4).
4. The restriction on processing special personal information, which includes information about a person's race, ethnicity, religion, biometrics, health, and sexual life, does not apply when the processing is done for research and the goal is in the public interest, when obtaining consent seems impossible or would require an unreasonable amount of work, or when there are sufficient safeguards in place to ensure that the processing will not negatively impact a person's privacy.	Special personal information processing: S. 27(1).
5. Personal information about inherited characteristics may not be processed unless it is required for a research activity.	"Authorisation concerning the data subject's sex or health life" (Part B, s. 32(5)).
6. Prohibition on processing personal information of children is not applicable if it is for research purposes, serves a public interest or obtaining consent seems to be difficult or would require an undue amount of work, and enough safeguards are in place to ensure that the processing will not adversely impact the child's personal privacy in an undue manner.	Processing of children's personal information is generally prohibited: Part C, s. 35 (1).

3.2.8 POPIA and broad consent for biobank research

There is academic support for the argument that consent under POPIA should be explicit, as was noted in the previous section. The broad consent model of the Act is supported by some scholarly theories, nonetheless. As noted in Chapter 1 section 1.1,

Staunton et al. (2019) maintain that POPIA permits broad consent for the use of personal information, but Thaldar and Townsend (2021) contend that this is not the case. Clarification is necessary due to conflicting interpretations of section 13(1) of POPIA's definition of "specific, explicitly defined, lawful purpose" as it relates to the collection of personal information. This would guarantee that limitations on the use of broad consent, particularly in the context of biobank research, do not impede the urgently needed human health research agenda while still providing necessary protections for study participants.

Since POPIA is not a research framework in and of itself, it is not surprising that there is a difference between POPIA and the NDoH Ethics Guidelines with regard to consent. Nonetheless, these differences draw attention to the need for a more simplified regulatory framework, especially in the context of obtaining broad consent for future uses of biobank research data. POPIA Code of Conduct for Research is being developed by ASSAF to help research institutions and researchers comply with POPIA while also ensuring that proper measures are in place to preserve research data and to hold those who violate POPIA accountable. At the time of the current study, the most recent version of the Code was made available for public comment on September 23, 2022. The Code makes a distinction between (1) POPIA consent, which is the consent required by POPIA for the use of personal information, and (2) research consent, which is the consent required for research under section 12(c) of the Constitution, the NHA, and the NDoH Ethics Guidelines, and thus consent for medical and scientific experiments. Version 8.7, section 4.3.3.3.5 of the Code outlines the legal justifications that must apply when research does not contain special personal information and stipulates that (1) POPIA consent should not be speculative and must clearly indicate the specific purpose for which personal information is being

processed; (2) for future uses of the personal information, provided that such uses are described "as fully as possible;" and (3) restricts further use of the personal information. According to Section 4.3.5 of the Code, it is also acceptable to reuse personal data without the research participant's POPIA approval provided it is exclusively used for research and will not be disseminated in an identifiable form. Nonetheless, participants may be notified of further processing in accordance with Condition 6 (Openness and Notification requirement). As a result, version 8.7 of the Code acknowledges that participants' consent will frequently depend on information sharing (whether to POPIA Consent or research Consent). In other words, researchers must ensure that participants have adequate information to make an informed decision while using POPIA Consent (s 4.3.7.2.1).

When using broad consent, this condition of "adequate information" could provide a challenge. Furthermore, the Code does not specify whether broad consent is acceptable for processing personal information in the field of health research, despite the fact that it does not prohibit it. The current study has brought to light the various ways that POPIA has been interpreted in relation to the legitimacy of broad consent. The ramifications of such diverse interpretations permit the processing of personal information that does not align with the consent that was obtained, which may lead to regulatory non-compliance. On this premise, I argue that, despite the fact that POPIA has exceptions, it is still uncertain and confusing whether or not broad consent is acceptable for research. In order to ensure consistent interpretation in biobank research, clarification is necessary.

3.3 Defence of the claim that the current regulatory framework, specifically POPIA, is ambiguous and unclear regarding the permissibility of broad consent

As mentioned in the preceding section, divergent interpretations of the permissibility of broad consent for the use of personal information for research purposes under POPIA cast doubt on already established health research practices. This necessitates clarity. There are several types of ambiguities in law, including (1) lexical ambiguity, which refers to a phrase or word with multiple valid meanings; (2) syntactic ambiguity, which refers to a sentence with more than one valid grammatical interpretation regardless of context; (3) referential ambiguity, which is a grammatically sound sentence with a reference that the reader might misunderstand given the context (Massey et al. 2009). The ambiguity in section 13(1) of the POPIA could be argued to be referential ambiguity because, while the words "specific, explicit, lawfully defined purpose" are clear, confusion arises due to the context provided. Ambiguities make it difficult to read, comprehend, and analyse legal texts (Massey et al. 2009) This could mean the difference between compliance and non-compliance with regulatory requirements (Massey et al. 2009). According to Massey, original legal text may be written ambiguously in order to allow courts to determine what is appropriate or reasonable (Massey et al. 2015). In cases where legislation is ambiguous or absent, principles decided by judges in case law may take precedence (Martin 2008). However, there is no case law in SA to this effect regarding personal information.

In terms of its application to genomic research in South Africa, the fundamental problem with POPIA, which is the requirement for consent that is for a specific, explicitly defined purpose, appears to be cause for concern (Staunton et al. 2020). The authors specifically mention genomic research in this paper. However, Thaldar and

Townsend (2021) point out that section 13(1) of POPIA is problematic for health research in general because it limits the purpose of personal information collection. Staunton et al. (2020) go on to say that specific consent is not the only type of consent for responsible research. Furthermore, as evidenced by the table of exceptions provided in section 3.2.5, POPIA allows for broad consent for further processing of health data for research purposes. Divergent interpretations of the law and their implications merit discussion, which is presented below.

3.4 Divergent views on interpretations of the law

Perkins (2021) asserts that we must take into account a number of factors in order to find the most reasonable interpretation of legal texts.: (1) the pre-statute status quo of human behaviour; (2) the type of concerns that legislature members had when proposing the statute; and (3) the intention behind statute promulgation in addressing their specific concerns. The difficulty with statutory interpretation is that seemingly unambiguous statutory provisions can cause serious problems in practice (Brannon 2018). Statutory interpretation can take several forms (Manning 2006) (1) textualism, which emphasizes semantic context (word usage), whereas (2) purposivism emphasizes a policy context approach to interpretation (problem-solving). Although both categories of statutory interpretation acknowledge conceptual common ground, textualists criticize purposivism for entailing an ineffective search for arbitrary legislative intent (Manning 2006). The purposivism-textualist debate is complicated because determining the meaning of words without acknowledging the purpose is difficult (Colinvaux 1997). Furthermore, the need to interpret a statute may indicate that the law is only partially complete. As a result, clear, unambiguous regulation is critical. Although the constitution is acknowledged as the supreme law, this does not

mean that the optimal constitutional interpretation theory will be based only on the constitution's text (Fallon 1999). In this context, constitution refers to any constitution, not necessarily the Constitution of RSA. As a result, constitutional theories have been classified as (1) text-based theories, which seek validity through interpretation of constitutional text, and (2) practice-based theories, which are based on judicial decisions in court cases and go beyond interpretation of constitutional text (Fallon 1999).

Horowitz contends that legal interpretation cannot be ethical in a narrow sense and that context is critical (Horowitz 2000). When applied to the context of broad consent for biobank research, this means that specific (narrow) consent would result in little or no biobank research being conducted in SA, because broad consent is the preferred consent model for biobank research (Mahomed 2020; Tindana et al. 2020; Mwaka and Horn 2019; Moodley and Singh 2016). This, combined with the fact that samples and their associated data (which may contain personal information) are linked, necessitates clarification of a perceived conflict in research between the NDoH Ethics Guidelines and POPIA. As a result, an enabling framework that takes into account the various research contexts and uses of personal information is required.

The position I advance in the current study is that the South African regulatory framework should legally permit the use of broad consent for personal information given the future-oriented nature of biobanking and the current NDoH Ethics Guidelines, which allow the use of broad consent as long as it protects participants' rights, including the right to decide whether or not to participate in research (autonomy). As a result, a framework geared towards biobank research will be necessary. Regulations for biobanks should not be unduly strict, instead, they should

guard against exploitation in research in order to advance science and, ultimately, improve the health of the populations concerned (Staunton and de Vries 2020).

3.5 Consequences of the law limiting biobank research

According to Laurie, some of the challenges in health research include regulatory silos in which different aspects of research, such as those dealing with participant data, tissues, and embryos, are subject to different legislation, resulting in a lack of reflecting reality in research practice (Laurie 2016). This has the potential to impair the effectiveness of regulatory oversight, which is critical to health research. Furthermore, fragmented regulatory frameworks or silos do not improve compliance. The terms "oversight" and "accountability" are frequently used interchangeably to refer to biobank regulation (Rothstein 2005). In the context of the current study, "oversight" refers to the broader regulation of health research in addition to the former definition.

Hallinan (2020) discusses a purported limitation of the General Data Protection Regulation (GDPR) on broad consent, but also points out that the Article 29 Working Party issued additional guidance regarding the specificity of the consent required in regards to scientific research in 2017 after the GDPR's adoption. Under the predecessor of the GDPR, Directive 95/46, the Article 29 Working Party was the entity charged with interpreting data protection law at the EU level. Representatives of the national Data Protection Authorities (DPAs), the organizations tasked with interpreting and upholding data protection legislation in EU Member States, constituted the committee. Adversely, the Working Party's 'Guidelines on consent under Regulation 2016/679' contain significantly less sympathetic declarations on Recital 33 and broad consent. It is possible to interpret two components of the Working Party's advice as particularly troublesome for broad consent. Secondly, the guidance seems to try to

narrow the extent of applicability of Recital 33 and hence of broad consent. This implies that, in theory, projects involving scientific research can only use personal data with authorization if they have a clearly defined goal. Article 33 permits as an exception the purpose of data processing to be expressed at a more general level in the instances where the purposes for data processing within a scientific research project cannot be specified at the outset. Second, the guideline appears to support the necessity for periodic rolling granular consents rather than a single, ex ante, broad consent in circumstances where Article 33 would still apply. The term "ex-ante" refers to an estimate of a variable when there is ambiguity regarding its value before a process has begun (Lexis Nexis 2023). Ex ante, which means "before," is a Latin term. Ex post refers to the term for an unclear variable that is known after the process has concluded (after the fact) (Lexis Nexis 2023). Consequently, the scope to which consent may ever be a practical basis for processing in the context of banking personal data and associated samples has been severely reduced as a result of Article 33 guidelines in terms of interpreting and restricting the use of broad consent for research (Peloquin et al. 2020).

Through their gatekeeping roles on research protocol review and approval, RECs and BECs contribute to the regulatory oversight mechanisms for health research. According to Laurie (2011), such REC gatekeeping, as well as many of the legal frameworks that govern scientific research, are problematic. This is because they create oligarchies of science regulation that are driven by bureaucratic inspections that favour a tick-box mentality over genuine engagement with genuine ethical quandaries (Laurie 2011:351). In the South African context, where exploitation of African samples and data is not a thing of the past, and where the nature of research

is constantly changing (due to scientific and legal developments), the role of RECs must also change (Mahomed and Labuschaigne 2019).

Laurie (2011) suggests "reflexive governance" of biobanks in awareness of the law's limitations in regulating biobank research. Who are the relevant actors in respect to this approach, then, is a crucial question. This query may elicit a broad response in the context of biobanks and, beyond those in charge of the biobank itself, may involve funders, participants, regulators, ethics committees, or even the general public. But, if we adopt this viewpoint, we run the risk of creating a recommendation that is just impossible to implement. Additionally, this falls short of capturing the idea of governance partnership, which Laurie (2011) contends must also be at the core of any system of reflexive governance. Like any other relationship of this kind, it will be built on mutual respect, trust, and a shared desire to see the biobank succeed; in other words, trust will result from shared adherence to the idea of integrity of purpose. The parties will occasionally dispute on what is the appropriate thing to do, just like any critical friend; in these situations, the principle of proportionality of action will serve to direct and restrain behaviour. It is a good idea to have a backup plan in case something goes wrong. Critically, this reflexive governance system must work in concert with the advancement of the scientific enterprise, ensuring that, like any vital friend, advice and direction are available at every stage of the shared journey. By operating in this way, a system of reflexive governance can create value where none already exists. Reflexive governance, according to Laurie (2011), offers a framework for organic policy evolution through time. This can take into consideration a variety of values and interests, most crucially those of the participants, who can and will change over time. It is simultaneously responsive to the project's requirements and can take them into account. A reflexive governance approach's potential limitations are acknowledged,

and it would be dishonest to ignore them. Particularly, the reader is likely to have these queries in mind. (1) How, if at all, may participants or other stakeholders be included in the reflexive governance model? (2) Is the reflexive governance model still viable in the absence of strict legal penalties? The answers are as follows for each of these inquiries individually. In response to the first query about participant involvement in the model, some have argued that this is a crucial component of a sound governance framework because there is often perceived to be an "agency gap" in many biobank governance regimes, which is often taken to mean a lack of direct representation for participants on biobank decision-making bodies. Nevertheless, it is less certain if this is a suitable or efficient approach for large-scale, population-based efforts such as the UK Biobank. This may work effectively in the case of biobanks particularly established to address the health needs of its participants. This is true for a number of reasons. In the first place, it presents a significant practical challenge to achieve true representativeness for a diverse group of 500,000 individuals, and in the second place, it contradicts the far more comprehensive goal of such efforts that are carried out to further the public interest. It is suggested that the model can quickly become ineffective and/or lose its legitimacy in response to the second point, which questions if reflexive governance can function in the absence of hard law sanctions, without resorting to law. This, however, misses the mark in terms of what a reflexive governance regime can accomplish and, more importantly, what it cannot. A tick-box approach to top-down regulatory control is not a part of reflexive governance, nor is it about monitoring compliance, risk-benefit analysis, or ticking boxes. The irony is that if legal action must be taken even within established regulatory frameworks, the frameworks have already failed. Reflexive governance, on the other hand, focuses on creating and implementing principles and policies that remain appropriate for the task at hand for the duration of

a project. It also focuses on understanding and cooperating to meet expectations and address challenges as they arise. According to Laurie, the three basic principles of reflexivity, proportionality and integrity offer the ideal foundation for policy formation in the context of biobanking and may be accomplished without the use of the legal system. I discuss other, potentially viable, biobank governance solutions in chapter 5 section 5.3.3.

The national Department of Science and Innovation (DSI) Draft Policy on Open Science is another regulatory development worth considering. It demonstrates SA's support for the worldwide shift towards open science and extensive data sharing. This emphasizes the significance of obtaining broad consent for research (Draft policy 2022).

3.6 Analysis of the Draft National Open Science Policy in relation to personal data access and use

As previously stated, POPIA protects personal information in SA. Although POPIA is a restrictive piece of legislation, its implementation must be balanced with the less restrictive practices of open science, which SA is moving towards. There is a need for a clear legislative framework that will establish rules for data disclosure and other research inputs and outputs for the public good, ensuring equitable data access while protecting personal information (Draft Policy 2022). In recognition of the global trend towards open science, the Draft Policy (2022) was developed with the assistance of the SA-EU Open Science Dialogue Process (Draft Policy 2022). Through the help of an appointed Expert Task Group, a multi-stakeholder open science Steering Committee was formed. The goal was to facilitate an initial consultative workshop to engage key stakeholders. This forum discussed key issues, including compiling a report that was reviewed at a second workshop on February 21st, 2022, by

stakeholders who attended this workshop (Draft Policy 2022). The Draft Policy is intended to apply to publicly funded research. One of its goals is to increase national and international scientific collaboration for societal benefit through economic and ecological benefits, evidence-based policymaking, and a well-informed society (Draft Policy 2022). It adheres to the "as open as possible, as closed as necessary" principle to ensure that all publicly sponsored research yields the most benefit (Draft Policy 2022).

Transfers of sample associated data, which can include the transfer of personal data during research collaborations, as discussed in Chapter 1, predispose the data to misuse that is inconsistent with participant consent. As a result, the Draft Policy recommends long-term stewardship and curation of publicly funded research data by appropriately resourced public entities. This may be difficult to achieve because once data is transferred to a third party, the provider has little to no control over what happens to it. The Draft Policy was made available to stakeholders who attended the consultative workshop via email after the workshop, even though it had not yet been published at the time of the current study. As a result, it is relevant to the discussion on how to balance privacy requirements with open science initiatives.

Given that the concept of open science is based on unrestricted data access for any purpose, the issue of balancing research participants' autonomy and unrestricted data use requires further discussion. The Policy mentions that it is intended to promote protection of consent and privacy, presumably through the proposed open science framework, although the Policy does not address this aspect. The Policy, on the other hand, recognizes the need for a clear legislative framework for establishing the rules for data disclosure that will, among other things, protect personal information and commercial interests (Draft Policy 2022). The Policy's Annexure A refers researchers

to the Promotion of Access to Information Act No. 2 of 2000 (PAIA), presumably in relation to data access, despite the fact that the Policy does not make any further mention of the Act. PAIA governs information access, including the protection of a public entity's research data (PAIA 2000). Section 69 of PAIA refers to mandatory protection of a third party's research information in that access must be denied if disclosure is likely to expose the third party, the individual conducting the research, or the research subject matter.

In the current study, a number of issues have been raised in the previous discussions including the following: (1) on the surface, POPIA recognizes only specific consent, (2) this can result in limitations when interpreting POPIA for health research, particularly in the context of biobank research, and (3) research specific exceptions allow for further personal information processing, but whether this extends to applying broad consent in its traditional format is unknown. (4) As already mentioned in chapter 1, section 1.10, divergent interpretations of POPIA cause confusion in the research sector, given that the restrictive nature of POPIA must be balanced with the less restrictive practices of open science, and (5) the Draft Policy on Open Science mentions the need for a clear legislative framework for establishing data disclosure rules, which will protect personal information and commercial interests in the face of open data access, among other things.

3.7 Open science and data commercialisation

Given the increased pressure from funders to facilitate open science, it can be challenging for biobanks to acquire private funding (Joly et al. 2015). A formal requirement for funders includes the idea that researchers should make their findings available for commercial use. Moreover, the regulations of funding organizations

reflect a need for research networks to cooperate and commercialise their research findings (Caulfield et al. 2012). Commercialisation is defined differently depending on the context. For example, it is associated with human material misuse (exploitation) or exchanging samples and associated data for money (payment) and/or in a different context, namely the advancement of science such as drug and vaccine research. Although large collaborations that enable open access and data sharing, such as the Human Genome Project for mapping the human genome, contribute to significant scientific advances, participant privacy and confidentiality have been identified as ethical challenges for open science (Bisol et al. 2014; Atteveldt et al. 2021; Dennis et al. 2019; Phillips and Knoppers 2019).

The difficulty with open data access is in fostering creativity while guarding against improper, privacy-invading applications of such data (Borgman 2018). When data elements from one or more data resources are combined, the possibility of misuse and abuse increases. Misuse of human material would be a violation of participant autonomy (negative commercialisation), whereas scientific progress would benefit the public good (positive commercialisation). Patenting research outputs has also been considered commercialisation in the literature (Webster and Jensen 2011). The Patents Act No. 57 of 1978 permits and governs patenting of research outputs, although Section 60 of the NHA forbids payment for human samples (commercialisation) other than the costs of collection. People routinely unknowingly or intentionally share their personal information with organizations that use it to process, sell, or transfer it to other organizations for a number of objectives. Even if there is a legal framework in place to safeguard the privacy and confidentiality of personal information, this still occurs (Botes et al. 2021). When genomic data sharing is not managed correctly in accordance with the regulatory framework requirements, this

creates problems. This is due to the fact that the creator of the data set has IP rights and benefits from the curated dataset(s), while the individual from whom the data was collected does not (Botes et al. 2021).

When research sample-related data is used for commercial purposes, access can be revoked unless sample donors grant consent for commercialisation (Fortin et al. 2011). Data Transfer Agreements (DTAs) are a useful tool for regulating data access (Shabani et al. 2021). The SA MTA addresses IP, a type of commercialisation, by referring the parties to relevant laws pertaining to the applicable protocol (SA MTA 2018: Section 12). The Intellectual Property Laws Amendment Act No. 28 of 2013 and Section 60 of the NHA, which forbids the commercialisation of human samples, are the appropriate legislation in this situation. As indicated in the Sanger case discussed in Section 1.6.1 of Chapter 1, research collaborations complicate sample associated data commercialisation and protecting and safeguarding of materials due to the difficulty in controlling the fate of the materials once in the hands of third parties.

Borgman (2018) explains how two methods can be used to balance the benefits and risks of big datasets in order to prevent data misuse. One strategy is to follow the guidelines of limited collection, high-quality data, use specification, and purpose specification. Controlling how data is used after it has been obtained is the second method. Specifying who has access to what data, when, and under what conditions should be part of governance, as does defining what uses are acceptable and unacceptable.

The only document that regulates broad consent and future sample use in research, with a focus on consent information that should be given to participants, is the NDoH Ethics Guidelines. The Guidelines also recommend that participants be informed of

the potential for harm or discomfort. Participants should also be informed about risk-mitigation measures. In particular, when identifiers are retained, they should be informed of the type and extent of specific risks of harm linked with the use and storage of materials. Participants should be made aware that where there is a low risk of harm, a REC may accept a consent waiver for material secondary use. This is relevant when doing the research would be impossible without the waiver and the participant's interests and rights are unlikely to be harmed. Participants should also be informed about the implications of genomic research, genetic or genomic testing, such as paternity testing, and the risks associated with confidentiality. However, some aspects of consent information are not addressed in the NDoH Ethics Guidelines consent considerations, such as the provision for rules of access to the biobank (to safeguard the confidentiality and privacy of participants), commercial use of materials, benefit sharing, and material sharing with other countries. As a result, the following section examines the WMA Declaration of Taipei (2016) in order to improve SA's current framework for biobank research consent. International perspectives must be taken into account while interpreting the Bill of Rights, according to Section 39(1)(b) and (c) of the Constitution, which also states that foreign law may be taken into account.

3.8 WMA Declaration of Taipei, 2016

The WMA Declaration of Taipei offers ethical guidelines on health databases and biobanks. This guidance includes, among other things, provisions for valid consent in terms of information that participants should be given with regard to materials that are to be maintained in a biobank. The Declaration and the NDoH Ethics Guidelines, which are also largely included in the SA MTA, are somewhat aligned in relation to this information. As a result, Table 2 below outlines some of the important validity apects

relevant to consent for the storage and potential use of personal data and human samples. In an effort to enhance the NDoH Ethics Guidelines Consent Form Template indicated in section 3.1, Table 2 compares these instruments.

Table 2: Comparison of the NDoH Ethics Guidelines, SA MTA and the WMA Declaration of Taipei in relation to consent for storage and future use of human samples and personal data

Key information aspects for participants	**NDoH Ethics Guidelines**	**SA MTA**	**WMA Declaration of Taipei**
Purpose of sample collection or biobank	✓	✓	✓
Nature of material to be collected	✓	✓	✓
Risks associated with material collection, use, and storage	✓	X	✓
Investigate the possibilities and, where applicable, explain genetic research and its implications	✓	X	X
A choice between samples remaining identifiable or for de-identification of samples, explaining risks and benefits for each option	✓	X	✓
That samples will not be sold for profit	✓	X	X
Research conducted must have been approved by a REC	✓	✓	✓
The right to refuse and withdraw from research participation	✓	X	✓
If materials are no longer identifiable, the participant may not know what their material is used for and will not be able to withdraw consent	✓	X	✓
How privacy (WMA) and confidentiality (NDoH) will be maintained	✓	✓	✓
Procedure for return of results which includes IFs	X	X	✓
Rules of biobank access	X	X	✓
When applicable, commercial use, benefit sharing, IP, material sharing with other countries	X	✓	✓
Regulating transfers of personal data/personal information	✓(limited)	✓	✓

When the NDoH Ethics Guidelines, the SA MTA, and the WMA Declaration of Taipei are compared for their important informational elements, it becomes clear that the SA regulatory framework generally provides sufficient guidance on the consent information that should be given to biobank research participants. The Ethics Guidelines and the SA MTA are complementary to each other. The fact that neither of the two instruments mentions access rules to the biobank may be compensated for by the fact that the NDoH Ethics Guidelines require the biobank to state how confidentiality will be maintained. The NDOH Ethics Guidelines should be expanded to include guidance for commercial uses, benefit sharing, IP rights, and material sharing with other countries. Personal information (data), privacy, and confidentiality are all required by all three documents examined. The NDoH Ethics Guidelines do not provide any specific guidance for consent for data use. However, the SA MTA and the WMA Declaration of Taipei require that consent be obtained for data use. To ensure ethical processing of research data, the NDoH Ethics Guidelines must address not only consent for sample use but also consent for data associated with the samples. Although consent for the use of personal information and consent for the donation of samples for research are two distinct things, in the context of biobank research, sample transfers may also involve the sharing of personal information. Thus, mechanisms for data protection should be included in the consent framework.

3.9 Conclusion

According to the above analysis, specific consent appears to be a requirement under section 13(1) of POPIA, and that using broad consent, which is typically unspecified, could be a violation of the Act. There are conflicting interpretations of POPIA section 13(1). So, it is argued that POPIA casts doubt on whether broad consent is permitted,

even though there are exceptions for the processing of personal information for research purposes. Also, it is important to clarify a perceived incompatibility between POPIA and the NDOH Ethics Guidelines, which expressly permit broad consent in the context of biobank research. The identified consequences of legal limitations on biobank research in this chapter are regulatory silos or fragmentation, which impede regulatory oversight and compliance. Given the preceding discussion of differing interpretations of POPIA pertaining to broad consent use, as well as the regulatory gaps identified in the NDoH Ethics Guidelines and DNOSP, the regulatory framework pertaining to broad consent for biobank research should be amended. By not restricting the use of broad consent, this would ensure that the much-needed human health research agenda is preserved. As a result, Chapter 5 presents a proposal and argues for what changes to the current framework would be required to allow for ethically justifiable broad consent. Chapter 4 discusses consent in research that involves humans and other elements required for valid consent.

Chapter 4

Informed consent in research involving humans

4.1 Introduction

The foundation for the in-depth examination of the ethical defence of broad consent in Chapter 5 is laid forth in this chapter. A review of SA's regulatory framework in relation to broad consent for biobank research was provided in Chapter 3. My investigation revealed discrepancies between POPIA and the NDoH Ethics Guidelines. Additionally, the latter allows for the use of broad consent for biobank research, but the former seems to restrict the collection of personal information (sample associated data) to purposes that are explicit and lawfully defined. The provision of POPIA implies limitations on the use of broad consent for future research uses of data associated with human samples.

To trace the development of informed consent, Chapter 4 discusses the historical context of unethical conduct in human research. This historical backdrop shows how important informed consent is to ethical research. Moreover, the relevance of this chapter is to address the questioned legitimacy of the validity of broad consent as mentioned in chapter 1, section 1.1 to determine the minimum requirement for valid informed consent. In research, informed consent has been seen as a way to exercise the right to autonomy (self-determination) (Allen and MacNamara 2009). Consent should be sought not only to respect autonomy, but it should also meet certain criteria in order to be considered valid. The ethical standards for informed consent should be met by establishing a minimal threshold for informed consent. Different ethical guidance documents and other sources of literature establish different standards as

required elements of informed consent. These elements are discussed through an examination of the relevant sources. Moreover, these elements are required regardless of the consent model used.

Given that broad consent is one of the consent models used in human research, an examination of the doctrine of informed consent in general health research and biobank research is necessary. Finally, a summary of broad consent and alternative consent models employed in biobank research is provided, along with an explanation of how study-specific consent hampers biobank research as a common good. The discussion focuses on broad consent as an ideal model for biobank research. In this chapter, I respond to the current study's Objective 3.

4.2 Background to the development of informed consent in research

Knowledge of the pertinent historical occurrences and trends is essential for comprehending the ethics of using human volunteers in research (Resnik 2018). There have been numerous instances of unethical treatment of research participants in the past that have been documented in the literature. German physicians and scientists, for example, inflicted a variety of fatal and vile treatments on vulnerable populations and prisoners of concentration camps between 1933 and 1945 (Leaning 1996). This occurred in Nuremberg, Germany, during World War II (Leaning 1996). The unethical research conduct atrocities inflicted on research participants who were war victims (inmates) included the failure to obtain informed consent; torturing and disfiguring the participants, resulting in thousands of deaths; violent reactions resulting in intense pain and suffering; exposing them naked to freezing temperatures for hours, causing them to freeze to death; and forcing them to drink sea water until they grew so thirsty that they became mentally unstable. Moreover, incisions were made in the participants'

legs, causing the development of gangrene that was accelerated by the addition of septic foreign matter, and inmates were artificially inoculated with cholera, malaria, yellow fever, typhus, and spotted fever, all of which proved fatal (ICC Legal Tools Database 2010). Additional atrocities included subjecting prisoners to poison gas, mustard gas, phosphorus, and sulphur to show that these chemicals are deadly, which was not a current (original) scientific discovery; they were also injected with gasoline or phenol into the bloodstream, which resulted in immediate death (ICC Legal Tools Database 2010). The Nuremberg Code (1947) arose as a result of a judgment against the German physicians for atrocities committed against war victims in Nuremberg. The instrument appears to be the earliest form of documentation relating to informed consent for ethical behaviour guidance in medical research, and it refers to "voluntary informed consent" (University of North Carolina at Chapel Hill (UNC) 2021).

Another example of unethical behaviour in human research is a syphilis study launched in 1932 by the US Public Health Service (USPHS) in collaboration with the Tuskegee Institute. In this study, 600 black men were enrolled, 399 of whom had syphilis and 201 of whom did not (CDC 2021). A number of unethical violations were inflicted on the participants. For instance, participants were misled into thinking they were receiving therapy for "bad blood"; no informed consent was acquired; and even after penicillin became available in 1943, they were not given treatment. As a result, many died or infected their partners, who in turn infected their new-borns (CDC 2021). In 1972, an advisory panel deemed the study unethical, and it was halted the following year. The Belmont Report was developed in 1979 in response to the ethical violations committed during the Tuskegee study (Sierra 2011). It was part of national law in the U.S to guide ethical conduct in human research, including providing guidance on informed consent (US Department of Health & Human Services 2018). There have

been reports of African Americans being wary of mainstream medicine in the aftermath of the Tuskegee syphilis study. The study has been cited as a factor in black men avoiding seeking health care and low clinical trial participation (Alsan and Wanamaker 2018).

Table 3 displays a timeline of earlier and later instances of unethical behaviour in human participants research, according to Resnik (2022). In order to build the groundwork for the discussion on the need of informed consent in research, this section's only focus on atrocities related to informed consent.

Table 3: Historical unethical behaviour timeline, according to Resnik (2022)

Year	Unethical conduct
1897	Without their consent, Giuseppe Sanarelli administers yellow fever bacteria to five patients. Three people died and each patient had contracted the disease.
1900	Walter Reed conducts tests to identify the origin of yellow fever. 33 individuals, including 18 Americans and 6 Cubans, were exposed to mosquitoes carrying the yellow fever virus or were given an injection of patient blood. Six people died, including two volunteer researchers. The consent forms, some of which were translated into Spanish, were all signed by the participants.
1990	The California Supreme Court determines in the Moore v. Regents of the University of California case that researchers have IP rights in a cell line produced from Moore's tissue but that Moore had no such rights in his own tissue. The Court further decides that by failing to disclose to Moore their financial interests in his tissue sample, the researchers violated his right to informed consent. Following this decision, the majority of courts have ruled that patients no longer have any legal claim to tissues left over following operations or other treatments or tissues donated to researchers.
2011	A book regarding the case of Henrieta Lacks is published by journalist Rebecca Skloot. Upon speaking with Lacks' family, it came to light that, contrary to their wishes and without offering the family any recompense at the time, researchers had cultured Lacks' tumour cells without her knowledge or consent. Skloot made the decision to give the family a portion of the book's proceeds. The NIH and Lacks family came to an agreement in 2013 over access to the cell line's genomic information. The agreement allows the family discretion over who has access to the data and how they are acknowledged in academic publications. Thermo Fisher Scientific, the business that sold Lacks family's cell line, was sued in 2021. The business allegedly illegally benefited on Lacks' tissue without her consent, according to the lawsuit.

Despite the Nuremberg Code's safeguards, evidence of research participants being exploited emerged in the 1950s (Dhai 2014). The WMA established principles for ethical conduct in health research, and the resolution resulted in the WMA Declaration

of Helsinki in 1964 (most recent revision in 2013). The CIOMS Ethical Guidelines were developed in 1982 as a collaboration between CIOMS and WHO (the most recent revision was published in 2016). The goal was to lay the groundwork for developing countries to apply the principles of the Belmont Report, the Declaration of Helsinki, and the Nuremberg Code (Sierra 2011). The WMA Declaration of Taipei, which was developed in 2016 in conformity with the WMA Declaration of Helsinki, adds additional ethical guidelines for the use of biological material (samples) and associated data, particularly in the context of biobanks and health databases. Informed consent for human research and consent in relation to the collection of biobank material are both covered by this guidance. The previous discussion on unethical behaviour in human participants research served as the foundation for the subsequent discussion on the importance of informed consent in research.

4.3 The significance of informed consent in research

Informed consent was not always required when collecting human samples for research purposes. It is thought to have been implemented in 1947 as a consequence of the Nuremberg war crimes trials (University of North Carolina (UNC) 2021). Human biological samples for studying disease mechanisms and identifying disease markers have been collected and stored since the 17th century. This was before such practices were classified as biobanking, which occurred only about 30 years ago (Kinkrova 2016, Malsagova et al. 2020).

Informed consent has two objectives, according to Mikkelsen et al. 2019: (1) to inform participants of the potential risks and benefits of the research; and (2) to provide participants the option of accepting or declining an invitation to engage in research (i.e., respect participant autonomy). In human research, informed consent is required

both ethically and legally (Nijhawan et al. 2013). Seeking informed consent represents the distinction between ethical and unethical behaviour in medical research. Adherence to this doctrine, in turn, denotes professionalism and responsibility on the part of researchers (Brekke et al. 2006). Furthermore, the doctrine of informed consent demonstrates respect for persons and a recognition that research participants are not merely reduced to an "experimental tool" or merely as a means to an end (Porteri and Borry 2008:137). This can be interpreted as the objectification of another person in order to achieve certain goals. When a person is viewed as a means to an end, this is referred to as objectification (Orehek and Weaverling 2017). There are several ways of objectifying people, including by denying them their autonomy (Orehek and Weaverling 2017). Respecting people (research participants) entails respecting their right to self-determination. It also entails treating them with respect (Grant and Sugarman 2004). A standard for determining valid informed consent is required to meet these ethical requirements.

4.4 Elements of ethically valid informed consent

Consent procedures have been designed to allow for self-determination. Consent protects patients and research participants while also encouraging medical professionals to act responsibly (Beauchamp and Childress 1994:142). The required elements of ethically valid informed consent presented in this study are based on international ethical guidance and other literature sources. The Belmont Report mentions three aspects of informed consent. Voluntarism, information, and comprehension are examples of these. Voluntary consent, legal capacity to consent, and freedom to choose without deception or coercion are the elements required for seeking informed consent, according to the Nuremberg Code (1947). Participants

should also be adequately informed and comprehend the research's subject matter in order to make an informed decision about participating in the research (UNC 2021). The Code only mentions these two aspects of consent. The Code, on the other hand, specifies basic principles that researchers must follow. These include considering the good of society as motivation for the research, avoiding unnecessary injury, and the researchers' competence. Participants should also have the freedom to withdraw from the study at any moment, and the possible risk should not outweigh its significance. Consent requirements outlined in the Declaration of Helsinki include voluntariness, the right to refuse (dissent) or withdraw from participation, participants' understanding of the information provided, that consent should not be granted under duress, and that legal representatives should grant consent on behalf of incapable participants in addition to the latter's assent where possible. According to the WMA Declaration of Taipei, consent requirements include free voluntary consent, consent in accordance with the WMA Declaration of Helsinki, participants' rights to change or withdraw their consent, and capacity to consent. Furthermore, it entails providing participants with adequate information on, among other things, the type of material to be collected, the risks and burdens associated with material collection, the purpose of the biobank, use and storage, privacy protection of their materials, an option for return (disclosure) of incidental findings (IFs) by researchers, and biobank governance arrangements. According to CIOMS, the required elements of informed consent are voluntariness, relevant information, adequate understanding of the material facts, consent that is free of deception (withholding relevant information), and undue influence or coercion. Sufficient opportunity and time should be given to participants to make their decision regarding participation, it also reads. Finally, it includes the researcher's ability to respond to any questions from participants.

Informed consent court cases also establish requirements for the doctrine. One such requirement is that participants be given adequate information during the consent process (Beauchamp 2011). Participants' understanding of the information provided in consent documents, according to Taub (1986), is one of the factors influencing the consent process. According to Grady et al. (2015:4), the "reasonable person standard," which stipulates that information presented to participants should be based on what a reasonable person would want to know in order to decide whether or not to donate his or her samples, can be used to evaluate the validity of consent.

A number of common themes are highlighted from the analysed sources. These include emphasis on voluntariness for participation, providing participants with adequate information that they are able to understand (comprehend), participants' right to withdraw, consent that is free from coercion, and capacity to consent. Based on these common themes, the next section discusses each of these elements in detail as they seem to be a common standard for valid consent. According to empirical evidence, broad consent is reasonable because it gives people the choice of whether or not they want their samples used for research (i.e., autonomy is not only restricted to specific consent) (Grady et al. 2015). This means that even when broad consent is used, participant consent is still required for obtaining samples as recommended by various instruments, including the NDoH Ethics Guidelines, the Declaration of Taipei, the Declaration of Helsinki, and the CIOMS Ethical Guidelines.

4.4.1 Voluntariness for participation in research

When it comes to research, voluntariness typically refers to the decision to participate being made voluntarily, hence compulsion undermines voluntariness (Agrawal 2003). Duly, the component of voluntariness implies research involvement free from coercion

and undue influence according to the Belmont Report (UNC 2022). If there is no proof of undue influence or coercion on the side of the individual making the decision, it is assumed that the decision was made voluntarily (Appelbaum et al. 2009). The ability to withdraw from research at any moment is another aspect of voluntary research involvement (Nelson and Merz 2002). As a result, in addition to voluntariness for research participation, this section also discusses consent that is free of coercion and consent withdrawal. Voluntariness and coercion are interconnected concepts, as demonstrated in the following discussion.

It is critical to have a mechanism in place for determining appropriate incentives for each study within the domain of research ethics review. This is to consider what might be undue influence or coercion for research participation in order to ensure voluntary consent (Fisher 2013). According to empirical research on the meaning of the concept of voluntariness among research participants in Nigeria, this concept is interpreted as the dialectical relationship between self-determination and the absence of coercion for participation to be truly voluntary (Marshall et al. 2014). This illustrates the significance of personal autonomy and free will in the absence of coercion, as well as the necessity of the option to withdraw from research as a key component of voluntary participation (Marshall et al. 2014).

Nelson and Merz (2002) list traits that discourage people from taking part in research. These include socioeconomic and disease status, reduced cognitive or other capacities, and family situation. Cultural, political, and social variables that could impede participants' ability to voluntarily decide to participate in research should be recognized by researchers (Bull and Lindegger 2011). Furthermore, participants believe they are less able to make voluntary judgments regarding the research the higher the power differences between researchers and participants (due to education

and poverty). This is despite the fact that there is no objective evidence that the participants are being controlled by the researchers (Bull and Lindegger 2011). Notably, the presence of influencing factors does not always imply that a decision was not made voluntarily. Rather, it means that a decision is not voluntary if it is influenced by outside, illegitimate, or intentional forces and is causally related to the research participant's choice (Appelbaum et al. 2009). Thus, intentional influences must be intentional in order to negate voluntariness (Appelbaum et al. 2009). The observed characteristics that influence voluntariness may be risk factors for the vulnerability of research participants. This implies the need for restrictions and special precautions aimed at empowering participants to make decisions free of coercive and "manipulative pressures" (Nelson and Merz 2002:V-70).

The capacity of potential participants to decide whether or not to participate in research is undermined by coercion, which is incompatible with valid consent (Wendler and Wertheimer 2017). Autonomy is based on a rational decision that is free of coercion (Glick 2000). Furthermore, one could argue that coerced consent is morally worse than no consent or deceived consent because the former impairs participants' interests more severely (Wendler and Wertheimer 2017). Notably, study-related incentives in the form of payment for participation are not considered coercive by Lynch (2019) on the basis of the notion that they do not involve a threat to make a participant worse off. Lynch (2019), on the other hand, admits that, unlike reimbursements, which should cover out-of-pocket expenses for research participation, such as travel costs, these are ethically required in order for fairness to prevail. As a result, incentives should be at the discretion of the researchers to avoid undue influence.

Coercion is frequently confused with other moral violations related to offers, such as undue inducement or exploitation (Hawkins and Emanuel 2005). Undue inducement entails providing a genuine good in large quantities. The inference here is that the size of the offer is probably going to push the potential participant to make hasty judgments in order to get a short-term benefit (Hawkins and Emanuel 2005). Wertheimer and Miller (2008) point out that, while the size of the incentive may be more effective in convincing people to accept a proposal, a larger offer is not more coercive. Two essential presumptions underlie the use of undue inducements (Macklin 1981). In order to get enough people to actively participate in research, some kind of inducement is first needed. Second, there is a theoretical and practical distinction between "undue" (morally unacceptable) and "due" (morally acceptable). The validity of a person's consent would be questioned due to the effects on his or her capacity to consent if an incentive results in an individual making an illogical decision about participating in research (Millum and Garnett 2019). Voluntary consent must provide the option to withdraw participating in research (Nelson and Merz 2002).

The option to withdraw participating in research includes the option to withdraw the usage of participants' data in future studies (Melham et al. 2014). Providing participants more information resulted in fewer future withdrawals from the initial consent, according to research by Matsui et al. (2005). If potential participants' anxiety, lack of trust, misunderstanding, or comprehension is not addressed, these participants are likely to change their minds and withdraw from the study later (Matsui et al. 2005). According to Edwards (2005), the right to withdraw consent protects those who would not have consented if they were fully aware of the implications of the research. Edwards (2005) maintains that rather than simply accepting a withdrawal, researchers should devise conditions under which a participant may withdraw. Thus, in order to

protect participants' autonomy, they should not have "unconditional or absolute withdrawal rights" (Edwards 2005:114). This claim, however, is unsubstantiated. On the surface, it appears to violate autonomy by not allowing participants to choose whether or not to continue participating in research. It is a violation of autonomy to use someone only as a means (i.e., to act in a way that furthers the aims of others without taking into account their own goals) (Beauchamp and Childress 1994f:125). Yet, Schaefer and Wertheimer (2011) contend that a person's autonomy should by definition grant that person the freedom to renounce a right if they so choose. They also argue that not allowing participants to agree to pay a penalty if they withdraw from a study violates their autonomy and may prevent a mutually beneficial agreement from being reached. Without any penalty, the right to withdraw may not provide any significant protections (Schaefer and Wertheimer 2011). On the basis that people are expected to fulfil their commitments and keep their promises outside of research settings, the ability to withdraw has occasionally been disputed (Lynch 2020).

A variety of potential defences against withdrawing consent in the context of biobank research are presented by Helgesson and Johnsson (2005). For starters, providing samples for storage and use could be considered a gift to researchers. This means that the donor no longer has any claim to the samples. Second, unlike the potential risk of physical harm if the research is conducted in humans, the donor is not directly harmed by the analysis of their biobank sample. Third, the claim that the right to withdraw consent from research involving body samples based on privacy and integrity is legitimate but that right to do so from research not involving such samples is unfounded. When biobank research participants wish to withdraw their consent, sample and data anonymization (de-identification) has been considered an acceptable solution (Eriksson and Helgesson 2005). Eriksson and Helgesson (2005) argue that

anonymisation should not be considered an acceptable response to such consent withdrawal requests, on the grounds that anonymisation may not always protect individual interests. Notably, the WMA Declaration of Taipei (2016) states that withdrawal of consent is not possible for material that has been rendered unidentifiable.

According to Schaefer and Wertheimer (2011), the right to withdraw should be an inalienable right without penalty for a variety of reasons. First off, asymmetry in information between participants and researchers regarding the benefits and risks of participation suggests that the right to withdraw can protect participants in the event that the initial consent failed to address the asymmetry. Second, the uncertainty of risks and burdens may be greater than the participants anticipated. Third, researchers hedging, which entails accepting a relatively low cost by stipulating a right to withdraw without penalty as a means of avoiding negative outcomes (risks). Fourth, because of the widespread acceptance of the value of bodily integrity, such a value appears plausible to protect people from having to choose between continuing to accept bodily invasions and paying a penalty if they withdraw. In addition, consideration should be given to autonomy, integrity, privacy, and trust in medical research while defending the right to withdraw from participating in research (Helgesson and Johnsson 2005).

The preceding discussion demonstrates that different people have varied views on what it means for participants to have the right to withdraw research participation. This is with respect to whether or not this right should be prima facie or absolute, and whether or not there should be any penalty for withdrawal. Therefore, it is important for researchers to strike a balance between safeguarding participants' ability to withdraw from the study and preventing coerced consent. For voluntary consent to be

ethically valid, other elements including adequate information disclosure to participants must be met (Agrawal 2003).

4.4.2 Adequate information and understanding (comprehension) as a requirement for informed consent

Key information elements that must be provided to research participants during the consent procedure for the storage and future use of human samples in research have been discussed in Chapter 3, section 3.3. They include, among other things, the reason for the collection, the type of data to be collected, possible risks and benefits (if any) of research involvement, regulations for material access, the option to withdraw, and privacy and confidentiality protections. After making sure that the potential research participant is aware of the information provided, the researcher should simply seek consent (WMA Declaration of Helsinki 2013). Understanding is used in the context of human research to refer to a participant's objective comprehension of material shared throughout the informed consent procedure (Nishimura et al. 2013). Comprehension is one of the measurement tools that have been used in empirical research surveys as variables for measuring how participants understand consent information (Sand et al. 2010). It is assumed that the informed consent procedure results in the participants fully understanding what they are consenting to in order for research participants' autonomy to be respected (Pietrzykowski and Smilowska 2021). The Belmont Report (1979) states that it is the obligation of the researchers to ensure that the participants have understood the information to the point where they might be asked to take written or oral comprehension tests. Poor communication techniques by the researcher due to a lack of time, illiteracy, and unfamiliarity of the participants with medical research conduct are some of the elements that may contribute to inadequate comprehension of consent information (Kadam 2017). According to Sand et al. (2010), questionnaires have been

used to measure understanding in the majority of empirical research, with the participant's overall understanding being assessed by adding up all of the correct answers.

Notably, such measurements are regarded as proxy measures because they do not directly measure comprehension (Sand et al. 2010). Based on this finding, Sand et al. (2010) argue that participants must narrate basic consent information in order to measure actual understanding. Contextual factors identified as influencers for research participant understanding include (1) recruitment circumstances; (2) level of education, literacy, and reading (presumably reading ability as this is not elaborated on further in the article); (3) consent model used; (4) location; and (5) demographics such as gender, age, and income, (6) consenters (the authors do not explain how this is a contextual feature), and (7) time spent explaining consent (Eisenhauer, et al. 2019). The reasonable person standard addresses the issue of what constitutes adequate information for consent to participate in research. This standard was developed to determine the information that a reasonable person would want to have in order to decide whether or not to participate in research and, as a result, grant consent or dissent (Odwazny and Berkman 2017). In the US, the reasonable person standard has a lengthy history extending back to the 1970s, when courts and legislatures utilized it to evaluate the appropriateness of patients' information disclosure when making decisions about their medical care (Dresser 2018). Applying this criterion to the field of medicine or healthcare, a clinician would be able to avoid being held accountable for medical malpractice or negligence by demonstrating that a patient gave their consent to a procedure despite being aware of the potential risks (Sykes et al. 2017). The reasonable person standard also applies in tort law,

particularly in cases of negligence (Harlow 2007). In the current study, my analysis of the concept will be limited to health research.

Although the reasonable person standard was developed in the healthcare context, medical researchers adopted it to determine information disclosure to research participants (Dresser 2018). The reasonable person standard is of significance in practice because few of the experts who conduct research have personal experience as research participants, are more educated, affluent, and healthier than the average research participant, and may thus downplay matters that study participants would consider relevant to their choices (Dressler et al. 2018). According to Dressler, a good way to determine prospective research participants' information preferences is to ask those who have previously participated in research (Dressler et al. 2018). Dranseika et al. (2017) propose that the reasonable person standard is characterised by relevant considerations for a reasonable person in terms of information disclosure when determining the solution for reasonability of information that should be disclosed. As a result, researchers and RECs should consider what information would be relevant to a reasonable person (Dranseika et al. 2017). Dranseika et al. (2017), on the other hand, argue against the reasonable person standard. They believe that the subjective standard for informed consent information disclosure in research is ideal. Their reasoning for this is that the former standard disregards the possibility that competent individuals may have different concerns, experiences, and values than the "idealized type-person" of the reasonable standard (Dranseika et al. 2017:218). The subjective standard necessitates an understanding of what information would be relevant for specific individuals based on empirical survey data, an understanding of an individual's cultural context, and an understanding of the target population's concerns and interests based on interviews with prospective participants (Dranseika et. al. 2017).

The concept of providing "relevant information" appears to be a recurring theme in discussions about required informed consent information (Steinsbekk et al. 2013; Dressler et al. 2013). (2018).

The National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research (the National Commission) rejected the Belmont Report's formulation of the reasonable person standard (1979). For evaluating informed consent in research, it proposed the "reasonable volunteer" standard. The National Commission's objection to the reasonable person standard stems from the belief that it is insufficient. The claim is that this is so because research participants volunteer to take part, and research, by its very nature and design, produces generalizable knowledge that is not primarily meant to benefit the participants. Due to this, it is possible that they need a lot more information than people seeking treatment for their own benefit (Odwazny and Berkman, 2017). The reasonable volunteer standard is based on the notion that the scope and nature of the information should be such that a reasonable volunteer "can decide whether they wish to participate in the furthering of knowledge, knowing that the procedure is neither necessary for their care nor perhaps fully understood" (Belmont Report 1979: Part C); that the volunteer should understand the possibility of benefits and risks as well as the voluntary nature of participation (Belmont Report 1979).

Understanding consent information and retaining that information long enough to make a decision are two of the factors used to assess consent capacity (Hardicre 2014). If a participant has difficulty in any of these areas, he or she cannot participate in research because such difficulty would imply a lack of capacity to consent (Hardicre 2014).

4.4.3 Capacity to consent

The capacity to consent, often referred to as decision-making capacity, is the ability of prospective or current participants to understand the information provided about a research project and to understand the potential repercussions of their decision to participate or not (Tri-Council Policy Statement (TCPS) 2018). Assessing decision-making capacity requires determining whether a participant (or prospective participant) sufficiently comprehends the nature of a particular research endeavour, as well as the risks, repercussions, and potential benefits related to it (TCPS 2018). The capacity for self-determination, which necessitates the acceptance of autonomy and the protection of those with impaired autonomy, is one of the conditions for respect for persons, according to the Belmont Report (1979). The principle of autonomy in modern biomedical ethics relates to the idea that a person's life is defined by own decisions and preferences (Beauchamp and Childress 1994g:58). In addition, the principle establishes a standard for treating autonomous people's decision-making abilities with respect (Beauchamp and Childress 1994a:38).

One commonly accepted criterion of vulnerability is the capacity to consent to research involvement (CIOMS 2016). Vulnerable groups of people include those in hierarchical relationships (e.g., students and subordinate personnel); institutionalised people in mental institutions, nursing homes, and prisons; women in studies of female sex workers, intimate and sexual partners in violence studies, women in abortion studies in countries where abortion is illegal, trafficked women; pregnant women; children and other groups of people such as those receiving welfare and social services (CIOMS 2016).

Humans are vulnerable when they are unable to protect their own interests (CIOMS 2016). For instance, if individuals lack the decisional competence, education,

resources, strength, or other traits essential to protect their own interests (CIOMS 2016). Vulnerability in the context of research participation entails difficulty understanding information and making decisions. For instance, those who lack capacity, such as immature children or individuals with cognitive impairment, those who do not lack capacity but are in circumstances that prevent them from exercising that capacity, and those who are unable to communicate effectively due to language barriers (Gordon 2020). In the instance of minor research participants (children under the age of 18), assent should be granted with the assistance of a parent or guardian due to the minor's legal incapacity to grant consent (NDoH 2015). Different levels of maturity can exist among children of the same age. The capacity of a child of a given age to make mature decisions is therefore not always evident (Grootens-Wiegers et al. 2017). Decisional capacity, which includes consent capacity, is typically determined by a person's capability to comprehend relevant information, think critically about available treatments, recognize the potential negative effects of their choices, and convey their choice (CIOMS 2016). Cherry (2017) contends that adolescents, including so-called "mature minors," lack the necessary development and emotional capacity to consent to medical research. Those who suffer from incapacitating medical problems such as a stroke, dementia, or severe learning difficulties may lose their capacity to consent (Shepherd et al. 2019).

An authorized legal representative may represent an individual with diminished capacity to consent (Biros 2018). When capacity is an issue, researchers should have a methodical plan for assessing capacity (Gordon 2020). A set of standards for determining consent capacity has been developed. These include: (1) the participant's capacity to communicate a yes or no decision for all risk/benefit levels; (2) the participant's comprehension of pertinent information and ability to explain what the

research procedures and consent information include for all risk/benefit levels; (3) the participant's comprehension of the situation of the research and its likely repercussions (applicable to all research involving more than minimal risk); and (4) when the participant is aware of the research circumstance and its expected outcomes. For instance, are choices in line with a person's moral, religious, and other views (important for the worst risk/benefit ratios)?

The examined informed consent elements reflect support for protecting participants from unethical behaviour by ensuring that they participate voluntarily and without coercion, that they understand the information presented to them (which should be adequate), and that they have the decisional capacity to consent to the research. After discussing the importance of informed consent and what constitutes ethically valid consent in human research, a discussion of the various types of consent in research and biobank research will be presented, with the goal of demonstrating that consent is not a one-size-fits-all approach for the various research contexts.

4.5 Informed consent in research and biobank research

There are various recognized models of informed consent that are represented in Table 3 below:

Table 3: Various recognized informed consent models

Type of informed consent	Definition
1. Blanket	Consent for all types of research with no additional permissions required (Thompson et al. 2017).
2. Meta	A participant chooses whether or not to grant consent for each and every future study (Ploug et al. 2017).
3. Broad	Consent for future research use (unspecified) of samples, as frequently used by biobanks, with REC/BEC oversight (NDoH 2015).
4. Dynamic	Technology/internet-based, modified consent over time that allows participants to change their consent preferences in response to changing circumstances (Kaye et al. 2015; Steinsbekk et al. 2013).
5. Waived	When consent is waived subject to REC's approval if there is only a slight chance that participants will suffer harm, their interests will not be harmed, and the research cannot proceed without the waiver (CIOMS 2016).
6. Tiered	Consent for the primary study with a choice to allow storage and subsequent use of samples and data (NDoH 2015)
7. Narrow (specific)	Consent for a single use of donor material with no permission for storage or sharing and new consent required for subsequent use (NDoH 2015).

Table 4 below shows that while guidance relating to consent for storage and future use of samples in high income countries (HICs) is clear, guidance in African countries is generally non-specific and unclear with broad consent mostly being prohibited in the countries studied. This consent model is generally not prohibited in HICs.

Table 4: Comparison of consent models used in specific regions for storage and use of HBMs in biobank research (De Vries et al. 2017)

Country	**Informed consent model use as per frameworks**
Australia	Specific, broad, tiered (The Australian National Statement 2018).
Canada	Specific, broad (TCPS 2018).
Europe	Specific, broad, tiered (Council of Europe 2006).
UK	Specific, broad (Human Tissue Authority 2023).
US	Broad (US Department of Health & Human Services 2023).
Selected African countries' frameworks in relation to consent for sample storage and future research (De Vries et al. 2017)	
Benin, Ghana, Guinee, Kenya, Lesotho, Mauritius, Namibia, Swaziland, Togo Zimbabwe	No specific guidance for consent for storage and future research. According to Kenyan national guidelines, sample donors must either re-consent for future usage or a waiver should be obtained from the ethics committee.
Botswana, Sierra Leone, Senegal, Uganda, Cameroon, Nigeria, South Africa, Sudan, Rwanda, Nigeria, Ethiopia	Future unspecified research is allowed with conditions. Guidelines from Senegal, Uganda, Botswana, and Sierra Leone stipulate that consent for any future usage must be obtained using a different form; this appears to be a regulatory preference for tiered consent. The guidelines for Cameroon, Nigeria, South Africa, and Sudan provide that participants must be informed of plans to store samples for future research rather than requiring separate consent forms for future usage, although the ethical practice around consent for future research may differ. Regulations in Sudan mandate that participants (not only for biobank research) be re-consented at "regular intervals," even if the research aims do not change. However, they do not specify the intervals or what constitutes a fair time frame. According to the guidelines for Rwanda, Nigeria, and Ethiopia broad consent may be used to collect samples for future use. However, ethics committees have ultimate authority over whether the consent models proposed for research are suitable.
Malawi	Not explicit but a suggestion that broad consent may not be used. Future unspecified use of samples is prohibited.
Tanzania	Not explicit but a suggestion that broad consent may not be used.
Zambia	Specific consent

Table 4 shows that while guidance relating to consent for storage and future use of samples in high income countries (HICs) is clear, guidance in African countries is generally non-specific and unclear with broad consent mostly being prohibited in the countries studied. This consent model is generally not prohibited in HICs.

4.5.1 How is study-specific informed consent a hindrance to biobank research?

Given the future-oriented nature of biobanking, specific consent would not be ethically justified for biobank research. This is because it is impossible to obtain specific

consent for an objective that was not thought of at the time of sample and data collection (Caplan 2009). When using materials for a single, specific study, specific consent is used (i.e. consent to use the materials) (Eisenhauer et al. 2019). One defence of specific consent is that it shows respect for donors or participants (Hansson et al. 2006). This argument, according to Hansson et al. (2006), would be valid if the process of seeking specific consent did not put the quantity and calibre of research that can be carried out in jeopardy, particularly in the context of biobank research (Hansson et al. 2006).

Specific consent is challenging to put into practice due to the practicalities of biobank research (future-oriented research with ambiguous goals and methodologies) (Mikkelsen et al. 2019). This includes the magnitude of research studies and the frequency of new investigations. Also, unlike clinical research, the structures and procedures used in biobank research are very different (Mikkelsen et al. 2019). Furthermore, different biobanks take different approaches to consent withdrawal. Some biobanks have tiers of different aspects from which participants can withdraw consent, whereas others allow participants to withdraw consent for all aspects of the research (Melham et al. 2014). Moving away from the "all or nothing" approach of consent withdrawal ensures that participants can withdraw from specific, limited aspects of biobank research without withdrawing consent from the entire study (Melham et al. 2014). Given the difficulty of applying specific consent to biobank research, it is clear that specific consent is likely to limit the utility of biobank research (Mikkelsen et al., 2019). As a result, alternate consent models for biobank research are required. By abandoning the "all or nothing" method of consent withdrawal, participants can opt out of only a small portion of biobank research without withdrawing their participation from the entire project (Melham et al. 2014). Given how challenging

it is to apply specific consent to biobank research, it is obvious that this model will likely limit the usefulness of this type of research (Mikkelsen et al., 2019). Other consent models for biobanks are therefore necessary.

4.5.2 Broad consent and alternative consent models for biobank research

In the US, the requirement to safeguard participant confidentiality led to the emergence of broad consent (Fisher and Layman 2018). This was specifically in reference to researchers using potentially identifiable personal information in a secondary manner for purposes other than those for which it was originally collected, including those that materially diverged from the original consent (Fisher and Layman 2018). This form of consent was not always regarded as appropriate. For instance, a few RECs in Germany around ten years ago refused to approve biobank research that employed a broad consent model. In this setting, consent to research should be based on specific information about the research, as required by the Declaration of Helsinki and data protection legislation (Strech et al. 2016). To create broad consent template forms that would be accepted by all 53 German RECs, a task force was established as a result of the rise in German biobank projects (Strech et al. 2016).

Alternatives to specific consent include broad consent, blanket consent, dynamic consent, tiered consent, and meta consent (Steinsbekk et al. 2013; Mikkelsen et al. 2019). According to Mikkelsen et al. (2019), the participant protection requirements for biobank research are different from the security precautions that traditional consent models are intended to offer (in relation to known specific risks associated with a particular study). As a result, rather than making comparisons with traditional consent models, any reasonable assessment of biobank research consent models must be based on criteria specific to biobank research. The acceptability of broad consent over

alternative consent models for ethical and pragmatic reasons is discussed in more detail in the section that follows. The importance of practical reasons for choosing broad consent cannot be overstated. The practical reasons for choosing broad consent are significant because practicality is a key feature for enabling biobank research. This summary is the basis for Chapter 5's defence of broad consent as the ideal consent model for biobank research.

4.5.3 An overview of acceptability of broad consent for biobank research over alternative consent models based on ethical and practical reasons

The justifications for accepting broad consent model differ, according to the literature on the acceptability of broad consent. Justifications are also predicated on ethical and other issues, the majority of which centre on the applicability of broad consent and the regulatory response to it. Charitable reasons related to altruism, gratitude, reciprocity, and solidarity (Richter et al. 2018); broad consent motivated by participants' trust in researchers (Barazzetti et al. 2020); the claim that broad consent appeals to autonomy (Sheehan 2011); REC oversight (Tindana et al. 2020); and using broad consent as long as participants are informed about the usage of their samples through ongoing communication (Grady et al. 2015). These ethical considerations are elaborated on in Chapter 5. Other arguments in favour of broad consent centre on the feasibility of applying this consent model to biobank research. In this study, I consider practical reasons for selecting a consent model for biobank research to be critical, given the future-oriented nature of biobanking. As a result, such a decision should be based on a combination of ethical and practical considerations. This is due to the fact that future study's precise research details, which are typical of biobank research, are usually impossible to ascertain. Finally, regulatory responses to broad consent are considered from the perspective of a few countries studied.

4.5.4 Support for broad consent based on practical applicability reasons

In a study of 48 participants recruited by the University of Iowa Hospitals and Clinics (UIHC Biobank) in the US, broad consent received the most support over study specific and tiered consent in two focus groups (Simon et al. 2011). Given that the biobank was unsure of the type of potential future research, participants in this study believed that broad consent was the proper approach (Simon et al. 2011). Steinsbekk et al. (2013) prefer dynamic consent to broad consent for biobank research, arguing that the former allows for a more interactive follow-up process for participants than the latter. Although dynamic consent is difficult to implement in an African setting due to technological limitations, particularly in rural areas, its supporters see it as appealing due to the potential for ongoing communication between participants and researchers. They believe that doing so will boost participant trust and confidence in the research and researchers (Tindana et al. 2020). The practicality of dynamic consent in an environment with limited technological resources cannot be overstated. As a result, an alternative model of consent should be considered in such contexts, especially if access to resources cannot be improved due to limited funding. Dynamic consent has been considered as a resource-intensive procedure because of the added costs associated with continual communication, which could be detrimental to the quality of the research if individuals regularly changed their minds about participation and this significantly affected datasets over time (Teare et al. 2020). In light of the researcher's experience as a medical scientist in SA conducting health and biobank research, the reality is that securing funding for research is a daunting task in and of itself, made more difficult by the fact that biobank research funding agencies are generally limited.

4.5.5 Regulatory framework responses to broad consent

In a number of African nations, broad consent is not forbidden nor encouraged by law, suggesting that it can be employed (de Vries et al. 2017). There seems to be some ambiguity in the GDPR 2016/679 of the European Union (EU) regarding consent for the collection of personal data (GDPR 2016). While Regulation 33 admits that it is not always possible to identify a clear purpose for data collection, Regulation 32 of the GDPR requires specific consent for the collection of personal data. Hence, data subjects should have the option of giving consent only to particular areas of research or sections of research projects, to the extent that this is permitted by the intended objective (GDPR 2016). It is interesting to see how EU Member States have used their discretion to define the scope of consent for processing personal data in the context of biobanking because, aside from the GDPR's implied definition of "broad consent" in regulation 33, no other place in the regulation makes this model of consent explicitly clear (Tzortzatou et al. 2021). This is due to the GDPR's provision for derogations from its regulations. Consequently, Member States have the authority to determine the specific regulatory guidance regarding data protection regulation (Reichel 2021). As a result of this derogation, biobank regulatory frameworks in Europe are fragmented. However, in Finland, broad consent is widely accepted, whereas in France, there is no explicit mention of biobanks in the regulatory framework, but sample transfer is permitted. Furthermore, in the Netherlands, consent can be waived if the research is motivated by "public interest" (Kaye et al. 2016:198).

Proponents of tiered consent argue that, while it allows for future research use of samples, it is more specific than broad consent in terms of information provided to participants regarding prospective use of samples (Mikkelsen et al. 2019). The claim

states that tiered consent is intended to allow participants to retain a higher degree of control over the use of their samples and data (Mikkelsen et al. 2019). Yet, tiered consent almost always contains a component of broad consent since it involves the future use of samples. Contrary to broad consent, the more specific information offered in tiered and meta consent includes categories of research aims, methodologies, and tiers in which their materials (samples and data) can be utilized as a way to limit consent from uses they would not approve of (Mikkelsen et al. 2019).The notion that the research will be done in the future limits the extent to which "specific" future research details relating to categories of research aims, methods, and tiers of material use can be provided. It is unavoidable that the research will have limitations in providing specific details. As a result, whether tiered and meta consent models are superior to broad consent remains debatable. To adequately respond to the question of whether tiered and meta consent are more specific than broad consent, an analysis of information provided during the use of these consent models in the context of biobanking is required, which is discussed in the following section.

Although SA researchers have differing opinions on the best consent model for biobank research, they generally agree that broad consent is the preferred model (Mwaka and Horn 2019; Moodley et al. 2016). In Africa, researchers and study participants believe that broad consent is sufficient and even desired because tiered consent is thought to be too time-consuming and challenging to communicate to research participants (Tiffin 2018). The answer to why broad consent is considered more ideal or superior than tiered consent, despite the fact that both entail future research use of materials, is that providing "specific" future research details relating to categories of research aims, methods, and tiers of material use is limited by the notion

that the research will be done in the future. Furthermore, as previously stated, there is bound to have limitations in providing specific research details.

To some extent, the ethical reasons for broad consent presented herein are related to the defense of biobank research as a common good. These include motivation for granting broad consent as a reflection of values such as altruism, gratitude, and reciprocity, as well as motivation for broad consent based on the public or common good (beneficence). Other ethical arguments in favour of broad consent include the idea that this consent model appeals to respect for autonomy by asserting that autonomy does not specify the scope of choices (i.e., it does not require autonomy to be limited or restricted to a specific consent model, keeping in mind that participants are allowed to withdraw from research at any time, regardless of the consent model employed). Last but not least, biobank research is subject to REC assessment prior to starting the research, just like any other medical research involving humans, in order to assess and decrease the possibility of participant harm as well as to ensure that research has social and scientific value (CIOMS 2016). A thorough ethical justification for using broad consent in biobank research is provided in Chapter 5.

As previously stated, tiered consent almost always includes an element of broad consent because it involves future use of samples, with the distinction of more specific information being provided in the former versus the latter. As a result, for the sake of clarity, the next section analyses the specificity of the information provided when using tiered and meta consent.

4.5.6 Analysis of specificity of information provided during the use of tiered and meta consent

The goal of this section is to explain what it means for tiered and meta consent to be more specific than broad consent in terms of information provided to participants, as mentioned in section 4.5.2.2. To reiterate, these consent models suggest potential sample use in the future. But, as was already mentioned, there are limitations on disclosing specific research information for subsequent studies. As a result, it is still up for debate whether tiered and meta consent models are better than broad consent. Nembaware et al. (2019) suggested a framework for tiered informed consent in the context of African genomic research. Overall, the information on the consent form is focused on giving consent for a specific area of research (for instance, research into sickle-cell disease, where participants are asked whether or not they consent to having their samples and data used for specific research reasons) (Nembaware et al. 2019). Obtaining consent for: (1) research into the genetics of sickle cell disease; (2) more future research into the genetics of sickle cell disease; and (3) research into the genetics of other diseases or biological processes would normally be part of sample and data usage research (Nembaware et al. 2019). According to Ram (2008), psychological research findings support the notion that tiered consent provides "abundant choice" or "hyper-choice" (Ram, 2008:269). Information overload, avoidance of decision making, arbitrary selection, and regret are some of the identified pitfalls of such abundant choice. Nonetheless, it is acknowledged that in order to comply with the criteria of truly informed consent, the research categories should be increased under this consent model (Ram 2008).

The National Cancer Institute (NCI) of the National Institutes of Health (NIH) provides recommendations on information categories for tiered consent. They include whether or not participants consent to having their materials stored and used for secondary research on the prevention and treatment of diseases, secondary research on the prevention and treatment of a specific research area (such as cancer), consenting (or not consenting) to have their samples associated with their medical history or records, and consenting (or not consenting) to be contacted about future research (NCI 2016).

The NDoH Ethics Guidelines include recommendations for future research using human samples in a number of contexts, including a Consent Form Template. Participants are given the choice to grant permission for the storage and use of their samples in future research with a variety of alternatives on consent forms categories of specific information, including: (1) giving permission for future research only if it is of the same research topic; (2) giving permission for any type of future approved research; and (3) giving permission for future research and specifying exceptions to which they do not consent. Although this Consent Template follows the approach of the aforementioned tiered consent models, sample-associated data is missing and not included in the Template. The issue with this scenario is that not only human samples, but also sample-associated data, are vulnerable to misuse (Tindana et al. 2014).

4.6 Conclusion

Unethical behaviour in human research has resulted in the development of informed consent documents dating back to 1947. The Nuremberg Code appears to be the earliest guidance developed in response to the Nuremberg war crimes, which involved unethical medical experiments on war prisoners. The WMA Declaration of Helsinki was developed in 1964 as a result of the widespread rejection of the Nuremberg Code

among scientists. Documents discussing informed consent have evolved over time. As a result of the Tuskegee syphilis study ethical violations, the Belmont Report (1979) was developed, and the CIOMS ethical guidelines were first developed in 1982 (latest revision in 2016). Other documents have since followed. These include the WMA Declaration of Taipei, which was created in 2016 to provide ethical guidance for biobanks and health databases. Nationally, requirements for biobank-specific informed consent models are included in the NDoH Ethics Guidelines, which were updated in 2015. The discussion about the significance of informed consent in research is built around these ethical guidance documents. The goal of informed consent is to give participants information on the benefits and risks of participating in research while simultaneously allowing them to exercise their autonomy. Giving participants sufficient knowledge (i.e., based on what a reasonable person would want to know; the "reasonable person standard") demonstrates respect for their autonomy, which is one of the qualities of ethically valid consent. In addition to providing adequate information to research participants, there are required elements of informed consent identified from ethical guidance documents and other literature sources that have been set as different benchmarks. These include participants' voluntariness (willingness) to participate; their right to withdraw; and consent that is free of coercion and capacity to consent. The acceptance of broad consent over alternative consent models is based on ethical and practical considerations. The practical reasons for choosing broad consent are significant because practicality is a key feature for enabling biobank research. To some extent, the ethical justifications for broad consent presented herein are related to the defence of biobank research as a common good. These include motivation for providing broad consent as a reflection of altruism, gratitude, and reciprocity values; REC oversight; and ongoing communication with participants.

Other ethical arguments in favour of broad consent include the idea that this consent model appeals to respect for autonomy by deducing that autonomy does not specify the scope of choices. These ethical reasons serve as the foundation for the ethical defence for broad consent presented in Chapter 5.

Chapter 5

An ethical defence for broad consent use in biobank research

5.1 Introduction

In Chapter 4, the ethical acceptability of biobank research broad consent over alternative consent models was discussed. The regulatory framework's response to this consent model was also covered in chapter 4, taking into account the practical justifications for broad consent and the future-oriented nature of biobanking. The notion that broad consent appeals to autonomy because the latter is not limited to the scope of choices, taking into account participants' right to withdraw from biobank research at any stage; broad consent use provided there is REC oversight; and the use of broad consent provided that participants are informed of their sample use through ongoing communication. The ethical justification for broad consent is thoroughly described in this chapter.

The relationship between altruism and solidarity is that both appeal to assisting others without personal gain, whereas solidarity is related to reciprocity in that both promote the concept of "doing good" (Guttman et al. 2016:927). According to Beauchamp and Childress (1994d:259), one form of beneficence is to promote or do good. To some extent, altruism and beneficence overlap in that they are both motivated by concern for others (Glannon and Ross 2002). Based on these relationships and conceptualizations, it follows that broad consent use for biobank research for reasons of altruism, solidarity, and reciprocity is founded on the beneficence principle (doing good). To begin, this chapter argues for the use of broad consent because it promotes beneficence. Second, an explanation of what is meant by autonomy that is not limited

to the range of options is provided. This is done to demonstrate that respect for autonomy does not have to be limited to specific (narrow) consent. Broad consent, on the other hand, satisfies the requirement for respect for autonomy by allowing participants to choose to consent, dissent, or withdraw from research. In the sense that freedom of choice is a significant liberal ideal both in and of itself and as a component of the autonomy ideal, autonomy and choice mutually support one another (Dan-Cohen 1992). Third, the use of broad consent for biobank research is justified by the fact that the latter is subject to REC ethical evaluation, just like all other human research, with the main objective of preserving participants' rights (NDoH 2015). In light of this, the premise of the third argument is predicated on the idea of participant non-maleficence via BEC review. Fourth, provided participants are kept informed about the continued use of their materials, the use of broad consent for biobank research is justified. This maintains participant autonomy because they can choose whether or not their materials can be used for further research. Finally, as demonstrated by Barazzetti et al. (2020), motivation for biobank research participants was when they felt they could trust researchers. According to the study, this trust is a result of the researchers being open about the fact that they do not have specific research details for the prospective study. Due to the notion that trust is a virtue, it is fundamental to the concept of community, which is fundamental to communitarianism. This is a modernized version of virtue ethics (Shionoya 2001). In terms of a virtue ethics approach, broad consent is thus defended as being motivated by trust. The notion that broad consent interferes with participant autonomy by not providing adequate information (Sheehan 2011); the problem of understanding consent information when broad consent is used (Cheah et al. 2018); concern about ethical participant protection (Mikkelsen et al. 2019); the challenge of broad consent

withdrawal (Mikkelsen et al. 2019); and limitations of sample anonymisation are all criticisms for broad consent (Gross et al. 2021). Section 5.5 addresses these concerns. I align Chapter 5 with the current study's Objective 4.

5.2 Defence of the claim that broad consent for biobank research is ethically justifiable

As evidenced by empirical evidence, both researchers and participants generally accept broad consent. According to Tindana et al. (2020), research participants in Ghana who include a variety of stakeholders, namely, members of RECs and research participants generally support the recommendation for information on the use of their samples as well as REC oversight. In a study of 478 German patients, the willingness to grant broad consent for biobank research was 86.9% (Richter et al. 2018). When asked why they were willing to grant broad consent, the majority of participants said it was for charitable reasons such as altruism, gratitude, reciprocity, and solidarity (Richter et al. 2018). Quality acts such as charity, generosity, and kindness are represented by beneficence, which refers to actions or rules aimed at assisting or promoting the good of others (Beauchamp 2008). Because of the relationship between these charitable concepts and the principle of beneficence, the premise of the argument in favour of broad consent for charitable reasons is based on the principle of beneficence.

As mentioned in chapter 1, section 1.6, some researchers in SA are opposed to using broad consent, citing concerns that it is incompatible with respect for autonomy and building trust (Moodley 2017). However, the NDoH Ethics Guidelines do not prohibit broad consent, and it is a consent model that is commonly used by South African researchers (Moodley 2017). The argument that broad consent lacks legitimacy is based on the notion that this consent model is not informed consent; nevertheless, the

response to this is that broad consent can be informed consent and is ethically justifiable by virtue of its appeal to the principle of respect for autonomy (Sheehan 2011). An essential factor to take into account is that respect for autonomy justification and the associated idea of self-governance is not specific with regards to anything about the scope of the choices and decisions that an individual is entitled to make in relation to the way in which they control their lives (Sheehan 2011). As a result, there is no justification in the requirement for seeking consent that the nature of choice must be restricted or limited (Sheehan 2011). Similarly, the second premise of the argument in favour of broad consent is that this consent model is ethically justifiable on the grounds that autonomy is not limited to the range of options.

Another reason I argue for broad consent over other consent models highlighted in the current study is the practice of biobank research protocol review by BECs to reduce the likelihood of participant harm. As a result, the third premise of the argument for broad consent is based on allowing broad consent as long as participant non-maleficence is ensured through BEC.

Widespread support has been given by a number of countries for the use of human samples in research in the future (Grady et al. 2015). As an illustration, from 2011 to 2014, the United States of America (USA) implemented the required regulatory adjustments to allow the use of broad consent in several regulatory instruments (Grady et al. 2015). Following this, the NIH conducted a workshop on the ethical acceptability of broad consent for subject-matter leaders. Participants agreed that broad consent is ethically justified if initial broad consent is obtained, future research oversight and approval is obtained, and ongoing communication or information to donors is provided (Grady et al. 2015). The researchers' and participants' communication processes can

be reviewed later in the research (CIOMS 2016). In the context of the current study, I submit that providing participants with information on how their materials will be used through ongoing communication is a good way to respect their autonomy (i.e., withdraw their consent if they so wish). In light of this, the fourth premise of my defence of broad consent is its usage under the condition that participants are continuously informed about the use of their materials. Research relating to perceptions and attitudes of biobank practices in SA is generally limited to those that involve biobank experts, researchers and REC members as research participants (Moodley et al 2017; Mwaka and Horn 2019, Staunton et al. 2018; Singh et al. 2022). There is little to no evidence of such research in the general population or SA rural communities that are led by chiefs and traditional leaders as gate-keepers for that specific community, specifically with regard to access of researchers to community members for community engagement and research purposes. Human Heredity and Health in Africa (H3Africa) (2017) notes that in order to ensure sustainability of biobanks, African political and traditional leadership must be made aware of biobanking and genomics research. Moreover, clear authority structures, such as those established by village chiefs and elders, are often present and must be respected when engaging communities and such settings (H3Africa 2017). Thus contextualising the approach used to a particular group or community is necessary (Moodley and Beyer 2019). It is advantageous to approach the chief in traditional African communities and seek his permission, support, and assistance (Moodley and Beyer 2019). A notable study which involved research participants from the general population in the Western Cape and Gauteng provinces of SA, indicated that the idea of storing samples was acceptable to 77.5% of the participants (Moodley et al. 2014). The most frequently stated justification for agreeing to sample storage was that they (participants) would not need

the sample once it was donated, therefore storage would not have an impact on them. On the other hand, 12% said they would like to be informed of the reasons for storage and provide consent for such. Although the majority of participants expressed no issue to the storage of their samples, 49.5% of the participants indicated they would want to be notified each time the sample was utilised again. Almost half the number of participants in this study would prefer to be re-contacted before providing consent, whereas the remaining half would let a REC provide consent on their behalf (Moodley et al. 2014). This finding of participants having a preference for being re-contacted is consistent with that of Grady et al. (2015).

According to a study by Barazzetti et al. (2020), biobank research recruiters' honesty in stating that they do not know specifics of future research has been connected to a trusting relationship with participants who were therefore driven to give broad consent. Broad consent is considered in terms of a virtue ethics perspective as being driven by trust on the basis of the idea that trust is a virtue and essential to virtue ethics. As previously stated, the first four arguments for biobank research broad consent use considered are based on principlism; therefore, a discussion of this theory is necessary prior to the development of arguments.

5.2.1 Principlism

The term principlism refers to an approach that employs a framework of Beauchamp and Childress' four biomedical ethics principles, namely respect for autonomy, non-maleficence, beneficence, and justice (Beauchamp and Rauprich 2016). The earliest documentation of thses ethical principles appears to date back to the 1970s, as documented in the Belmont Report. Clouser and Gert appear to have coined the term "principlism" in 1990. Moral reasoning is justified by an appeal to reflective balance

and common morality, according to principlism (Beauchamp and Rauprich 2016). Principlism also has universal applicability because it establishes boundaries for what constitutes ethical behaviour in all countries when it comes to medical research and practice while correlating to fundamental human rights.

Given that Beauchamp and Childress (1994a:38) were the authors of the principles, their framework is the one that is used to analyse principlism. Principles are general guidelines for the formulation of more detailed policies and laws, and they provide great latitude for decision-making in certain circumstances. One of the assumptions made by Beauchamp and Childress was that principles can be developed as rights, virtues, or values in other frameworks and that they are central to biomedical ethics. The four guiding principles are as follows: (1) respect for autonomy, which is the norm of respecting the ability of autonomous people to make decisions; (2) beneficence, which is a group of norms that balances benefits with risks and costs; (3) non-maleficence, which is a norm of avoiding harm; and (4) justice, which is a set of norms for the fair distribution of benefits, risks, and costs. There are various kinds of rules that specify principles and direct actions. These are substantive rules such as confidentiality, privacy, fidelity, truth-telling rules for healthcare allocation and rationing, withdrawal of treatment, and physician-assisted suicide; rules of professional authority, such as those governing who should accept or disregard a patient's decisions if such decisions are medically harmful, and distributional authority and rationing rules, specify who may and should conduct acts (e.g., determining eligibility for scarce medical resources). Beneficence, autonomy, and non-maleficence are the principles used to defend broad consent use for biobank research.

5.2.2 Broad consent use based on beneficence

Beneficence, according to William David Ross (1877-1971), is the idea that we should be kind to others and try to improve their health, happiness, security, wealth, wellbeing, and wisdom (Wrenn n.d.). Benevolence, on the other hand, is a morally admirable quality that involves being willing to act in others' best interests (Wrenn n.d.). Beauchamp (2008) defined beneficence as behaviours or laws that benefit others. In the current study, I use the two concepts interchangeably. Philosophers have historically interpreted the concepts of beneficence and benevolence in a variety of ways (Beauchamp 2008). For example, David Hume considers benevolence to be the most important moral principle of human nature and defines it as a set of virtues based on generosity, goodwill, and love directed towards others, manifested as charity, compassion, friendship, and so on (Beauchamp 2008). Beauchamp goes on to argue that benevolence is largely responsible for what he refers to as "the origin of morality." John Stuart Mill, on the other hand, asserted in 1859 that the utility principle dictates that actions are right if they bring happiness to all beings (Beauchamp 2008). Consequently, this is a principle of beneficence. Actions are morally correct if they produce the greatest balance of beneficial consequences, according to utilitarianism. Mill's moral theory is based on goodness and is understood to be welfare oriented. Although Immanuel Kant rejects the utilitarian model of beneficence's supremacy, he still believes that beneficence plays an essential part of the moral life. Kant defined moral character as that which is universally beneficent as a duty rather than an inclination (Kant 2002). One of the universally valid principles (maxims) of duty, according to Kant, is beneficence. Furthermore, Kant contends that everyone has a duty to help others within their means without expecting any form of personal gain,

thus a duty of beneficence towards others. Although Kant admits that everyone has a duty to be beneficent, neither Kant nor Mill define the boundaries of beneficence.

According to Beauchamp and Childress (1994d:259), morality entails not only refraining from harming people and treating them autonomously, but also contributing to their well-being. According to The Belmont Report (1979), beneficence is the idea that, in order to treat people ethically, one must both protect them from harm by, for instance, respecting their decision and make efforts to secure their well-being. The two formulations that have been developed as complimentary expressions of beneficent actions are: (1) do not harm and (2) maximize potential benefits while avoiding potential harms. According to the Belmont Report, in relation to medical research ethics, the obligations imposed by beneficence affect not only researchers but society as well. In addition, the former have a responsibility to think about how to maximize the benefits of research while limiting the risks, whereas members of society have a responsibility to think about the potential long-term benefits and risks that may be the result of advances in knowledge and medical technology advancements. Ross identified beneficence as one of the primary duties that could be incorporated into a single duty to promote intrinsically good things (Wrenn n.d.). According to Ross, a prima facie duty is always conditional and never absolute. As a result, duties (obligations) may conflict with one another. In order to clarify what Ross means by saying that duties may conflict with one another, Ross gives an analogy (Wrenn n.d.). My choice to stop and help an accident victim (a duty of beneficence) might conflict with my duty to attend a crucial meeting (a duty to keep commitments), or it might go against my doctor's advice to stay away from stressful situations (a duty of self-improvement). What should one do in these situations? According to Ross, there will always be one duty that is more important or urgent than the others, and that duty,

which Ross refers to as one's duty proper, is what one should do in a certain circumstance. Of course, that does not imply we can always say with absolute certainty what that duty is. Perception controls that decision.

In the context of the current study, based on first, empirical evidence demonstrating that biobank research participants gave broad consent due to charitable reasons in the interest of promoting research (Richter et al. 2018), expressed as beneficence. Second, applying broad consent in the context of biobank research (considering the practical applicability of this consent model) is ethically justified on the basis that biobank research would benefit society at large, based on the conceptions of beneficence discussed previously. This should be done while avoiding harming research participants, because fulfilling the principle of beneficence necessitates fulfilling the principle of non-maleficence. Furthermore, beneficence is defined as not only providing benefits but also balancing such benefits against risks (Beauchamp and Childress 1994a:38). In the current study, I concur with Ross that the obligation to be beneficent should be prima facie and not absolute in the sense that upholding the principle of non-maleficence should take priority, in contrast to Kant's and the Belmont Report's views that beneficence is absolute. By doing so, the utility of broad consent to enable biobank research would benefit society as a whole, with the limit to beneficence being treating participants autonomously while not harming them.

By virtue of the notion that beneficence is defined as doing good, this principle therefore has the potential to benefit the greater good (Kinsinger 2009). Based on this premise, the case for broad consent justified by societal benefit (beneficence) in terms of scientific advancement is linked to the case for biobank research as a common good. In this section, the argument for broad consent in terms of beneficence is more about societal benefit than individual participant benefit. As a result, discussing

beneficence in terms of societal benefit is prudent. Beneficence aims to do good (wellbeing) not only for the individual but also for the community (Pandit 2021). Despite their differences, all ethical theories agree on the normative significance of beneficence in morality (Pandit 2021). In deontology, we have a responsibility to promote what is good for others. Utilitarianism, for example, focuses on consequences (telos) to maximize good (wellbeing) for others. In virtue ethics, the focus is on fostering the good nature of the moral agent. The notion of encouraging good for all, whether through regulations or the cultivation of virtue, is what unites all three ideologies. According to Pandit (2021), humanity's basic nature is one of goodness. Every human being possesses a certain common good. The moral concept of beneficence derives from each person's inherent humanity. In other words, the beneficence concept encapsulates human dignity and defines it in its purest form. In spite of their original differences, utilitarianism, deontology, and virtue ethics all recognize this innate humanitarian inclination to do good for others (Pandit 2021).

According to Pandit (2021), this version of beneficence differs from the utilitarian viewpoint because it is derived from an understanding of humanity (i.e., appeals to humanity as a virtue). Pandit (2021) makes two distinctions between beneficence: (1) beneficence as a universal moral principle or ideal moral ought that is anchored in humanity (i.e., humanitarian); and (2) beneficence as an active principle suited to specific conditions for effective implementation in daily life. As a result, there is some recognition that beneficence is context dependent and does not have to apply in all situations all of the time. According to Gillon (1994), we do not have a duty to be beneficent to everyone. However, healthcare workers have a beneficent duty to their patients (i.e., the latter represents at least one group of people for whom the duty of beneficence is owed). This commitment is affirmed by the societies in which the

healthcare workers practice through laws and regulations that guide the duties of care of healthcare professionals.

The Belmont Report (1979) claims that because beneficence requirements encompass both individual research projects and the entire research enterprise, they have an impact on not only the researchers themselves but also society at large. According to the concept of beneficence, it is the responsibility of researchers to make plans in advance to maximize the benefits of their work and reduce any potential risks. Society has an obligation to recognize the potential long-term benefits of the research (i.e., improved knowledge and medical development).

Weinbaum et al. (2019) introduce the concept of "duty to society" (Weinbaum et al. 2019:5), which means that research and researchers must contribute to society's well-being. According to this viewpoint, the duty to society contradicts beneficence in the sense that, while the research may benefit society, it may unknowingly and unintentionally harm research participants. As a result, involving community members can aid in the design of research that achieves an appropriate balance. Weinbaum et al. (2019) found that all professional societies studied required their members to fundamentally serve the public with the outcomes of their research and practice, despite the fact that the duty to society has been defined differently across disciplines. Furthermore, the vast majority of statements about this duty are concerned with protecting public welfare.

5.2.3 Broad consent is ethically justifiable on the basis that autonomy is not specific to the scope of choices

Originally used to describe the self-governance or self-rule of independent city states, the word autonomy comes from the Greek phrase autos ("self") nomos ("rule," "governance," or "law") (Beauchamp and Childress 1994f:120). The phrase is not a

clear notion; it has subsequently been applied to people and has taken on other connotations, including "free will," "individual choice," "liberty rights," and others (Beauchamp and Childress 1994f:120). The right to autonomy is described as the freedom to make choices that will directly reflect the decision maker's values and goals (Luków and Róyska 2015). One who is autonomous is able to make and carry out decisions that direct their behaviour (Littlewood 1996). Capacity is determined by ability and willingness (Littlewood 1996).

According to Luków and Róyska (2015), autonomy as a right is limitless and is granted to an individual under two conditions. The individual possesses certain morally significant characteristics such as: (1) rational thinking capacity and (2) awareness. In accordance with Beauchamp and Childress (1994f:121), choosers are seen as autonomous when they behave in ways that are: (1) intentional; (2) cognizant; and (3) unaffected by outside forces. Ronald Dworkin (1986) presents a somewhat perplexing view of the requirements for autonomy. According to him, in order for someone to act in his or her own best interests, we must also permit them to act in a manner that they recognize is not at all in their interests (Dworkin, 1986). The latter had been the subject of a heated debate about whether rationality is possible when someone acts against their best interests (Dowrkin 1986). Christman (2003) defines self-rule (or autonomy) as the ability and mental capacity to act in accordance with one's desires. Autonomy also necessitates acknowledging and accepting each person's "free choice" (Rathor et al. 2016), even if that choice appears inappropriate or even life-threatening.

In the sense that we appreciate free choice partly because it contributes to our autonomy and we respect autonomy partially because it supports the right to make a choice, autonomy and choice mutually reinforce one another (Dan-Cohen 1992). Choice autonomy and will autonomy have been distinguished as two types of

autonomy. The two types of autonomy are assumed to be choosing and willing (Dan-Cohen 1992). In the current study, I consider Sheehan's (2011) viewpoint in expanding on the notion that autonomy is not limited to the scope of choice and decisions. An essential point to note regarding the principle of respect for autonomy and its associated concept of self-governance is the fact that it makes no mention of the variety of decisions and choices that a person is permitted to make regarding how they are going to spend their lives (Sheehan 2011). A person has the right to make decisions and to opt not to make some decisions based on autonomy (also known as self-governance in this context) and its moral significance. For example, an individual may decide that they no longer want to do something. Another conceivable example is when an individual chooses to. This example is a decision to commit and, in some ways, a decision to continue to choose. If one chooses to live in one area over another, that is a self-determined decision that pertains to future decisions that one is willing to make. An example of a level of decision that is analogous to biobank research broad consent is someone named Fred who is in a restaurant with several colleagues. Without having seen the menu, Fred is then excused owing to a phone call, but he insists that someone chooses dinner for him. His dietary restrictions and the kinds of food he prefers are briefly discussed with the one assigned to choose dinner for him. Fred's meal is then ordered on his behalf by his companion. The rationale behind this comparison is that Fred's choice is typical, demonstrates his autonomy, and is comparable to obtaining broad consent for biobank research. Using the broad consent analogy typical of biobank research, Fred and the designated companion may decide that the former will confer with other companions before reaching a choice. The designated companion may even suggest a strategy for handling a scenario in which he places an order for something Fred does not want, and they agree that in that case,

Fred may back out of the agreement and the designated companion will have to either consume the meal or it will be returned. The decision to withdraw by Fred and the consultation with other partners both represent the inherent governance and withdrawal rights in biobank research. Nothing in the argument for informed consent suggests that choice must be limited or constrained in any way. There is nothing that only requires your specific consent. Furthermore, independent people frequently make choices for the future that are akin to the choice to take part in biobank research.

It is worth noting that the scope of unlimited choice in relation to autonomy does not apply in all circumstances. For example, the ethical foundation of blood alcohol consumption (BAC) laws is that they not only protect drinking drivers but also protect other road users (Morain and Largent 2018). Broad consent as a nature of choice does not need to be specific in terms of giving participants specific study details on the grounds that nothing in the basis for the need to obtain consent necessitates that it be constrained or limited (Sheehan, 2011). If participants' right to choose whether or not to participate in biobank research is honoured, this includes adhering to the minimal requirement for adequate information specified in Chapter 4 section 4.4.2.

5.2.4 Broad consent use provided participant non-maleficence is ensured through biobank ethics committee review

In order to be ethically acceptable, human research must adhere to certain ethical principles, including the principle of non-maleficence (Shade et al. 2019). Through their process of ethics protocol review, RECs protect future research participants from harm (Kerasidou 2017, Phillips et al. 2017, Ursin et al 2009). The perspective of Beauchamp and Childress is taken into account in conceiving the principle of non-maleficence. The duty to not wilfully harm others is upheld by this principle (Beauchamp and Childress 1994e:189). Non-maleficence obligations are sometimes

stricter than obligations of beneficence (Beauchamp and Childress 1994e:191). An obligation not to endanger a research participant through low-risk procedures, for example, is typically not more stringent than an obligation to rescue a participant who has been injured by research procedures. If the injury to a participant is minor, the obligation of beneficence takes precedence over the obligation of non-maleficence (e.g., swelling caused by needle prick, but there is major benefit such as a life-saving intervention as an outcome of the research). In general, compared to beneficence requirements, non-maleficence obligations are stricter (Beauchamp and Childress 1994e:191). When acting beneficently results in the best outcome, obligations of non-maleficence take precedence over obligations of beneficence. When there is a conflict between beneficence and non-maleficence, non-maleficence is usually the deciding factor. Yet, there cannot be a priori rule that prioritizes non-maleficence over beneficence because the relative importance of these moral principles varies depending on the situation. Without recommending a hierarchical framework or normative ordering, Beauchamp and Childress (1994e:192) distinguish the principles in the following manner. Non-maleficence: 1) One must refrain from doing evil or harm. Beneficence: 2) One should stop evil or harm. 3) Evil and harm should be eliminated. 4) One should carry out or encourage good.

The contrast between non-maleficence and beneficence that was established above indicates that whereas non-maleficence only calls for refraining from doing harm, each of the types of beneficence calls for action by aiding, namely: preventing harm; removing harm and promoting good. Generally speaking, maleficence (also known as harm) in the context of human research refers to the possibility of research participants suffering bodily or mental harm (Shade et al. 2019). Although there is no risk of bodily harm when participating in biobank research, there is a risk of violating participant

privacy and the potentially harmful consequences of such violations (Ursin 2010). Harm can be intentional or unintentional (negligent) (Shaw and Barrett 2006). Risk of harm assessment entails addressing negligent harm in order to reduce the possibility of non-negligent harm (Shaw and Barrett 2006). Mwaka and Horn's (2019) research findings on South African researchers revealed a perceived lack of emphasis by study participants (who were researchers) on the benefit/risk assessment by RECs during ethics review. The significance of maintaining proper community and stakeholder engagement in biobank research is highlighted by this finding, which emphasizes the need to increase awareness among REC members and researchers. This recommendation would not only allow communities to play an active role in determining research agendas, but it would also help to identify potential community harms (Mwaka and Horn 2019). According to Eriksson and Helgesson (2005), it is fair to have distinct ethics review standards for research involving biobanks compared to study involving human participants because the former does not directly endanger the individuals' physical safety.

RECs evaluate the risks of harm that research may bring about by ensuring that those risks are proportionate to any potential benefits (Shaw and Barrett 2006). Broad consent must be obtained in accordance with the NDoH Ethics Guidelines in SA and BECs must approve biobank research procedures for ethical reasons before biobank research can begin. Over and above ethics committee approval for individual research protocols, the NDoH Ethics Guidelines require REC approval when establishing new biobanks. BECs and RECs perform the same function, with the exception that the former only reviews biobank research protocols. The NDoH Ethics Guidelines, Chapter 4, provides recommendations for RECs and state that a REC's primary responsibility is to safeguard research participants' interests. It is imperative to bear in

mind that the recommendations include instructions for collecting and storing samples and associated data. The Guidelines make a number of recommendations for assessing the risk for participant harm. These include training for REC members, particularly on reviewing high risk research; a requirement for research that involves a moderate increase in risk above minimal risk to include monitoring schedules and persons responsible, as well as their contact information; that only research with a very low risk of harm should be subject to expedited review; and that monitoring of risk of harm should be done on a regular and consistent basis, reflecting the extent and degree of risk of harm to participants. In order to reduce the privacy risks associated with samples and associated data, RECs must assess the extent to which materials could be used to identify a participant (donor).

The Guidelines also provide a few examples in that regard: (1) materials with direct identifiers can be used to identify a donor; (2) if security and confidentiality measures are inadequate, coded materials may identify a donor; (3) materials that have been anonymized but are not linked to donors are unlikely to identify a donor; and (4) materials that have been acquired without any identifiers are unlikely to identify a donor. The Guidelines also state that genetic markers allow for the re-identification of population groups rather than just individuals. Furthermore, RECs should focus on eliminating or at least minimizing the risks to privacy and autonomy that could result from such re-identification. Avoiding group maleficence is especially important in the African research context, where some population groups with distinct cultures, languages, and belief systems may be marginalized or discriminated against (Yakubu et al. 2018). In terms of secondary use of materials, if samples have been made anonymous and the results of the research do not pose a risk of harm (social, psychological, legal, or economic) to any individual, family, or community, no new

consent is required. If a link to identifiers exists but is inaccessible to the research team and the findings of the study do not indicate a risk of harm (social, psychological, legal, or economic) to any individual, family, or community, new consent is not required.

A research ethics committee should assess and authorize the establishment of any biobanks used for research or other purposes, according to the WMA Declaration of Taipei. The Declaration further urges the ethics review committee to confirm that the consent obtained is adequate for material use and that no more measures are necessary to protect the donor. Additionally, the ability of a biobank to oversee continuing operations must be granted to the ethics review committee. The committee can also establish mechanisms and procedures to protect participants' autonomy, dignity, and privacy. Such procedures are only acceptable if strict data protection rules are followed. Due to this, data and biospecimen access committees (DBACs) are being established by biobank and genomics research programs for secondary sample use review and consideration of risks posed to study populations (Yakubu et al. 2018). The biobank Ethics Advisory Committee (EAC) provides guidance, suggestions, and advice on ethical matters to the biobank board (UK Biobank 2022). The EAC also provides participant interest advice and keeps track of the UK Biobank's compliance with the Ethics and Governance Framework (EGF), reporting its findings to the public. The UK Biobank Access Sub-Committee is in charge of making key material access decisions, particularly those concerning sample use.

There is no justification why broad consent for future research use of human materials should not be acceptable if (1) the risk of harm (alternatively, maleficence) is low and adequately well controlled; (2) participants voluntarily accept the level of risk; and (3) a mechanism for withdrawal exists (Staunton and Moodley 2013). Additionally, it is the

responsibility of RECs to establish whether research investigations are of the type to which participants broadly consent to when they give their broad consent to participate in a particular type of research (Ursin et al. 2020). According to the authors, the dependence on widespread agreement for biobank research "is thus a reliance on trust" (Ursin et al. 2020:10).

5.2.5 Broad consent for biobank research provided that there is ongoing communication with participants on the use of their materials

Continuous communication is defined by Mikkelsen et al. (2019) as communication with participants who are still alive and competent in the context of biobank research. Such communication would describe and provide information on the work done within the biobank since the previous communication, as well as notable study findings, future plans, and newly approved research. They suggest making such data accessible at predefined regular periods (e.g. once a year). The proposal is that providing information on a continuous basis should be mandatory when broad consent is granted, thus making broad consent a necessary condition of compliance. The consent form must further specify that potential participants must agree that the biobank must continue to provide them with information on a continual basis as outlined above in order for their consent to be valid. The benefits of continued communication guarantee that participants are constantly informed of the results of the process of ethical review. As a result, people are informed about the research being done and can decide whether or not their values still line up with those of the biobank's operations before continuing to participate. Continuous participation has the additional benefit of ensuring that participants (who are still competent) are always informed of their right to withdraw as well as their participation status. Mikkelsen et al. (2019:10) also raise the issue of participants experiencing "information fatigue" when

they are bombarded with information in real time. This could be a concern since people who receive information frequently in an invasive and unwanted manner might develop "information fatigue" (Mikkelsen et al., 2019:10). In addressing this issue, they acknowledge that it may be possible to provide participants with only relevant changes that are in line with the participant's preferences. First, it is feared that communication may become so infrequent as to render the information provided ineffective in assuring participation awareness (Mikkelsen et al. 2019). Additionally, judging when relevant or significant modifications have been made would require making broad assumptions about participant preferences, which would fall short of offering all participants the same level of protection. Second, any risk posed by the information as indicated is probably not as severe as the risks associated with consent fatigue. Trust, confidence in researchers, participant retention, and desire to engage in future research may all increase with ongoing communication with biobank participants regarding the use of their samples (Mester et al. 2015). Communication is necessary for developing trust and rapport during the research process (Kondowe and Booyens 2014). Tracking participants requires generic skills such as good interpersonal skills (Patel et al. 2003). According to Mester et al. (2015), the majority of participants preferred to get study updates. A majority preferred yearly updates, but a small number was unconcerned about getting them. The inclination of many individuals was also to give researchers information on their health. Bidirectional communication strategies that allowed participants to inquire about the use of their materials were favoured by a sizeable number of the participants. A study involving the Mayo Clinic Biobank is an example of how trust can be built through communication with participants (Mester et al. 2015). According to Mester et al.'s findings, biobank research participants in this study considered yearly newsletters and emailed updates to be acceptable forms of

communication with researchers. According to a separate study by Meagher et al. (2020), ongoing communication is important for enabling trust and transparency, acknowledging the ongoing relationship between participants and researchers, and ensuring participant values are upheld. Members of the Mayo Clinic community advisory board (CAB) in this study viewed letters as the most reliable and authoritative form of communication, whereas emails and text messages were viewed as less reliable, with texts garnering the most unfavourable reactions (Meagher et al. 2020). Letters and e-mails should follow the rules of written professional correspondence (Patel et al. 2003). Some participants respond positively when an institution's letterhead is used, along with a handwritten note and an original signature. Coloured ink, fliers, envelopes, and letter paper have been shown to increase response rates (Patel et al. 2003). These findings on communication modality preferences show that ongoing communication with participants is not a one-size-fits-all approach, and that different participant groups prefer different communication modalities. This implies that prior engagement with targeted communities is essential, or that participants' communication preferences should be determined during the consent process at the very least. Notably, ongoing communication with research participants differs from public engagement in that the latter includes activities designed to gain public understanding, promote trust, and support for the proposed project via a consultative process prior to seeking informed consent (Watanabe et al. 2011).

There is a proposal for broad consent use with restrictions based on the findings of a 2013 workshop organized by the NIH Clinical Centre Department of Bioethics. Participants in the session included a variety of subject matter specialists with various perspectives on the application of broad consent (Grady et al. 2015). The workshop conclusions resulted in a proposal to allow broad consent use under the condition of

ethics approval and, where possible ongoing communication with participants while recognizing that communication may not always be possible (Grady et al. 2015). Members of the Mayo Clinic CAB also saw ongoing communication as a supplement to broad consent (i.e. broad consent ethical acceptability based on ongoing communication) (Meagher et al. 2019).

In relation to ongoing communication for biobank research broad consent use, trust and transparency appear to be recurring themes. Given the preceding discussion on biobank research participants' perspectives, it is prudent to incorporate participants' perspectives into biobank governance systems. This is because if biobanks do not consider public perspectives on biobank governance, biobank endeavours may fail (Hawkins and O'Doherty 2010). In the context of biobanking, it is essential to distinguish between trust in people and trust in institutions since interpersonal trust (i.e., participant trust in the person taking the sample) does not always convert into institutional trust (Dive et al. 2020). Regarding transitivity, which is the ability of a connection between two parties to move to a third party that is a specific relational partner of one of the others, it may be said that the transition from interpersonal to institutional trust is related to this concept. If individual A has confidence in (person or institution) B, the transitivity question is whether or not A's confidence in B could extend to (person or institution) C with whom B is affiliated (Dive et al. 2020).

So, the credibility of the biobank representative plays a significant role in determining the credibility of a biobank (Dive et al. 2020). Establishing and retaining trust depends on transparency (Gibson et al. 2017). A crucial aspect of biobank governance is transparency, which guarantees the availability of biobank research information (Gibson et al. 2017). According to Canadian biobank stakeholders interviewed for a study by Gibson et al. (2017), posting a comprehensive material access policy online

would not necessarily increase transparency for the general public. Instead, they said that shorter explanations of material access are desired. Although there appears to be widespread support for transparent biobank governance, the question of how much information should be made available to participants remains unclear (Gibson et al. 2017). Given the preceding discussion, broad consent use based on ongoing communication with research participants about the use of their materials has the potential to increase trust and transparency in biobank representatives. As a result, I argue that biobanks that use broad consent should have a transparent and trust-based approach to material access, as well as ongoing communication with participants about the use of their materials. In turn, this will guarantee the long-term sustainability of biobank research.

5.2.6 Defence for broad consent motivated by participants' trust in terms of a virtue ethics approach

As previously stated, in research conducted by Barazzetti et al. (2020), biobank research recruiters' honesty that they do not have details of future research was attributed to a trust relationship between the recruiters and participants, who were then motivated to grant broad consent. As a result, it can be argued that biobank personnel's truthfulness and trustworthiness have the potential to influence participants' motivation to grant broad consent. The relational viewpoint (relationships between research participants and researchers) considers how consent models can undermine or strengthen trust in medical research and healthcare institutions (Wiertz and Boldt 2022). The foundation of human relationships is truthfulness (Sanney et al. 2020). Furthermore, how truthful we are with others has a significant impact on trust. Aristotle defined virtue as that which is praiseworthy and divided it into virtue of thought and virtue of character (Irwin 1999:31). Teaching produces virtue of thought, whereas

habit produces virtue of character. Thus, virtues develop in us either naturally or through acquisition, and they are completed through habit. According to a virtue ethics perspective, character considerations must be taken into account when determining whether an action is right or wrong. There are two ways to interpret the term "character" (Pellegrino 1989). In general, it refers to the type of person we are as evidenced by the virtues and vices we exhibit. A person of character is defined as someone who can be trusted to behave honourably and take others into account when making decisions (Pellegrino 1989). Principles and rules are needed to supplement virtues (for example, the corresponding virtue for veracity (rule) is truthfulness) (Beauchamp and Childress 1994c:67).

Pellegrino (1989) defines "ethics of the professions" as the moral obligations derived from the types of activity in which professions engage in, consisting of the rational and systematic ordering of duties, principles, rules, and virtues intrinsic to achieving the ends to which those professions are dedicated. According to Pellegrino, the many virtues of professional life are primarily reducible to two virtues: fidelity to trust and beneficence, which follows from fidelity to trust. Furthermore, these two character traits serve as the foundations upon which other virtues and principles of professional ethics are built. Pellegrino believed that virtues could be taught in the same way that family, church, and schools shape a student's character before they enter professional schools. The latter must also teach what a good professional should be like.

Meara et al. (1996) assert that professional conduct is rarely either absolute or completely relative. Due to this, exercising professional judgment calls for morally virtuous and competent people. Furthermore, professional codes aid professions by recommending a standard of behaviour to guide professionals in their work. These codes represent ideals that professionals are encouraged to strive for. Aspiration

towards ideals and the development of character virtues (traits) that enable attainment of these ideals are central to virtue ethics. Beauchamp and Childress (1994c:69) contend that virtues alone are insufficient, and that in many cases, rules and principles are required to guide behaviour. According to the Health Professions Council of South Africa (HPCSA), one of the core ethical values and standards for good practice in the healthcare professions is truthfulness (HPCSA 2016).

Based on empirical research that demonstrates the importance of trust in scientific research, Tindana et al. (2019) advocate for a "entrustment" approach to solve the issues surrounding biobank research consent in Africa. In order to further scientific research, the entrustment model presupposes that sample donors (or alternatively, biobank research participants) view themselves as entrusting their samples to research institutions. The main prerequisite for entrustment is trustworthiness. Among the ramifications for the entrustment model as a justification for broad consent is that it is only justifiable in the context of a genuine attempt to develop reliable organizations with solid trust relationships to the communities where the samples are obtained (Tindana et al. 2019). Entrustment implies responsibility and establishes a moral relationship between researchers and participants. This means that researchers cannot do whatever they want with the samples because they have a responsibility and accountability to protect the samples from inappropriate uses that may harm participants' values and well-being. Tindana et al. (2019) propose several methods for an entrustment framework to support broad consent. These include promoting the research institution's trustworthiness; establishing clear guidelines for the institution; community engagement and strengthening consent practices; and ethics review processes that improve and foster trust. Key guidelines for fostering institutional trustworthiness include having honest objectives and motives, being open and

transparent, maintaining scientific integrity, and reducing risks and harm that relate to sample and data use. Frequent research meetings with field employees and local workshops can be useful tools for fostering these principles.

Empirical questions about trust may influence normative questions about its appropriate use (Johnsson 2013). According to Johnsson (2013:70), empirical findings can contradict a normative theory that is based on an empirical statement's "truth value". Generally, ethicists who are working on theoretical work utilize empirical assertions sparingly. But, in practical ethics, like in daily life, such arguments are employed more liberally to support one's assertions. Empirical data are taken into consideration as described in the following section to assess the generalizability of the finding that participants in biobank research are more likely to give broad consent when they trust biobank staff.

5.2.7 Empirical evidence of trust as motivation for participants to grant broad consent

Between October 2013 and November 2014, Bosisio et al. (2021) carried out a qualitative study on broad consent at the Lausanne Institutional Biobank (BIL) at the Lausanne University Hospital in Switzerland in order to determine how recruiters influenced patients' decisions to sign up for this consent model and how they developed trust in the organization. The results of this study reveal that recruiters have a significant role in broad consent by improving the clarity, lowering the level of confusion, and, where possible, promoting acceptability of consent forms. Fostering a relationship that is based on trust between participants and BIL necessitates conditions such as recruiters' attitudes toward patients' decision-making competence; acting as mediators and answering questions; connecting patients with BIL management for further explanation; and being compassionate listeners.

According to Saskia et al. (2017), participants in a hypothetical biobank that uses open data sharing and broad consent would be less likely to engage and would have a more unfavourable view (2017). The results of the study, however, imply that broad consent biobanks might not necessarily have less success recruiting participants than those that rely on specific consent models. This study found a connection between acceptance of broad consent and tailored recruitment efforts for underrepresented groups, such as informational initiatives and addressing certain attitudes regarding participation. Sixty-one percent (61%) of respondents said they trusted the medical researchers, while two-thirds (64%) reported that they trusted the healthcare system.

In Simon et al.'s (2011) study on the perception of different consent models, research participants reported that in order to grant broad consent and assume that their samples would be handled responsibly, they would need to trust researchers and science. The participants realized that in order for the biobank to properly manage access to their samples and data, they would need to have faith in the biobank. The confidence that this choice will be made available to them via a prospective opt-in consent process may be related to participants' readiness to give broad consent. With opt-in consent, consent is explicitly expressed (Giesbertz et al. 2012).

Given the conceptual analysis and empirical evidence that participants in biobank research are more likely to trust biobank staff members (or recruiters) when they have a trust relationship, trust is a crucial component in determining people's willingness to give broad consent for biobank research. According to Johnsson (2013), understanding trust relationships reveals motivations to participations in biobank research in ways that trust assessments cannot (e.g., surveys). Johnsson (2013) defends this claim in several ways. To begin, when asked about our reason(s) for trusting, we interpret the question on grounds that are epistemological rather than

strategic. Hence, if we describe trust in terms of the benefits it offers, we are describing something else. Second, on the basis of betrayal, which can be argued. Using the term necessitates moral rather than empirical justification because, when asked why they feel betrayed, the expectation is for those who betrayed them to provide reasons, such as what occurred and why certain things need to have been handled differently. Betrayal appears to imply a relationship with another. Johnson observes that in order to understand trust properly, we must distinguish between predictive (what will happen) and normative expectations (what ought to happen). Although this conceptualization has focused on interpersonal trust, it can also be applied to institutional trust if moral agency can be attributed reasonably. As a result, as demonstrated by empirical data, an institution's moral agency depends on the individuals who constitute its membership. The following section examines the arguments against using broad consent for biobank research.

5.3 Counter-arguments to broad consent for biobank research

Arguments against broad consent use in biobank research are based on the ideas that (1) broad consent provides insufficient information, which interferes with participant autonomy (Sheehan 2011); (2) the difficulty of understanding information when broad consent is used (Cheah et al. 2018); (3) concerns about ethical participant protection (Mikkelsen et al. 2019); (4) the difficulty of broad consent withdrawal (Mikkelsen et al. 2019); and (5) the drawbacks of sample anonymization as a critique of broad consent (Gross et al. 2021). These concerns are addressed in the sections that follow.

5.3.1 Interference of broad consent with participant autonomy

The requirement to provide adequate information to study participants in order to enable participant decision-making is the primary ethical challenge with broad consent

use for biobank research, as previously noted in Chapter 1, section 1.4. (Hansson et al. 2006, Steinsbekk et al. 2013). This concern is about participant autonomy and the participant's trust in the biobank researcher that their materials will be used in accordance with the consent granted. Commentators who oppose the use of broad consent argue that insufficient information interferes with participant autonomy (Sheehan 2011). This point of view contends that broad consent poses ethical challenges because it falls short of providing study participants with all the information they require to make an informed, autonomous decision (Sheehan 2011). The main concern is that there are no known research details at the time of sample collection. As a result, the participant cannot be made aware of the precise nature of the research for which consent is being requested.

5.3.2 Understanding of information when broad consent is used

Understanding the details of data sharing is a crucial component of obtaining broad consent, according to researchers who took part in a study in Thailand (Cheah et al. 2018). One of the study's findings was that other study participants who were clinical trial participants did not clearly understand data sharing in the same context as the study's researchers (Cheah et al. 2018). These participants had previously agreed to data sharing despite not understanding the concept as well as the researchers. Clinical trial participants from Bangkok, where the majority of the population is accustomed to using the internet and social media, were asked to characterize data sharing. Many compared it to sharing information on social media. This may be due to the similarities between the Thai words for "data" and "information," "*khor moon*" and the fact that one common usage of the word "share" alludes to pressing the share button to make information publicly available on social media (Cheah et al. 2018).

Richter et al. (2018) recruited research participants for a study in order to evaluate their comprehension of particular facets of broad consent use. The study was divided into two phases: E1 (before the consent brochure was improved in terms of language clarity) and E2 (after the consent brochure was improved in terms of language clarity). Some aspects of the research were poorly understood by participants when objective understanding was tested in phase E1. These included the "absoluteness" of data protection (21%), the "scope" of material usage (34.8%), and the potential for material use by other researchers (35.1%). Better outcomes came from other comprehension-related factors. The findings also included the right to object (71.6%) and the absence of a benefit to the consenting party (52.4%). Notably, when specific consent is sought, the goal of health research is not (or should not be) to derive personal benefit. Rather, health research is generally conducted for societal benefit (Hofmann et al. 2009). As a result, expecting broad consent to benefit individual participants would be unrealistic. Section 5.4 addresses these and other concerns about broad consent use.

5.3.3 Concerns over ethical participant protection

According to Mikkelsen et al. (2019), broad consent does not provide participants with adequate ethical protection. They contend that the value and duration criteria are not met by this consent model. In accordance with Mikkelsen et al. (2019), the value of participants' right to withdraw is debatable if they are unaware of the nature of the research they are enrolling in, and the duration criterion relates to appropriate ethical protection for the period of their involvement. The argument relating to the ethical protection of participants when broad consent is used makes two claims: (1) broad consent provides shallow protection because it does not provide enough detail and clarity of the scope of research; and (2) it is unlikely that broad consent will be extended to changing research objectives and methods over time. The defence

continues by claiming that there is a chance that participants will be coerced into taking part in research that they would not have accepted if they had been asked for study-specific consent.

5.3.4 The challenge of broad consent withdrawal

According to Mikkelsen et al. (2019), participants who have given broad consent for biobank research are prone to forget about their right to withdraw when there is little or no ongoing communication with them. Clarity surrounding the process of withdrawing consent from research is lacking in the literature (Melham et al. 2014). Notably, the challenge of withdrawal is not limited to consent withdrawal in biobank research, but to consent withdrawal in human research in general. Different biobanks have mechanisms in place for participants to withdraw their consent. These include the Canadian CARTaGENE Population Biobank, the Dutch Biobank Lifelines, the Swedish LifeGene biobank, HUNT Biosciences, and the UK Biobank (Melham et al. 2014). Regarding the withdrawal of samples from a biobank, it is unclear whether such samples should only no longer be used for research purposes or whether they should also be disposed of (Melham et al. 2014). Although there is a paucity of literature on biobank research participant withdrawal, there is evidence of such withdrawal from the Lifelines biobank in the Netherlands. Only 4% of those asked to participate in a new study agreed to give consent (Broekstra et al. 2020). Those who declined stated that they had no interest, were unavailable, and were unwilling to devote more time to Lifelines research (Broekstra et al. 2020). Two of those who had previously withdrawn consent cited too much data collection (financial information in addition to medical details) as a source of concern that their data would be misused, causing significant disruption in their lives. Furthermore, all former participants who

withdrew felt misinformed or that they were not given enough information (Broekstra et al. 2020).

5.3.5 Limitations of sample anonymisation as criticism for broad consent

According to Gross et al. (2021), while broad consent and de-identification of human samples minimize burdens on patients and maximize the benefits of learning from healthcare, these approaches fall short in terms of engagement, privacy, and transparency. Gross et al. (2021) cite the infamous Henrietta Lacks case, in which Henrietta's cells (the HeLa cells) were de-identified but used for further research without her permission. The problem in this example is not necessarily that broad consent was requested and utilised, but rather that consent was not sought and granted. Gross et al. (2021) discuss how de-identification exacerbated ethical violations in Henrietta's case in their article. They proposed non-fungible tokens (NFTs), a blockchain technology innovation that, in their opinion, may help to solve the problem of unethical behaviour.

5.4 Addressing broad consent counterarguments and concerns

In this section, the following counter-arguments and concerns about broad consent are addressed: (1) broad consent provides insufficient information, which interferes with participant autonomy (Sheehan 2011); (2) the difficulty of understanding information when broad consent is used (Cheah et al. 2018); (3) concerns about ethical participant protection (Mikkelsen et al. 2019); (4) the difficulty of withdrawing broad consent (Mikkelsen et al. 2019); and (5) the drawbacks of sample anonymisation as a critique of broad consent (Gross et al. 2021).

5.4.1 Broad consent provides inadequate information and therefore interferes with participant autonomy

My ethical examination of the present study on the use of broad consent identifies the fundamental ethical issue with this consent model. According to Hansson et al. (2006) and Steinsbekk et al. (2006), broad consent use should adequately inform participants on the intended use of their materials if it is to be ethically justified (2013). According to Helgesson (2011), the idea of being "properly informed" should be regarded as follows. Helgesson points out that one method to further the argument of those who oppose broad consent is to suggest that being properly informed necessitates that every prospective study participant gets all information that can be expected to be relevant to at least their decision to participate. Such information must be included since it is reasonable to assume that someone would at the very least prefer to receive study-specific information. Helgesson (2011) offers an alternative strategy, saying that rather than selecting what information should be included in a list, we should consider why information should be provided. If this is the case, then the primary goal of informing potential research participants is to support their autonomy in choosing whether or not to participate. A one-size-fits-all method in relation to research information is insufficient since people differ in what information they find pertinent for such decision-making. People are willing to participate in scientific research under a variety of conditions. For example, some people need specific information about a study before they will even consider it, whereas others are content with general information about the conditions that must be met for biomedical studies involving humans, such as ethical review, data storage and protection, confidentiality, etc., before they will be willing to donate their samples for biobank research. It is argued that if individuals in the latter group (those that are content with general information)

genuinely obtain, comprehend, and act upon pertinent and accurate general information, they are sufficiently informed and their consent is valid because it is based on the pertinent information in their opinion. In fact, the perspective that participants are adequately informed to the extent that they are provided with and comprehend the information they find relevant for their decision performs better in terms of respect for autonomy than the perspective that participants must have study-specific information in order for their decision to be properly informed, because individuals may want less information than what the latter view requires. As a result, it is acceptable to include a choice on consent forms where the subject offers general assent to being enrolled for research in the future. This idea might not appeal to everyone, but it does not make it unworthy of consideration. It is advised that this option be included on consent forms addressing the storage and use of human biological samples because broad consent is not only acceptable from an autonomy standpoint but also the most practical consent alternative from a research perspective.

The idea that the definition of autonomy in the context of biobank research solely includes the absence of deception is an intriguing one. This definition does not involve giving participants full disclosure at every stage of the research (Beauchamp and Childress 1994f:158). However, as stated in Chapter 4, section 4.4, sufficient disclosure should cover the objective of material collection, the type of material to be collected, potential risks and benefits (if any) of research participation, the right to decline participation, guidelines for material access, and privacy and confidentiality safeguards. Furthermore, the proposed use of broad consent entails providing participants with information on the broad area of proposed research.

The need for ongoing communication goes a long way towards addressing the concern about providing adequate information when broad consent is used. In addition

to the information supplied during the consent procedure, participants should also be informed about how their material will be used, as indicated in Chapter 4, section 4.5.2.1, and Chapter 5, section 5.2.4. When informing participants about the purpose of material (sample and data) collection, it should be sufficient for them to understand the broad scope of the proposed research. Given the future-oriented nature of biobanking, one example would be genomic research on a particular disease as relevant but not necessarily the precise aims and diagnostic research methodologies. Participants cannot be physically harmed if they do not have information on the diagnostic research methods that their samples will be used for because the analysis will be done on their materials without physical intervention, as is typical of general health research. The risks associated with biobank research are discussed in Chapter 1, section 1.5.1. These are related to the disclosure of personal information, which causes social and dignitary harms (Dhai and Mahomed 2013). For instance discrimination and stigmatisation, particularly genetic stigmatisation because it is frequently group-based (Dhai et al. 2015). An example is the case of the Havasupai tribe (appellant) v. the Arizona Board of Regents (defendants), 204 P.3d 1063 (2008) 220 Ariz. 214, which was represented by researchers from Arizona State University (ASU). Between 1990 and 1992, ASU researchers conducted diabetes genetic research on community members of the Havasupai tribe of the Supai village in Arizona.

Despite the fact that the research was halted, scientists at ASU and elsewhere continued to study tribal members' blood samples and to publish their findings, with some of their articles concentrating on evolutionary genetics as opposed to medical genetics. In contrast to the Havasupai tribe's belief that early humans originated in the Grand Canyon, some published research focused on their prehistoric voyage from

Asia to North America. One of the tribe's claims was that the researchers violated its legal, cultural, and religious rights by purposely causing emotional discomfort.

The notion that granting broad consent equals to choosing to forgo all future possibilities or choosing ignorance is used in the argument that broad consent is not informed consent based on the claim that it does not present participants with enough information. An individual could, for instance, be born with a fatal genetic disorder (Sheehan 2011). This assertion relates to the right not to know. There are several exceptions to the right not to know (such as having a fatal disease), and comprehending these exceptions necessitates considering one's own opinions towards such a right. Sheehan (2011) responds to this assertion by arguing that the argument for broad consent is not about defending the right not to know but rather about making decisions with the proper level of information to make them an informed, autonomous decision (Sheehan et al. 2011)

Sheehan (2011) continues by asserting that this consent model is appropriate and that it makes use of the principle of respect for autonomy to argue that broad consent is informed consent. This argument is based on the notion that the explanation for respecting autonomy does not include any information about the variety of decisions and choices that a person is permitted to make regarding how they will conduct their lives (Sheehan 2011). Self-governance in this perspective is managing oneself on all levels, not just the most fundamental ones. This assertion is related to the earlier point made in section 5.2.1.2 about decisions to be in a long-term marriage or to live in a specific area, which are decisions that affect future decisions. Thus, whether or not the latter decisions restrict liberty, they have no effect on autonomous decision-making. In the current study, to further the idea of autonomous persons and decision-making in the context of broad consent, I draw on Beauchamp and Childress's idea

that people are autonomous in the first place because they determine and provide the moral law for themselves out of their inherent rational, as independent individuals with opposing interests (Beauchamp and Childress 1994g:59-60). Furthermore, an autonomous person is one who acts freely according to a self-determined plan. Self-governance abilities such as independent choice, deliberation, reasoning, and understanding are characteristics of an autonomous person. A decision-making discussion focuses on autonomous choice, which is actual (self) governance. Even autonomous beings who are capable of self-government occasionally make poor decisions. This could be due to temporary limitations imposed by disease, coercion, ignorance, or other factors that limit options.

Even though they did not act autonomously, a person who signs an informed consent form without reading or comprehending it nevertheless qualifies to act autonomously by granting informed consent. Persons who are not autonomous (those who lack the characteristics of autonomous people) can also make autonomous choices. Some patients in mental institutions who have been declared legally incompetent and unable to care for themselves, for example, can make autonomous decisions regarding meal preferences, phone calls to acquaintances, and refusal of some medication. Thus, being autonomous is not dependent on the type of consent granted, according to this contextualisation. It is instead based on other factors such as incapacity caused by diseases such as mental illness and other characteristics such as coercion, ignorance, or other conditions that limit options. As a result, broad consent, as a type of consent, cannot render people non-autonomous; rather, being autonomous is a matter of possessing the characteristics of an autonomous person.

Beauchamp and Childress' analysis of autonomous actions is used to determine whether or not those who choose broad consent do so autonomously. Beauchamp

and Childress study autonomous actions in terms of decision-makers who behave in a manner that is (1) deliberate, (2) with understanding and (3) free from outside influences (Beauchamp and Childress, 1994f:123). Except for the first condition, actions are either intentional or unintentional and are not graded. Actions can have varying degrees of autonomy. An activity must have a significant level of understanding, be unrestricted, be completely devoid of influence, or have no full comprehension in order to be considered autonomous. In the real world, where people's actions are rarely, if ever, entirely autonomous, limiting patients' autonomous decision-making to the ideal of completely autonomous decision-making eliminates these acts from any significant place. Understanding and independence from controlling influences in the healthcare (or research) setting should not be greater than, say, understanding and influence when buying a new house, selecting an investment, or attending university. Such consequential decisions are far from fully autonomous, despite being substantially autonomous. Similarly, I argue that an autonomous decision to grant broad consent does not require full information because this would be impractical, but rather that (1) a substantial amount of information should be provided (as discussed thus far in the current study) to enable substantial understanding by participants; and (2) the consent process should be free of controlling influences (i.e., free from coercion as recommended in Chapter 4, section 4.4.1). Given this account of autonomous actions, it would be unreasonable to expect a comprehension of consent information beyond that suggested in Chapter 4, section 4.4. 2. According to Sheehan (2011), it is essential to include governance mechanisms with regard to broad consent because doing so would acknowledge that the biobank would make judgments in the future about how it will use its materials. Consequently, the inclusion of the biobank's broad research program would be a recognition that the

research done would be of a more specialized kind. For instance, broad consent can mention the goals of the research (i.e., the scope of projects that will be conducted under the auspices of the biobank).

5.4.2 Understanding or comprehension of information when broad consent is used

Understanding is a cognitive process that requires prior knowledge in order to relate to and make sense of new information (Sand et al. 2010). In order to be able to understand, there must be some level of familiarity between prior knowledge and the new information (Sand et al. 2010). Furthermore, advanced age or serious illnesses can have an impact on motivation for understanding and cognitive ability to process information. Concerning the issue of participants' understanding of broad consent information, one way to improve understanding is to simplify consent information (Cheah et al. 2018). Regardless of the consent model used, South African RECs require researchers to translate consent documents into a language that participants can understand. To enable comprehension, effective scientific translation necessitates technical knowledge of the subject (Jhanwar and Bishnoi 2010). Richter et al. (2018) discovered that when consent text is modified in terms of clarity of language, there is significant understanding. These findings were obtained in a second phase of the study after the consent information was revised to improve clarity of language. This study also found that when participants felt they had a better understanding of the information (subjective self-assessment of understanding), they were more willing to grant broad consent. The level of understanding of broad consent is required to ensure that this consent model is not only practical but also ethically acceptable (Richter et al. 2018). In order for the participant to offer their informed consent, the participant must

receive and comprehend the necessary information to permit independent decision-making (Pandiya 2010).

Biobank research and the use of broad consent are not the only situations in which comprehending informed consent concepts is a problem. Comparing clinical research participants' understanding of informed consent information in an African context, it was found that only 30% of participants in six studies understood therapeutic misconception, compared to 48% of participants in six studies who understood placebo and 47% of participants in four studies who understood randomization (Afolabi et al. 2014).

Joffe et al.'s (2001) measurement of participants' objective (actual) understanding (i.e., that they comprehend the clinical trial well) and a measurement of their subjective (perceived understanding) of information provided to cancer clinical trial participants during the consent process is another study on understanding of information given to participants (e.g. that they adequately understand the risks for participation). Participant understanding was evaluated using a Quality of Informed Consent (QuIC) questionnaire. The scores for each domain were determined by averaging the scores for all completed answers in that domain. In this study, correct answers earned a score of 100, "unsure" answers received a score of 50, and the scores for each domain were determined. On the first administration, objective understanding scores averaged 77.7, and on the second administration, they averaged 79.8. While the average subjective understanding score was 87.2 on the first administration and 86.9 on the second administration. These findings indicate that participant comprehension still needs to be improved. In a study on the perceived understanding of informed consent in a clinical trial for ailments in Gulf War veterans, Guarino et al. (2006) discovered that 3.7% did not understand; 21.3% had some understanding; 40.3% mostly

understood; and 34.7% completely understood. To overcome the challenge of understanding consent information, clear guidelines for designing adequate tools for improving comprehension are required, as the existing tools are neither validated nor standardised (Cheah et al. 2018).

Pandiya (2010) makes several suggestions for improving understanding or comprehension. These include: (1) a readable consent form, which influences the willingness to read the document's text and thus may improve comprehension; and (2) review of consent forms by a lay person who is not a healthcare worker, which may aid in assessing the comprehensibility of translations. This type of review would ensure that the consent form information is appropriate for the patient population that may be included in the study. Regardless of the consent model employed, there must be a standard or uniform method of defining, applying, and measuring such an understanding for a critique of participants' grasp of consent information to be credible. Appropriately, for the current study, I take into account Sand et al.'s (2010) literature assessment on these criteria in relation to participants' understanding of consent information. Sand et al. (2010) conducted a literature review that revealed some of the challenges in studies aimed at measuring participants' understanding of consent information. In general, the methods used to assess comprehension vary greatly. Some of the researchers studying this variable have provided a rationale for why a specific combination of items would provide a valid measure of comprehension. Furthermore, there is variation in the instruments used to measure the variable of comprehension. This variation can result from the fact that the instruments have different definitions of what understanding is. These measurements are regarded as proxy measures because, in some investigations, general understanding cannot be assessed directly. If so, it is doubtful that the used questionnaires accurately assess

the level of understanding needed to provide truly informed consent for research participation (Sand et al. 2010). It is important to note that some consent information is more important to understand than others. For instance, it is crucial to understand the main goal of the research in order to avoid therapeutic misconceptions. Due to this, it may be reasonable for the understanding test to concentrate on the most important information. The issue arises when there is little agreement on what constitutes the most important information in such studies.

Another issue with understanding consent information is that it is difficult to operationalize because there is no consensus on what information is essential for participants to understand. An evaluation of understanding of consent information would suffice if it measured overall understanding based on agreement on the most basic information rather than recall of details. Some of the studies included in the review assessed comprehension long after the information was given and consent was granted. Given that it should be of importance to evaluate comprehension at the time of obtaining/granting consent rather than what participants remember weeks or months afterwards, it is unclear what was really measured. Even if the participant forgets some research-related specifics a few weeks after giving consent, the consent may still have been given/obtained with full knowledge at the time. Finally, measuring research participants understanding was mostly done with instruments that were inconsistent and not validated. Therefore, it is impossible to draw conclusions from such studies in order to suggest the optimal strategy for informing research participants before they give consent. A uniform definition of understanding could be the foundation for the development of measurement techniques. Comparing these assessments would also help in determining the best channels of communication for informed consent procedures. Regardless of the chosen consent model,

understanding consent information is one of the aspects necessary for ethically valid consent, as was previously covered in Chapter 4, section 4.4.2. As a result, it is an important aspect of ethical participant protection.

5.4.3 Concerns over ethical participant protection

Mikkelsen et al's (2019) duration criterion, which is based on the notion that the criterion provides ethical protection over the period of the participants' participation in the biobank, is central to the argument that broad consent does not provide sufficient participant protection. Additionally, the authors maintain that the criterion gives participants a chance to review their consent for that time frame and a "actionable" right to withdraw consent. Helgesson (2011) emphasizes the function of HRECs in the assessment of biobank research and reiterates that research initiatives must be appropriately examined by HRECs in defence for broad consent for future biobank research. HRECs must not only be able to recognize the ethically significant elements of the research and weigh the various principles, values, and interests at stake fairly, but it is also crucial that they evaluate each study on its own merits and refrain from ignoring some research simply because they have previously approved similar ones. Risks of stigmatization seem to be an especially urgent concern in relation to biobank research. There is no inherent guarantee that any of this will be handled correctly, and Helgesson (2011) notes of being previously informed by some Swedish HREC members that studies are not always treated as uniquely as they ought to be. The reaction to arguments like these from opponents of broad consent appears to be that we require specific informed consent procedures in which the individual can assume the duty of evaluating the benefits of each individual study. However, because they are unable to evaluate pertinent risks or the accuracy and calibre of study-related information, it is not appropriate to subject potential research participants to such

obligation. This implies that individuals who support specific consent must have some faith in HRECs or, in the absence of HRECs, in researchers. So, the most logical course of action is to try to fix any weaknesses in the processes used to handle research applications in HRECs.

Using the governance structure of a biobank as a model for the ethical protection of participants' materials (as it is the materials that need to be protected) throughout their participation is another option to address this problem. According to Boers et al. (2015), a meaningful viewpoint on consent within biobanking can result from interpreting broad consent as consent for governance. This defence is based on Grady and colleagues' (2015) assertion that empirical research has shown that prospective donors would want to indicate as to whether their samples can be used for research, but that the majority say that the specific details of the future research do not affect their willingness to participate. This defence could be used to argue for a change from specific consent to broad consent for a broad range of prospective uses. It might also support a shift away from a concentration on research content, given that it appears that potential participants care less about that. Additionally, they suggest that the original consent form should include details regarding how data and sample handling and the procedures for ethical oversight are handled. Second, even though it is hard to provide donors with specific study information, it is possible to provide them with information on the governance system that is unique to the biobank. This method makes it possible for autonomous decision-making since it makes it obvious what information can be offered and anticipated and what cannot. Third, placing a focus on governance allows for discussion and attention to be given to topics that are crucial to biobank research. Fourth, by developing structures that allow data and sample exchange, a strong governance model could advance communal interests (by

advancing public health). Finally, involving participants in developing standards for ethical oversight and evaluation. Trust is, after all, the foundation of consent for governance. This places additional obligation on researchers to manage samples and data in an ethically decent manner. Broad consent can be kept from turning into a tool that primarily defends institutions and researchers at the expense of participants by using an active governance approach that involves participants.

According to Steinsbekk and Solberg (2011), giving broad consent should be viewed as accepting a framework that includes participant impact, governance, and basic conditions for permissible use. They begin their discussion by examining the scope of participants' consent in medical studies. Do they approve of the project's specifics? Or do they approve of its "broad" nature instead? The best case scenario for this question is that they at least gain a general awareness. So, the empirical response to the issue of why people participate in research simply points us in the direction of the normative inquiry: What should people consider when consenting (or not consenting) to medical research? Is a general awareness sufficient or should we make a lot of effort to ensure that a potential participant is fully informed? Participants should focus on what matters in order to make informed judgments, and this a common and uncontroversial response to this query. Picking out the most pertinent and important information is more important for decision-making than absorbing as much information as you can. You must be aware of the details that can affect your decision to participate or not in order to be able to make an independent choice. These points can be used to support or refute arguments. Below is a list of potential and important issues that could make a difference: It matters whether or not a research project includes medical intervention. If the research has the potential to physically harm people, that also matters. It matters if I am going to take medicines that might have unintended consequences. It is

important if the research can find potentially disturbing results intended to be returned. It also matters whether the project will largely result in private gain rather than public gain. It matters if research is being done for contentious causes like human cloning or for ordinary and broad public health purposes. What kind of institutional control the research must follow matters. It matters whether the population, community, disease group, or me personally is the focus. Whether or not the samples collected for research can be used for other purposes is important. Whether or not the researchers perceive data to be anonymous matters. This list, while not complete, demonstrates the kind of information on research initiatives that is essential. These details are crucial because they directly address "what is at stake" for me as a participant and for the society to which I belong. My integrity and independence are at stake in these situations. It relates to my integrity in that the research activity I engage in should be consistent with the ideals that are significant to me as a person and as a contributor to society. It also relates to my integrity in a different way, namely in terms of what the research does to me overall, i.e. is there any possibility of bodily or informational harm that I do not want to experience, that would directly affect me and make me less sound? While choosing participants, a research project must consider the issues surrounding people's integrity in this dual sense. The solutions to the aforementioned questions will create a foundation for participation in biobank research, a framework that includes objectives, requirements for resource uses, governance, and participant interests. The decision to participate may alter if these conditions change, which is the premise on which consent is provided. So, a new consent is required if new activities alter the principles, the framework, on which broad consents to biobank research are granted. This could imply a breach of the participants' integrity.

As guidance for African countries lacking a legal framework for biobank research, Staunton and de Vries (2020) presented guidelines for the regulation of genomic biobank research in the region. They suggest that a national governance framework should guarantee accountability in the ethical and legal conduct of research. Also, it is a concern that there are no national norms or guidelines because it is not obvious what laws apply to the research in that situation. In such instances, local RECs will make impromptu, arbitrary decisions and it is unlikely that they will adopt a consistent strategy. In these circumstances, it is also not obvious if there are any protocols in place to guard against exploitative research and research practices. Staunton and de Vries (2020), citing the work of other researchers on biobank governance, suggest "reframing of the regulatory tilt" by African legislators in accordance with substantive and procedural norms that ought to be represented in governance frameworks of African biobanks. The procedural norms include accountability, participation from the community, reciprocity, and stakeholder involvement. They suggest specific guidelines for giving back to the community and reciprocity.

The newly reframed regulatory tilt's aim would be to safeguard both participants against exploitative research and the research enterprise from such relationships. As a result, the regulations ought to restrict material use and reuse by specifying the laws and principles for such regulation. Such a regulatory tilt should also include the requirements for collaborative research projects and non-exploitative research. Regulations promote non-exploitative research by setting limitations on research as well as preventing exploitative research through prevention. For instance, national laws may stipulate that materials must be used by a local principal investigator or that materials can only be used overseas if an African student is present. Stakeholder input should be crucial for developing the content of these regulations and influencing their

core provisions. Regulation of future use of samples and data; use, reuse, and material export; oversight of use and regulatory approval; sample ownership and custodianship; benefit sharing; capacity building; community engagement; and data sharing should be the bare minimum requirement. National engagement is important in terms of stakeholder engagement because of: (1) regional and cultural differences across the continent and (2) the need for those implementing the regulations to have broad support in order to avoid a disconnect between documented law and law in action. Engaging stakeholders may assist identify any issues with proposed regulations and current regulations, as well as to ensure that their execution is in line with the intentions of the lawmakers. It can also justify the rules in this way.

In order to address the issue of institutional oversight in terms of how to select an organization that would be in charge of this duty within a genomic biobank environment, Staunton and de Vries (2020) propose a corporate governance model that consists of a corporation, directors, and shareholders. Under this arrangement, shareholders contribute to the company but are not involved in day-to-day management.

They do, however, have the opportunity to contribute to the company's strategic vision during annual or extraordinary general meetings (AGMs) (EGM). In the interest of the shareholders, the directors oversee the company. The company, not the shareholders, is the object of the directors' fiduciary duty (except under specific circumstances). If such a model is modified for use in biobank research, the community from which the participants come, rather than the overall participants, will be the shareholders. By avoiding conflicts of interest, the biobank (business) must act in the interests of the biobank, exercising judgment in carrying out its functions, and adhering to the genomic biobank's governance framework. In this context, the best interests of the biobank

imply that material use should be for the benefit of the community. The biobank must therefore act in its shareholders' best interests (the community). Such a strategy has the advantage of defining accountability and duty precisely. The approach outlines the ongoing responsibility that the participant community should bear for preventing self-regulation of material use by researchers. Similar to the entrustment model for sample and data governance put out by Tindana et al. (2019), this concept proposes that the institution hosting the biobank have ultimate supervisory authority.

Staunton and de Vries' (2020) last benchmark for biobank governance is community participation, which includes both community representation in institutional policy development and engagement for research objectives. The community can participate in accountability measures by participating in the development and implementation of governance frameworks. Such an approach should be accompanied by resources to aid in training and implementation. In response to the concern that broad consent does not provide adequate ethical protection for participants, (Mikkelsen et al. 2019:9) advocate for "a strong and continuous ethical review process" when broad consent is used. Such a review's evaluation mandates should be based on: (1) whether planned research is permitted by broad consent; and (2) participants' continued access to information (Mikkelsen et al. 2019). The premise behind continuous ethical review is that every new study must undergo ethical review if participants cannot judge the study according to their values. The proposed new research must fall under the parameters of the already approved broad consent. This should be decided through an ethical review, thus for this process to be successful, the original broad consent must be explicit about the intended research scope. Consent documents are generally required to be attached to research protocol review applications when they are submitted to

RECs. When future research is planned, RECs (or BECs) could keep a copy of these consent documents on file for a specified period of time.

5.4.4 The challenge of broad consent withdrawal

Participants in biobank research, according to Mikkelsen et al. (2019:10), have a "meaningful" right to withdraw if they are regularly informed of how their data is being used. I concur in the current study that broad consent use should be combined with ongoing participant communication regarding the use of their materials, as per the recommendation stated in Chapter 4, section 4.5.2.1, and in the current chapter, section 5.2.4.The discussion of withdrawal of consent in the context of biobank research broad consent highlights the significance of providing participants with sufficient information during the consent process, as well as the need for biobank researchers to continuously provide information to participants as well as to ensure that participants understand that information. If broad consent meets these and other criteria, such as voluntariness, legal capacity to consent, and the freedom to choose without deception or coercion, there should be no reason why it cannot be used in biobank research. Given that withdrawal of consent for previously used materials is not always possible, withdrawal should thus concentrate on biobank activities that have not yet begun but would be permissible under the scope of broad consent (Melham et al. 2014). Participants' right to withdraw would be facilitated by ongoing communication because they would be aware of the intended material usage. Participants' communication preferences, as previously stated, should have been determined prior engagement or, at the very least, during the consent process. This would be advantageous in ensuring that participants could withdraw their broad consent if they so desired. According to Melham et al. (2014), biobanks take different approaches to consent withdrawal, with some biobanks having tiers of different

aspects from which participants can withdraw consent, while others allow withdrawal for all aspects of the research. Biobanks can thus choose whether to implement withdrawal of consent as a tiered or "all or nothing" approach, in which participants completely withdraw broad consent. If biobanks collect samples on behalf of researchers (as some do), such a decision should be made by the biobanks; otherwise, researchers should develop such a mechanism.

Hug et al. (2012) based the definition of the right to withdraw consent from research on a number of considerations, including donor harm and autonomy. Although the right to withdraw is related to autonomy, it has been claimed that even if autonomy (self-determination) were the dominant or only value, the idea that there should be a right to withdraw is not supported by this value. This assertion is supported by the argument that research using donated samples no longer has a direct impact on the person from whom they were obtained. The claim goes on to say that while you can choose whether to offer your sample for research in the first place, once it has been obtained, you cannot claim or decide what can be done because it is no longer a part of you or your body. However, it is simple to conceive how the participant (donor) would suffer if the material can be linked back to them. Such harm could include harm to the donor's personal integrity if unauthorised access to genetic information occurs. The freedom to withdraw at any time if one feels uncomfortable with their involvement might be seen as a precaution to protect participants from risks or harm associated with research. The pertinent question to pose in relation to biobank research risks that would justify withdrawal is if participants are at risk of harm after the samples have been taken. This means that if the justification for withdrawing consent is to protect participants from physical harm, then this right should be reconsidered after samples have been collected. Other potential harms have already been mentioned in Chapter 1, section

1.5.1. These are breaches of confidentiality or unauthorised use in the sense that information could be used in ways that were never consented to. This is addressed in the following section.

5.4.5 Limitations of sample anonymisation as criticism for broad consent

As previously stated, Gross et al. (2021) criticize broad consent on the grounds that sample de-identification facilitated ethical violations in Henrietta's case. The problem in Henrietta Lacks case is that her cells (the HeLa cells) were de-identified and then used for further research without her permission. The problem in this example is not necessarily that broad consent was requested and received, but rather that consent was not sought and granted. In order to solve the problem of unethical behaviour caused by sample de-identification, Gross et al. (2021) proposed non-fungible tokens (NFTs), a blockchain technology innovation that, according to them, may help circumvent this issue of unethical behaviour. Biobanks have software-based electronic inventory systems that serve as biobank information management systems (BIMS). These are used to store sample-related data in such a way that it corresponds to the precise location of the sample in a specific container, such as a cryo-box in a specific freezer rack, shelf, freezer and freezer room. Any sample retrievals or movement(s) from sample storage containers, whether it be freezers, freezer rooms, ambient storage rooms, nitrogen tanks, or any other storage locations, must be accompanied by corresponding BIMS adjustments. This measure is used by custodians to maintain material accountability. It is not only an ethical and legal requirement, but also a requirement of the International Organization for Standardization (ISO) standards for quality management systems (QMS). BIMS is an information management system that was developed to integrate biobank data from various research studies (Olund et al. 2007).

The goals of a system like this are to handle and constantly update data, query data, and control access (Ölund et al. 2007). The mechanism of action for Gross et al.'s (2021) proposal is that block-chain could enable sample use tracking, promoting transparency. Blockchain technology is a shared ledger (journal) that is used to record transactions and track assets, thereby increasing trust (IBM n.d.). Blockchain is described as a tool for community and patient engagement by Gross et al. (2021), thereby asserting patients' values and transparent community engagement without jeopardizing private identity (Gross et al., 2021). According to the authors, such a system could enable enforceable dynamic consent.

Anonymization of samples through coding connects the sample to its donor and such identification necessitates consent for further use (Elger and Caplan 2006). By virtue of the fact DNA sequencing can be used to identify the donor, DNA samples are not truly anonymous (Lin et al. 2004). Family members share DNA sequences (CDC 2022). As a result, when sequenced, an invasion of privacy of individual sample associated data has the potential to link family members. However, confidentiality can be increased by ignoring the precise genomic locations of single nucleotide polymorphisms (SNPs) (genetic variation of genetic sequences), thereby increasing the number of records (representing individual samples/individual persons) that share the same values (genetic sequences) (Lin et al. 2004).

Elger and Caplan (2006) have investigated consent and anonymisation in biobank research. They argue that because DNA is not truly anonymous as described above, the term "anonymous" can only be applied to archaeological samples. Although biobank research does not necessarily pose a physical risk to participants, materials stored in a biobank may be subject to a breach of privacy. This should be managed through biosecurity measures such as the installation of surveillance cameras at the

biobank, restricted access to the biobank, such as biometric and/or card access only for authorized personnel, password protected computer access, and BIMS as a means of ensuring sample associated data privacy. Notably, the biosecurity challenge is not limited to broad consent but would apply to any facility that stores human materials (research institutions or biobanks), regardless of the consent model used.

Based on a review of empirical research results in European biobankers, Rychnovská (2021) considered how risks and threats are anticipated and addressed in biobank governance and focused on elements of logic of risk (conceptualization of insecurity and "logic of risk" involved); referent object (what shall be protected from risk); risk factors (what is seen to contribute to the risks); technologies; (technologies involved in governance and how they structure social relations). Data security, privacy, and data misuse were shown to be the three risk logics for biobank governance. Data risks are defined in the context of ELSI as data manipulation, hacking, and blackmail. Access regulation, technological and physical barriers are used to mitigate these risks. These measures are regarded as trustworthy and uncontroversial. This method of technical risk management is generally accepted by ELSI experts.

The findings in this regard imply that biobank security is a technical domain issue, in the sense that if information technology (IT) and technical matters are followed correctly, there is no need to deal with security any further. A highly pertinent and technical issue, the rationale of risk that materials kept in and exchanged among biobanks is based on the idea that unauthorized access to biobanks is the main security risk. As a result, numerous precautions must be taken to protect the system (physical and electronic components). This reasoning makes it possible for stakeholders such as lawyers and IT specialists to recognize, control, and create defences against risks. Compliance is essential to preventing the community from

feeling pressured to take on responsibility for the problem beyond what the designated specialists are capable of. The individual is primarily referred to as the "referent object" (what shall be protected from risk) in privacy governance technologies, and to safeguard against risk factors such as disclosing private or personal information about a participant or using their data for unintended (i.e., unconsented) research reasons (Rychnovská 2021). The value of individual privacy is assessed against the overall benefits of biobanking in such a way that the possibility of privacy violations is contrasted with the possibility of biobank research failing to produce the promised benefits.

As a result, there are differences regarding the most suitable risk governance technologies, particularly those that have an ethical and legal component, as shown by the lack of clarity surrounding the interpretation and application of the GDPR. Data subjects are more empowered when privacy issues are addressed publicly, which helps biobanks better illustrate their security protocols and the benefits of their work for the general public. The unintended use of biobank data for potentially harmful purposes is a minor feature of the practice of biobanking that is addressed by the risk rationality of data misuse as a source of insecurity to society. In terms of potential exploitation of data stored in biobanks, the state is a relatively neglected stakeholder. This logic relates to the threat of third parties or the state using biobank data for discriminatory purposes such as genetic or medical profiling or other harmful purposes. The referent object in this instance is the entire society or those portions that might be exposed to unfair or harmful treatment. No strategies to deal with this kind of insecurity have been addressed, except suggestions to discuss these problems in the field. In the form that it is currently given, Rychnovská's (2021) anticipatory governance method to managing security and risk for biobank data comprises how

threats and risks are foreseen and addressed. The anticipatory governance approach is consistent with the recommendations made earlier in the section on how biosecurity in a biobank should be managed in terms of physical barriers.

5.5 Conclusion

Although I highlight practical efficiency and potential future research benefit for society as important aspects to consider when judging the applicability of broad consent in the current study, these two factors are insufficient. As a result, it is asserted that the ethical basis for this consent model continues to be crucial. Duly, in this study, I contend that broad consent is ethically justified based on empirical evidence of research participants citing altruism articulated as beneficence for society at large as motivation for granting broad consent; that autonomy is not specific to the scope of choices; broad consent use provided participant non-maleficence is ensured through BEC review; and broad consent use provided there is ongoing communication with the participants. As criticism for broad consent, counter-arguments include interference with autonomy, the challenge of understanding consent information, concerns about ethical participant protection, the challenge of broad consent withdrawal, and limitations of sample anonymisation. In response to these concerns, the current study emphasizes the view that autonomy is not limited to the scope of choices and that, as a result, consent need not limit participants if they are given the right to autonomy to grant broad consent; simplifying consent text in a language that participants can understand to improve clarity; ethical review of the research and ongoing communication with participants; participants should be able to withdraw their consent without hindrance if there is no coercion or deception.

Finally, as mandated by BECs and the WMA Declaration of Taipei, biosecurity of materials within a biobank should be a requirement for biobanks. Withdrawal of

consent in certain research contexts (e.g. after the creation of a cell line) may present unique challenges for researchers because these cell lines may end up in multiple laboratories around the world (Caulfield et al. 2007). It could be argued that withdrawal is inapplicable in such cases because the embryo is a "new entity with a special status" (Caulfield et al. 2007:1724). Where withdrawal may be impossible, this should be addressed in the consent document and explained to participants. Now that an ethical defence for biobank research broad consent has been presented, the following chapter proposes changes to SA's regulatory framework to allow for broad consent use.

Chapter 6

Proposed amendments to the South African regulatory framework which will enable ethically justifiable broad consent

6.1 Introduction

Law is a field of knowledge in which jurists employ a methodology to enhance their comprehension and application of the foundations, contents, and goals of the law (Carrillo 2020). Ethics on the other hand, is the philosophical field that studies good and bad as well as how they relate to morality and human behaviour. Since ethics considers every facet of human behaviour and decision-making, it is a vast and intricate subject of study with numerous subdivisions (WMA 2015). The area of ethics that addresses moral dilemmas in the practice of medicine is known as medical ethics. Bioethics, or biomedical ethics, is closely connected to yet distinct from medical ethics. Moreover, bioethics is a fairly broad field dealing with the moral questions posed by advances in the biological sciences more broadly (WMA 2015). In contrast to the legal domain, where both responsibility and obligation for noncompliance exist, ethics compliance is discretionary (Carrillo 2020). Notably, law that disregards ethics and social values runs the risk of losing its connection to the public will (Dunfee 1996). In a democracy, the interpretation and execution of the law must take into account generally accepted customs and practises as well as deeply held moral beliefs. This is one way that a sense of community is formed and community virtue is fostered, among other things. This is not to argue that these kinds of behaviours and attitudes should always take precedence over other factors, but rather that they should be given careful thought (Dunfee 1996). Moreover, in the health research domain, legal

integrity, ethical integrity and scientific integrity all go hand in hand. Participants may be subjected to needless risk of harm and burden due to poor research design and improper methodology (questionable scientific integrity), with little to no benefit in the form of useful knowledge gained (NDoH 2015). For example, the scientific integrity of a research project will be questioned if the ethical and/or legal integrity of the project is in dispute. Hence the need to consider the ethical aspects of broad consent (as presented in Chapter 5) in proposing legal framework amendments. In several regions of the world, regulatory frameworks for biobanks have been shown to have shortcomings. To name a few, in African countries (de Vries et al. 2017), Central American Integration (CAI) member states (Canario 2021), and the EU (Penasa et al. 2018; Reznik et al. 2017). In SA, Parliament has the authority to amend existing laws, which are then submitted to the President for approval (Department: Justice and Constitutional Development 2022). According to Venter (2014), the law is not intended to cover every eventuality. As a result, it occasionally has gaps (*lacunae*), and the closure of these gaps is frequently presented as a reasonable interpretation. As previously stated, the requirement to interpret statute implies that the law is only partially complete. This could mean the difference between compliance and non-compliance with regulatory requirements. This chapter provides an appropriate summary of the gaps identified in Chapter 3 in relation to SA's regulatory framework for broad consent, as well as the potential consequences of these gaps. Some commentators advocate regulatory framework harmonisation as a solution to regulatory framework gaps (Dove 2015). Harmonisation is the process by which points of convergence in legislation, policy, and regulation are identified and made substantially equivalent (Dove 2015). As an alternative to filling legislative gaps in human sample regulation, some researchers have attempted to self-regulate by

developing their own regulatory guidelines (Labuschaigne and Mahomed 2019). As a result, these remedies are discussed in order to determine their viability in filling regulatory framework gaps. Finally, amendments to SA's regulatory framework for biobank research broad consent are proposed. Chapter 6 corresponds to the current study's Objective 4.

6.2 Gaps in SA's regulatory framework pertaining to broad consent for biobank research

In the current study, I identify several gaps in SA's regulatory framework relating to broad consent for biobank research. Given that biobank research in SA is governed by the NDoH Ethics Guidelines, while personal information processing, which includes sample associated data, is governed by POPIA, the two instruments have been extensively studied in terms of broad consent for biobank research. As a result, the identified gaps in that regard are primarily in these two instruments. To a lesser extent, gaps in the Draft National Open Science Policy (DNOSP), the Children's Act 38 of 2005, and the Promotion of Access to Information Act 2 of 2000 have been identified (PAIA). Table 5 summarizes these gaps.

Together with the DNOSP, the Draft National Data and Cloud Policy (DNDCP) also supports open science. The primary objective of the latter policy is to create an environment that is supportive of data provision while removing legislative hurdles (DNDCP 2021). Promoting open science in the face of POPIA's strict personal information processing requirements is difficult due to the contradictory effects of open science principles (unrestricted data access use for any purpose). Furthermore, when reviewing protocols for determining ethical data access and use, REC members may

become confused because the principles of the two policies that promote open science do not align with POPIA requirements for processing personal information.

Table 5: Gaps identified in SA's regulatory framework in relation to broad consent for biobank research

Instrument	Identified gap	Consequences
1. POPIA	Does not provide specific rules for processing of personal information; none of the instruments address this aspect (Specific to health research bearing in mind that POPIA is not sector specific).	May allow for the processing of health information that falls under the definition of POPIA but is not in accordance with the consent granted.
2. POPIA	Section 13(1) is unclear and ambiguous because it seems to prohibit the use of broad consent for personal information while the NDoH Ethics Guidelines allow broad consent for future research use. Sec. 13(1) in terms of the words "specific, explicitly defined, lawful purpose," warrant clarity for the health research sector so that it is clear whether or not broad consent is permitted in light of the research exceptions stipulated in the Act.	The discord between the two instruments should be addressed because ambiguities in regulatory frameworks could mean the difference between compliance and non-compliance.
3. NDoH Ethics Guidelines	Data extracted from/ associated with the samples is missing from the Consent Form Template.	Potential for confusion regarding storage and future use of data.
4. NDoH Ethics Guidelines	Not specific on protection of personal information associated with samples that have been collected for future research use; refers researchers to POPIA which seems to require specific consent for personal information processing.	Using broad consent could be interpreted as a contravention of POPIA.
5. NDoH Ethics Guidelines	Mentions that research proposals should specify whether or not IFs will be communicated to research participants, but does not include this provision in the consent form template for sample storage and future use.	Providing inadequate information weakens participant autonomy.
6. NDoH Ethics Guidelines	The consent form template does not include the rules for access to the biobank; when applicable, commercial use of materials and benefit sharing, IP; and material sharing with other countries. This contradicts the consent requirements for biobank research outlined in section 3.5.2.3 of the same guidelines.	Providing inadequate information within ethico-legal templates weakens participant autonomy.
7. NDoH Ethics Guidelines, NHA and POPIA	Commercialisation (misuse) of data associated with human samples is unclear. However, the NHA prohibits sample commercialisation.	May create room for processing of personal information with potential commercial uses which is not in line with consent granted.
8. Children's Act 38 of 2000	Does not mention other types of consent including broad consent for research involving children. Provides for assent to be granted with parental involvement.	Potential for confusion as to whether broad consent for biobank research in children is permitted.
9. DNOSP	Does not address how data confidentiality and privacy will be maintained in the context of unrestricted open data access for any purpose.	May allow for the processing of personal information that is not in accordance with the consent granted.
10. DNOSP and PAIA	Does not address rules of data access but refers researchers to PAIA which does not seem to promote unrestricted data use for any purpose as per the principle of open science.	It is possible that data associated with samples will be accessed and used in ways that are not consistent with the consent granted.

6.3 Harmonisation of regulatory frameworks for biobank research

Karlsen et al. (2009) define harmonisation as a language issue that involves the sharing of a set of concepts and vocabulary in order to ensure communication and understanding and avoid confusion (Karlsen et al. 2009). They also state that social and ethical robustness should be the bare minimum for a harmonised regulatory framework (Karlsen et al. 2009). Harmonisation is context-specific and refers to approaches and methodologies that promote collaborative work (Harris et al. 2012). According to Zika et al. (2008), unharmonised biobank processes, such as informed consent and future sample use, may pose challenges for collaborative research (Zika et al. 2008). They acknowledge, however, that while standardisation, which entails practical and technical issues (lower level of standardisation) may be easier, regulatory harmonisation may be more difficult (Zika et al. 2008). Standardisation implies that all biobanks use the same standard operating procedures (SOPs)/protocols (Harris et al. 2012).

The GDPR was designed to harmonise data protection across Europe (Kaye et al. 2016). This instrument became operational in 2016. However, its true impact on unifying regulations relating to the processing of genetic and health data in EU member states was still unknown in 2021. (Shabani et al. 2021). There is an argument that the GDPR allows for different interpretations. For example, in terms of safeguards that should be established and additional conditions for data processing based on research exemption provisions (Shabani et al. 2021). Prior to the GDPR, data handling harmonisation in the EU had been achieved through the Data Protective Directive (DPD), but sample collection legislation harmonisation was lacking (Zika et al. 2008).

The Canadian Personal Information Protection and Electronic Documents Act (PIPEDA), a federal law for the protection of personal information during commercial activity, is another example of legal harmonisation (Tassé 2013). PIPEDA provides a common standard for personal information protection across provincial and federal jurisdictions in recognition of provincial legislation that is deemed substantially equivalent (Tassé 2013). Another example of legal (regulatory) harmonisation is the Canadian Association of Genetic Counsellors's (CAGC) recognition of the American Board of Genetic Counselling (ABGC) norms and guidelines, which allows American genetic counsellors certified by the ABGC to practice rights in Canada as if they were certified by the CAGC (Tassé 2013).

It is necessary to investigate the level of harmonisation required and to determine whether legal harmonisation or technical standardisation is the better approach (Zika et al. 2008). While standardization procedures are widely accepted in the field of biobanks, applied ethics emphasizes the limits of legal harmonisation due to technical limitations of the legal instruments themselves, allowing for normative creativity (Rial-Sebbag and Cambon-Thomsen 2012). Furthermore, regulatory convergence may be difficult to achieve (Zika et al. 2008). This is presumably because governments are to be considered sovereign and thus independent of one another (Slokenberga et al. 2017). Another harmonisation challenge is that of ethics as a cultural aspect of member states, in that there may be significant differences in how they address life sciences. This raises the question of whether harmonisation is ethically desirable (Da Rocha 2015).

Given the pitfalls of regulatory harmonisation between countries, harmonisation of the SA regulatory framework (rather than fragmented guidance) can achieved through the

recommendations and amendments proposed in this study. This will create a more enabling framework for biobank research that includes broad consent for personal information. Section 6.5 proposes these regulatory changes. Before delving into these amendments, another potential remedy for filling regulatory framework gaps, namely self-regulation, is discussed.

6.4 Self-regulation of biobanks

Where there is no guiding framework or regulatory authority, a form of self-regulation may facilitate institutional alliances and cross-border collaborations (Jordan and Hughes 2007). Some prefer self-regulation because: (1) it is easier to achieve and faster than government regulation; (2) it is more flexible than government regulation; (3) it can be tailored to the needs of a specific industry; and (4) it may offer improved incentives for adherence (Bregman-Eschet 2006). Self-regulation, for example, is regarded as an appropriate means of regulation in the healthcare and scientific research sectors in the Netherlands, owing to rapid developments in these fields (Hendriks and Hellemondt 2016). When the law and self-regulation rules conflict, the law takes precedence. As a result, while self-regulation is beneficial, it cannot eliminate all uncertainty (Aart et al. 2016).

In countries where biobanks are unfamiliar, self-regulation is a popular method of protecting the public's interest (Rial-Sebbag and Cambon-Thomsen 2012). Respondents in countries with higher levels of support for biobanks, on the other hand, tend to favour external regulation (by RECs, governments, national data protection authorities, and international organizations) over self-regulation (by researchers, medical doctors, and institutions) (Rial-Sebbag and Cambon-Thomsen 2015). Self-

regulation supporters argue that it protects privacy and controls what data is shared (Snell et al. 2012).

The Mexican biobank is an example of internal decision-making and self-regulation due to a lack of codified ethical standards (Gómez 2014). Notably, the Mexican National Commission of Bioethics (CNB) serves as the national advisory institute, as does the Federal Commission for the Protection against Health Risks (Comisión Federal para la Protección de Riesgos Sanitarios) (COFEPRIS), which is part of the Ministry of Health and protects the population from health risks (Gómez 2014). Furthermore, the lack of adequate regulations for genetic research in Russia forces organizations that conduct this type of research to self-regulate, despite the fact that genetic research self-regulation is underdeveloped in this region (Alimov and Leshchenkov 2021). An examination of data pertaining to the activities of relevant public and private institutions in the region revealed this finding (Alimov and Leshchenkov 2021). The problem is exacerbated by fragmented genetic research legal regulations and self-regulation, which results in violations of participants' rights (Alimov and Leshchenkov 2021). The fragmentation of regulatory frameworks poses a challenge for research collaborations (Tzortzatou et al. 2021). Furthermore, the EU DPD, which was superseded by the GDPR, has been criticized for being fragmented, whereas the latter has been cited as lacking the capacity to correct the divergent and fragmented landscape (Slokenberga 2021). Prior to 2018, biomaterial transfer in SA was self-regulated due to the lack of a national MTA. During collaborative sample transfer, researchers relied on their own institutional agreements. Moodley and Singh (2016) discovered that resistance to institutional MTA use by collaborators from HICs was expressed by SA researchers due to a lack of a national MTA. This finding emphasizes the importance of adequate national legislation in avoiding non-

standardised self-regulation. The SA MTA, which was gazetted in 2018, is legally binding on the parties involved, as is any legal contract.

Given the preceding discussion, the shortcomings of self-regulation and the consequences of fragmented regulatory frameworks all have an impact on research practices, including consent for health research. All things considered, these must be addressed before looking for alternatives to fill the gaps. As a result, in the current study, I argue that a more enabling regulatory framework for the use of broad consent in biobank research in SA is required, and I propose amendments to that effect.

6.5 Proposed amendments to the current regulatory framework relating to broad consent

In light of the identified legal gaps in SA's regulatory framework for biobank research broad consent, I propose the following regulatory changes. POPIA, the NDoH Ethics Guidelines, and the DNOSP are among the instruments that should be amended. Notably, I propose that POPIA-related amendments be incorporated into ASSAF's Code of Conduct for Research or within a Data Transfer Agreement (DTA).

6.5.1 POPIA

The ambiguity identified in (section 13(1)) of POPIA and disagreement with the current regulatory framework for biobank research should be addressed in the Code of Conduct for Research and/or in a DTA by making the following changes:

1. To address the discrepancy between section 13(1) of POPIA and the NDoH ethics guidelines, which allow for broad consent for future research use of human samples, and to address the ambiguity of the former, I propose that the words "specific, explicitly defined purpose" in that section be clarified within the

Code of Conduct for Research as applied within the health research sector. Currently, the latest draft version 8.7 of the Code of Conduct for Research does not permit broad consent for the processing of personal information in the health research sector. Although broad consent is not prohibited by the Code, the specificity required by section 13(1) of POPIA must be interpreted in light of the Act's research exceptions. To avoid confusion when conducting health research and biobank research, the Code should include more detail to guide RECs and researchers. The type of consent used should also be specified in a DTA where personal information is transferred. To protect participant autonomy, when seeking broad consent, participants should be given information about a field of research (e.g., genomic) or research on a specific disease, rather than specific details about the prospective research, as this would be impractical for future research;

2. Inclusion of specific rules for biobank research access and processing of personal information (interchangeably, data and sample associated data). To protect participants' rights to privacy and confidentiality, the custodian should make the following changes to data protection requirements:
    a. Data should be stored in a BIMS with an encrypted password system to prevent unauthorized access to sample-related data;
    b. According to the NDoH Ethics Guidelines, data should always be anonymized, for example, through coding, so that no donors can be identified;
    c. Data access, including network server access, should be restricted to authorized users who have login credentials (user identification (ID) and password);

3. Taking the rules in (2) into account, the terms for data transfer to third parties, including cross-border transfer, should also include the following:
    a. Appropriate safeguards for transferred data (explained in detail in point f. below) as per article 46 of the GDPR and section 72 of POPIA, which states that a legally binding agreement between the parties is one basis for international transfers;
    b. Given the limitations for specifying the purpose in cases of future research use, the purpose of data transfer should be as explicitly defined as possible. The broad scope of future data research that will be conducted should be stated;
    c. The purpose of data transfer should be consistent with the consent granted;
    d. The provider institution's responsibilities include obtaining REC approval for data access and use;
    e. The recipient institution's responsibilities include safeguarding the privacy and confidentiality of the data as specified in 2. above;
    f. According to section 72(1)(a) of POPIA, the recipient institution's country should have data protection laws in place that provide an adequate level of personal information protection; according to article 45 of the GDPR, an adequate level of data protection should include respect for the rule of law and human rights, relevant legislation pertaining to security, including implementation of such legislation, professional codes, data protection rules, and security measures. Although SA has not yet received a favourable adequacy assessment from the European Commission, it is important to note their requirements when concluding contracts and Codes that regulate transfers of personal information;

g. It should be explicitly stated in a contractual agreement (e.g., DTA) that profiting from transferred data is prohibited;
h. It should be explicitly agreed that in cases of confidentiality breaches, where South African data is being transferred or processed for research purposes, a civil action will be instituted in a South African court against the responsible party via the Regulator (Information Regulator) in accordance with Section 99 of POPIA.

6.5.2 NDoH Ethics Guidelines

Given the identified gaps in the NDoH Ethics Guidelines, including the Consent Form Template for future research use of samples (Appendix 3(4)), the following changes to the Consent Form Template (Appendix A) are proposed:

1. Participants should be informed that they will not be able to withdraw their consent in certain situations where materials have been rendered unidentifiable. Omitting this aspect during the consent process has the potential to reduce participant autonomy by not providing the participant with adequate information.
2. Adequate information should be provided to participants to strengthen their autonomy. As a result, the following changes are proposed to the Consent Form Template in Appendix 3(4) of the Guidelines:
    a. The heading of the consent form should include sample associated data;
    b. Point 1. above (i.e., that withdrawal is not always possible) should also be mentioned on the Consent Form Template so that participants are aware of the limitations of their right to withdraw consent;

c. The Consent Form Template should stipulate whether or not IFs will be communicated to research participants because this aspect is provided for in the guidelines;
d. The rules of access to the biobank should be explained to participants;
e. When applicable, commercial use of materials and benefit sharing, including IP benefit(s); material sharing with other countries and/or parties should be disclosed to participants;
f. Consent Template allows for tiered consent by providing participants with more specific information in terms of stored sample permissions for: (1) future research but only on the same research topic as the current research; (2) future research of any kind that has been approved; and (3) future research except for research on a specific topic. This section of the template should state that it provides for tiered consent, with an additional section inserted to provide an alternative for broad consent when permission for a broad area of research is sought.

3. To avoid confusion among researchers about whether or not broad consent is permitted in research involving children, guidance on whether or not broad consent is permitted in this population group should be provided.

6.5.3 Draft National Open Science Policy

1. Should address how data confidentiality and privacy will be maintained in the context of unrestricted open data access for any purpose, while respecting participant autonomy.
2. Should address data access rules to avoid access that is not consistent with consent obtained.

6.6 Conclusion

The identified legal gaps in SA's regulatory framework relating to broad consent for biobank research have the potential to: (1) allow for the processing of personal information that does not align with consent granted; (2) provide insufficient information, undermining participant autonomy; and (3) confuse researchers due to unclear guidance, potentially resulting in non-compliance. Chapter 6 argued that regulatory amendment is the best remedy for the identified legal gaps. This entails taking into account the disadvantages of regulatory harmonisation, such as the difficulty of regulatory harmonisation (Zika et al. 2008). This is most likely due to differences in national laws and guidelines, as well as a lack of self-regulation standardization. The proposal for amendments to SA's regulatory framework pertaining to biobank research broad consent is aimed primarily at amending the instruments governing biobank research (NDoH Ethics Guidelines 2015) and the protection of personal information (POPIA 2013). The proposed changes to the national regulatory framework may have the following advantages: (1) clarify POPIA ambiguity and the resulting divergent interpretation regarding the collection of personal information for health research in terms of the words used, "specific, explicitly defined, lawful purpose; (2) ensure adequate safeguards for research participants by specifying rules for data access and processing of personal information; and (3) Include the Consent Form information requirements specified in the NDoH Ethics Guidelines section 3.5.2.3 in the template, ensuring adherence to this aspect of the Guidelines.

Chapter 7

Recommendations and conclusion

7.1 Introduction

In the current study, I considered an ethico-legal analysis of biobank research broad consent in the South African context, with the goal of proposing a more enabling regulatory framework in this regard. As a reminder, the study's objectives are:

1. To defend the claim that biobank research is a common good on consequentialist/utilitarian grounds and for reasons based on solidarity and altruism thereby demonstrating that restricting the use of broad consent in biobank research potentially limits the utility of biobank research (as per Chapter 2).
2. To defend the claim that the current regulatory framework in SA is ambiguous and unclear about whether broad consent is permissible (as per Chapter 3).
3. To provide an account of informed consent in research involving humans with an intention to demonstrate that the standard study-specific model of informed consent in human research is inadequate for biobank research (as per Chapter 4).
4. To defend the claim that broad consent for biobank research is ethically justifiable using ethical principles and providing counterarguments to objections to this position (as per Chapters 4 & 5).
5. To propose and argue for what amendments would be necessary to allow for ethically justifiable broad consent (as per Chapter 6).

The current study's objectives have been met. Objective 1 was met by demonstrating that biobank research has the potential to benefit humanity significantly by improving medical research and, as a result, healthcare, which has also been identified as a common good. As a result, restricting biobank research would have a negative impact on the advancement of health research. Consequently, disease detection, management, and prevention would suffer.

Objective 2 was met by emphasizing the ambiguity and lack of clarity in POPIA regarding whether or not broad consent for biobank research is permissible, given the differing interpretations of section 13(1) of POPIA. Another aspect of SA's regulatory framework pertaining to the topic at hand that requires clarification is a perceived conflict between POPIA and NDOH ethics guidelines, which explicitly allow for the use of broad consent.

Objective 3 was met by providing an account of informed consent in human research, describing the various models, and emphasizing the choice for broad consent as an ideal model for biobank research.

Objective 4 was met by demonstrating the ethical justifiability of biobank research broad consent use, which includes charitable reasons such as altruism, gratitude, reciprocity, and solidarity; the notion that broad consent appeals to autonomy due to the latter not being specific to the scope of choices taking into account participants' right to withdraw from biobank research at any stage; use of broad consent with REC oversight; and use of broad consent with participants informed of the use of their samples through ongoing communication.

Objective 5 was met by proposing regulatory framework changes that would be required to allow ethically justifiable biobank research broad consent use. These include correcting the regulatory ambiguity pertaining to broad consent use in section

13(1) of POPIA in relation to the purpose of personal information collection (sample associated data in this context), which would align with the NDoH Ethics Guidelines in relation to allowing the use of broad consent; amendments that would ensure adequate safeguards for research participants by specifying rules for data access and processing of personal information; and amendments that would ensure adequate safeguards for research participants by specifying rules for data access and processing of personal information. In light of the findings of the study and the proposed regulatory framework amendments in Chapter 6, I make recommendations in the following section.

7.2 Recommendations

The following are the recommendations:

1. The following amendments should be incorporated into the Code of Conduct for Research:
    i. Those aimed at addressing the discrepancy between NDoH ethics guidelines and section 13 (1) of POPIA in relation to whether or not broad consent is allowed for health research purposes;
    ii. Those that stipulate specific rules for access and personal information processing; and
    iii. Terms for data transfers to third parties, including cross-border transfers.
2. The Consent Form Template in Appendix 3(4) of the NDoH Ethics Guidelines should be modified to include all information aspects that should be provided to participants, in accordance with section 3.5.2.3 of the same guidelines. The template is included as Appendix A, along with some proposed changes (highlighted in blue). The WHO Informed Consent Template for Consent for

Storage and Future Use of Unused Samples is the first section of the Template in Appendix 3(4) of the NDoH Ethics Guidelines.

3. In addition to point 2 above, participants providing broad consent should be given information on a broad area of the proposed research to protect their right to autonomy.
4. When broad consent is used, REC approval is required if new research is conducted that is outside the scope of the original broad consent.
5. When broad consent is used, ongoing communication with research participants should be a requirement to ensure that participants are informed of the use of their materials (samples and data). Due to the finding that different types of participants prefer different communication modalities, communication preferences should be determined during the consent process.

7.3 Conclusion

Clarification is needed regarding a perceived conflict between POPIA and the NDOH Ethics Guidelines, which explicitly allow for broad consent in the context of biobank research while the former is subject to various interpretations regarding the use of personal information. Given that samples and data (including personal information) are frequently transferred for biobank research purposes, this ambiguity and discord calls for a more enabling regulatory framework governing biobank research broad consent use. Although I emphasize the practical efficiency and potential future societal benefit of broad consent as important factors to consider when determining the applicability of broad consent, these two factors are insufficient. As a result, the ethical justification of this consent model remains paramount. As a result, it is argued that broad consent is ethically justified based on the notions that empirical evidence of

research participants citing altruism articulated as beneficence for society at large as motivation for granting broad consent; autonomy is not specific to the scope of choices; broad consent use provided participant non-maleficence is ensured through BEC review; and broad consent use provided ongoing communication with the participants regarding the use of their materials. In addition to the disagreement between POPIA and the NDoH Ethics Guidelines regarding broad consent use in biobank research, and the ambiguity in POPIA regarding broad consent use, I identify legal gaps in relation to the topic at hand. These include the lack of specific rules for accessing and processing personal information for biobank research, as well as the requirement to include information aspects in the Consent Form Template, as outlined in section 3.5.2.3 of the NDoH Ethics Guidelines. As a result, the proposed amendments would make the regulatory framework more conducive to the use of biobank research broad consent.

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Appendix 1: Consent Form Template

4. Consent for storage and future use of unused samples of biological materials

World Health Organization

Research Ethics Review Committee
(WHO ERC)

20, AVENUE APPIA – CH-1211 GENEVA 27 –SWITZERLAND – HTTP://INTRANET.WHO.INT/HOMES/RPC/ERC – HTTP://WWW.WHO.INT/RPC/RESEARCH_ETHICS

Amend heading to: Informed Consent Form Template for Consent for Storage and Future Use of Unused Samples and Associated Data

Informed Consent Form Template for Consent for Storage and Future Use of Unused Samples

Notes to Researchers:

1. Please note that this is a template developed by the WHO ERC to assist the Principal Investigator in the design of their informed consent forms (ICF). It is important that Principal Investigators adapt their own ICFs to the outline and requirements of their particular study.

The logo of the Institution must be used on the ICF and not the WHO logo.

2. The informed consent form consists of two parts: the information sheet and the consent certificate.

3. Do not be concerned by the length of this template. It is long only because it contains guidance and explanations for you which you will not include in the informed consent forms that you develop and provide to participants in your research.

4. In this template:

- square brackets indicate where specific information is to be inserted
- bold lettering indicates sections or wording which should be included
- standard lettering is used for explanations to researchers only and must not be included in your consent forms. The explanation is provided in black, and examples are provided in red in italics. Suggested questions to elucidate understanding are given in black in italics.

TEMPLATE ON FOLLOWING PAGE

Additional Consent to [*Name of Project*]

Include the following section if the research protocol calls for storage and future use of samples

This Statement of Consent consists of two parts:

- Information Sheet (to share information about unused samples with you)
- Certificate of Consent (to record your agreement)

You will be given a copy of the full Statement of Consent

Part 1. Information Sheet

Explain that you are seeking permission to store their unused samples for possible future use in either your own research or someone else's research. State that they need to make some decisions about their blood/tissue/sperm/ sputum sample because they gave you permission only to use it for the current research.

Explain that sometimes people don't want their samples used for research into areas they might not agree with, for example, research into birth control or reproductive technology. Use lay terms to explain research possibilities. If genetic research is a possibility, explain what this is and any implications for them. State that they can tell you if there is something they don't want their sample used for, or if they don't want their sample used at all.

Inform the participant that, at present, the researchers can trace which blood/tissue/sperm/sputum sample belongs to the participant. In most cases, the participant must decide whether they want to let the researchers keep the sample but get rid of all identifying information, or whether they are comfortable with the researchers knowing whose sample it is. Explain the risks and benefits of each of these options. Inform the participant of researcher obligations in cases where the sample remains linked. These obligations include informing the participant of results that have immediate clinical relevance. Inform participants as to after how long consent will expire. Explain to participants whether or not incidental findings (IFs) will be communicated to them.

Inform participants that their sample will not be sold for profit and that any research which uses their sample will have been approved. When applicable explain the following to participants: commercial use of materials and benefit sharing, including IP benefit(s); material sharing with other countries and/ parties.

Right to Refuse and Withdraw

Explain that the participant may refuse to allow samples to be kept or put restrictions on those samples with no loss of benefits and that the current research study will not be affected in any way. Inform the participant that they may withdraw permission at anytime and provide them with the name, address, and number of the person and sponsoring institution to contact. Inform participants that there will be no option to withdraw their consent in certain instances when materials have been made non-identifiable.

Confidentiality

Briefly explain how confidentiality will be maintained including any limitations. Explain rules of access to the repository.

You can ask me any more questions about any part of the information provided above, if you wish to. Do you have any questions?

Part II. Certificate of Consent

If any of the (TYPE OF SAMPLE i.e. blood, tissue) I have provided for this research project is unused or leftover when the project is completed (Tick **one** choice from each of the following boxes)

□ I wish my [TYPE OF SAMPLE] sample to be destroyed immediately.
□ I want my [TYPE OF SAMPLE] sample to be destroyed after ____ years.
□ I give permission for my [TYPE OF SAMPLE] sample to be stored indefinitely

AND (if the sample is to be stored) TIERED CONSENT

□ I give permission for my (TYPE OF SAMPLE) sample to be stored and used in future research but only on the same subject as the current research project : [give name of current research]
□ I give my permission for my [TYPE OF SAMPLE] sample to be stored and used in future research of any type which has been properly approved
□ I give permission for my [TYPE OF SAMPLE] sample to be stored and used in future research except for research about [NAME TYPE OF RESEARCH]

AND (if the sample is to be stored) BROAD CONSENT

AND I give permission for my (TYPE OF SAMPLE) sample to be stored and used in future research but only on the research focus area that I have been informed about and has been approved by a research ethics committee.

□ I want my identity to be removed from my (TYPE OF SAMPLE) sample.
□ I want my identity to be kept with my (TYPE OF SAMPLE) sample.

I have read the information, or it has been read to me. I have had the opportunity to ask questions about it and my questions have been answered to my satisfaction. I consent voluntarily to have my samples stored in the manner and for the purpose indicated above.

Print Name of Participant _____

Signature of Participant _____

Date _____

Day/month/year

If illiterate, a literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should make their mark.

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness _____ AND mark of participant

Signature of witness _____

Date _____

Day/month/year

Statement by the researcher/person taking consent

I have read out the information sheet to the potential participant accurately and, to the best of my ability, I have ensured that the participant understands that the following will be done:

1.

2.

3.

I confirm that the participant had the opportunity to ask questions about the nature and manner of storage of the samples, and that all the questions asked by the participant were answered to the best of my ability. I confirm that consent has been given freely and voluntarily.

A copy of this document has been provided to the participant.

Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Date _____

Day/month/year

Appendix 2: Open science stakeholder workshop email

Gmail **Mantombi Maseme <masememr@gmail.com>**

Open Science Stakeholder workshop on the South African Open Science Policy I 22 February 2022 I 09:00 - 12:00

1 message

Renate Venier <Renate@assaf.org.za> Mon, Feb 21, 2022 at 12:15 PM
To: Renate Venier <Renate@assaf.org.za>
Cc: Thandeka Halles <Thandeka.Halles@dst.gov.za>

Dear Webinar Registrant

Thank you for registering to attend the event: **Open Science Stakeholder workshop on the South African Open Science Policy I 22 February 2022 I 09:00 - 12:00.** To join the webinar, please follow the dedicated link sent to you upon registration. The event will also be recorded and live streamed to the ASSAf Facebook page.

Some house rules ….

1. When logging in, please type your full name and name of your organisation, e.g. Renate Venier (ASSAf).
2. Given the large audience, your microphone and camera have been disabled to ensure minimum disruptions during the event.
3. Attendees will be requested to type any questions and comments in the Q&A box. The questions/comments will be facilitated by Prof Himla Soodyall and will be directed to the relevant Expert Task Team member. In the event we run out of time to address all questions and comments, outstanding questions or comments that have not been addressed may be emailed to Ms Thandeka Halles at thandeka@dst.org.za
4. Should you experience technical difficulties, we will do our best to assist. Do try to logout and login again/a full device restart, and make sure your speaker volume is turned up. It may also happen that the Zoom screen is minimised on the taskbar accidentally. Please restore it from the taskbar if that is the case. The sound and connection will only be as good as the quality of your device and your Internet connectivity.

Please be advised that the information you provided upon registering will be protected under the Protection of Personal Information Act and will be used by ASSAf only for the purposes of this event including CPD validation by SACNASP (where relevant).

We are looking forward to welcoming you, and to your participation in the event.

Kind regards

Renate

Renate Venier

Governance Coordinator

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2 attachments

Programme Open Science Stakeholder Workshop 2022_Final.pdf
190K

Draft 0 OPEN SCIENCE POLICY v19.pdf
493K