Ethical issues in the Collection, Export, Storage and Uses of Human Biological Samples in Africa: an analysis of stakeholders' perspectives

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Abstract

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The collection, storage, export and use of human biological samples are important research practices in international collaborative research. However, the limitations of current ethical and regulatory frameworks to govern these research practices have resulted in inconsistencies in practice and a number of ethical concerns for researchers, institutions and research ethics committees (RECs).

The aim of this thesis was to contribute to an empirically-informed understanding of the ethical issues arising in the export, storage and future uses of human biological samples from sub-Saharan Africa (SSA). The thesis is based on an empirical bioethics project to examine stakeholders' perspectives of and responses to the ethical issues arising in these research practices. I employed a qualitative strategy of inquiry involving document review, observations, semi-structured interviews and focus group discussions with key stakeholders in Nairobi and Kilifi in Kenya and Navrongo in Ghana.

The project suggests that the ethical issues arising from the use of human biological samples depends on the nature of interactions between key stakeholders in biomedical research. Despite the compelling reasons for sample export, storage and use, and the existence of structures governing these research practices, the stakeholders I interviewed expressed several practical ethical concerns. These relate to consent, cultural sensitivities around blood, local control of samples, power-relations, capacity building and trust-relationships.

Drawing on these findings and existing literature, I argue that host research institutions bear the ultimate responsibility for the ethical conduct of research and should act as responsible stewards of research samples. I argue that it is important to refocus attention on important values in international research ethics such as trustworthiness to address the issues arising in practice. Recognising the limitations of current governance mechanisms and the uncertainties surrounding future uses of samples, I propose an entrustment framework to strengthen relationships between communities and host research institutions on one hand and between collaborating research institutions for research involving human biological samples in Africa. I also propose a set of 'points-to-consider' for research institutions, ethics committees and funding agencies.

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Dedication

TO GOD BE THE GLORY

In loving memory of my Dad, Samuel Sana Tindana
(15th June 1943 to 15th September 2009)

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List of abbreviations

AIDS: Acquired immune deficiency syndrome
AMANET: African Malaria Network Trust
CAB: Community Advisory Boards
CAST: Community Advice for Study Specific Teams
CCC: Consent and Communication Committee
CIOMS: Council for international organizations of medical sciences
CSKI: Cross-study key informants
DoH: Declaration of Helsinki
DNDI: Drugs for Neglected Diseases Initiative
EDCTP: European Developing Countries Clinical Trial Partnership
EE: Empirical ethics, used interchangeably with Empirical Bioethics
FGD: Focus Group Discussions
FW: Fieldworkers
GCGH: Grand Challenges in Global Health
HDSS: Health and Demographic Surveillance System
HIC: High-income countries
HIV: Human Immunodeficiency Virus
HSSR: Health Systems and Social Research group
ICH: International conference on Harmonisation
INDEPTH: International Network for the Demographic Evaluation of Populations and their Health
IRB: Institutional Review Board
KCR: KEMRI community representatives
KEMRI: Kenya Medical Research Centre
KDH: Kilifi District Hospital
KND: Kassena-Nankana Districts
KWTRP: KEMRI/ Wellcome Trust Research Programme
LMIC: Low and middle income countries
MalariaGEN: Malaria Genomic Epidemiology Network
NBAC: National Bioethics Advisory Commission
NCB: Nuffield Council on Bioethics
NHRC: Navrongo Health Research Centre
NIH: National Institutes of Health
OXTREC: Oxford Tropical Research Committee
PI: Principal investigator
QR: Qualitative research
REC: Research Ethics Committee
RES: Researchers
SSA: Sub-Saharan Africa
UNESCO: United Nations Educational Scientific and Cultural Organisation
VAST: Vitamin A Supplementation Trial
WHO: World Health Organization
WMA: World Medical Association

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Chapter 1: Introduction

The past two decades have witnessed an increase in biomedical research activities in sub-Saharan Africa (SSA) involving collaborative projects with researchers from High Income Countries (HICs). Together with the advent of new high throughput research methods such as those developed in the field of genomics – the study of the structure and function of an organism's genome and its related technologies – this has translated into an increase in the number of samples collected, stored and used for research (Collins, Green et al. 2003; Nyika 2009; Parker, Bull et al. 2009; de Vries, Bull et al. 2011). Due to limitations in the infrastructure needed to process these samples in SSA, the bulk of samples, particularly those used in genetics and genomics are currently exported to research laboratories in HICs (Langat 2005; Upshur, Lavery et al. 2007; Andanda 2008). It is also increasingly becoming the norm for samples to be stored both locally and in overseas laboratories for future research purposes and there has been a rapid increase in the establishment of biobanks[1], especially in HICs such as the United Kingdom and United States (Kaye 2006; Cambon-Thomsen, Rial-Sebbag et al. 2007; Gibbons and Kaye 2007; Harris, Burton et al. 2012).

These scientific developments and research practices have the potential to facilitate important research, and enable scientists to investigate the relationship between environmental exposures and diseases in humans while reducing research costs (Blatt 2000; Daar, Thorsteinsdottir et al. 2002; Collins 2003; Collins, Green et al. 2003; Zika, Schulte In den Baumen et al. 2008).

[1] A Biobank is defined as an organized collection of biological samples and the data associated with them (Kaye et al 2009).

However, the export, long-term storage and reuse of samples have recently generated discussions about widening health and economic disparities between HICs and Low and Middle-income countries (LMICs) (Upshur, Lavery et al. 2007). Important questions have been raised about appropriate ways to govern these samples, and to protect the interests of research participants and their communities (Langat 2005; Muula and JM 2007; MacQueen and Alleman 2008; Hawkins and O'Doherty 2010). Specifically, issues around consent, privacy and ownership of these samples have been highlighted in the literature (Emanuel, Wendler et al. 2004; Weijer and Miller 2004; Hansson, Dillner et al. 2006; Upshur, Lavery et al. 2007). However, without the necessary ethical and regulatory frameworks governing these research practices – especially in SSA – researchers, institutions and research ethics committees (RECs) are currently left to make their own judgments about what criteria specific projects need to meet to be acceptable. This has resulted in inconsistencies in practice and ethical concerns.

Against this backdrop, my research project aims to contribute to an empirically-informed understanding of the practical ethical issues arising from international collaborative research more broadly and specifically on the issues arising from sample export, long-term storage and future uses.

1.1. Background and motivation for this project

My interest in this research project grew out of my role as a member of the Navrongo Health Research Centre (NHRC) Institutional Review Board (IRB/REC) in Northern Ghana. My experiences as a member of this Board and my interest in research ethics led me to conduct empirical studies on consent issues and community engagement activities in Navrongo (Tindana, Kass et al. 2006; Tindana, Rozmovits et al. 2011; Tindana, Bull et al. 2012).

These studies highlighted the lack of community understanding of biomedical research projects carried out by the NHRC, especially projects involving blood samples, and illustrated the urgent need to identify appropriate mechanisms to improve research literacy in the community and to address the local fears and anxieties around the use of human biological samples in research.

As well as addressing these concerns, our IRB was constantly faced with several ethical dilemmas during the review of research projects involving international collaborators, especially when granting approvals for samples to be exported to HICs. This raised concerns about what kind of consent was appropriate for sample export, storage and future uses. Motivated by the current lack of guidance on appropriate ways of addressing these challenges, I decided to pursue these issues further through a DPhil project. I observed that it is highly likely that as the number of biomedical research activities increases in Africa, researchers, IRBs and research ethics committees (RECs) and other stakeholders of biomedical research will increasingly be faced with these ethical challenges[2]. Thus the need for further exploration of how the collection, storage and export of biological samples should be done, how it should be governed and what should count as best ethical practice.

1.2. Project description: An empirical bio-ethics project

My central research question was: 'what are the ethical issues arising in sample export, storage and future uses'? Ethics (moral philosophy), in broad terms is the philosophical study of morality or a branch of philosophy concerned with human actions or behaviour (Beauchamp and Childress 2009; Tangwa 2009).

[2] I have also served as a member of the Oxford Tropical Research Ethics Committee of the (OXTREC) during my DPhil studies (since 2010) and observed that the issues around sample export, storage and future uses were also relevant to RECs outside Africa.

As a practical ethics project, what I refer to as an *ethical issue* in my research is what is generally regarded as morally right or wrong, good or bad, permissible or not permissible, acceptable or problematic in the conduct of research involving human biological samples. To address this question I used research methods in the social sciences to examine the ethical issues arising in sample export, storage and future uses. I was however interested not just in identifying what the issues are from key stakeholders' perspectives but also identifying morally acceptable and practical solutions. This approach was based on the premise that empirical research and normative analysis can play complementary roles in addressing practical ethical issues arising in biomedical research. My research design thus falls within the remit of what has been broadly described as *empirical (bio)ethics* (Hope 1999; Ashcroft 2003; Croft, Sundar et al. 2006; Parker 2009).

Empirical bio-ethics: deriving values from the facts?

Sugarman uses the term '*empirical methods in bioethics'* to describe 'the application of research methods in the social sciences (such as anthropology, epidemiology, psychology and sociology) to the direct examination of issues in bioethics" (Sugarman 2004, p226). Other authors, such as Dunn et al have defined the term '*empirical ethics'* as a research strategy that aims to combine the collection and analysis of empirical data with moral philosophical analysis (Dunn, Sheehan et al. 2012). While there is a growing body of literature on the 'empirical turn' in bioethics and some convincing arguments about the value of combining empirical data with ethical analysis (Borry, Schotsmans et al. 2005; Parker 2007; Ives and Draper 2009), there is currently no consensus on the best approach for arriving at normative claims from empirical data or how we derive what 'ought' to be from what 'is' (Molewijk 2004; Emerson, Upshur et al. 2009; Parker 2009).

As a *bioethicist*[3] interested in understanding the ethical implications of biomedical research activities in Africa, I have engaged with both the fields of social science and bioethics to address the normative research questions around sample export, storage and future uses.

The need for empirical research arises because it is important to gain a practical understanding of (i) what is currently happening in sample export and long-term storage[4], (ii) what the real ethical issues arising in practice are and (iii) what the views, beliefs and concerns of key stakeholders are and their arguments for what ought to be done (or not). For this reason, I conducted empirical research in two African settings; Ghana and Kenya, to ensure that the recommendations I make are grounded in a real sense of what is going on and what the practical ethical issues are. I also aimed to take seriously the arguments made about what ought to be done, by people who are involved, informed and key stakeholders such as researchers, fieldworkers, IRB/REC members and community representatives.

Whilst empirical research on its own can describe and analyse the meaning of contexts and practices, it is also important to critically assess the strengths and weaknesses of the arguments made by interviewees, in order to contribute to the development of valid, coherent and empirically-informed positions on what should be done – that is, on recommendations for good practice. Given this need to bring together empirical work and ethical analysis, this project was structured as shown in Figure 1:

[3] Although there is no single definition of bioethics, Merriam-Webster OnLine defines the term as a 'discipline dealing with the ethical implications of biological research and applications, especially in medicine' Also see Jonsen's Birth of Bioethics (Jonsen 1993). In this thesis I am not going to focus on the debates around what is bioethics or who is a bioethicist but I would like to acknowledge that while people who work in this field of bioethics come from many different disciplines, a bioethicist is generally someone who has expertise in bioethics. As a bioethicist myself, I was initially trained in the humanities and obtained a master's degree in bioethics. Much of my career has focused on understanding the ethical implications of biomedical research activities in Africa and I have also served as a member of research ethics committees in Africa (Ghana) and Oxford (UK).

[4] I define long-term sample storage as storage beyond the duration of the initial research and for 10 years or more.

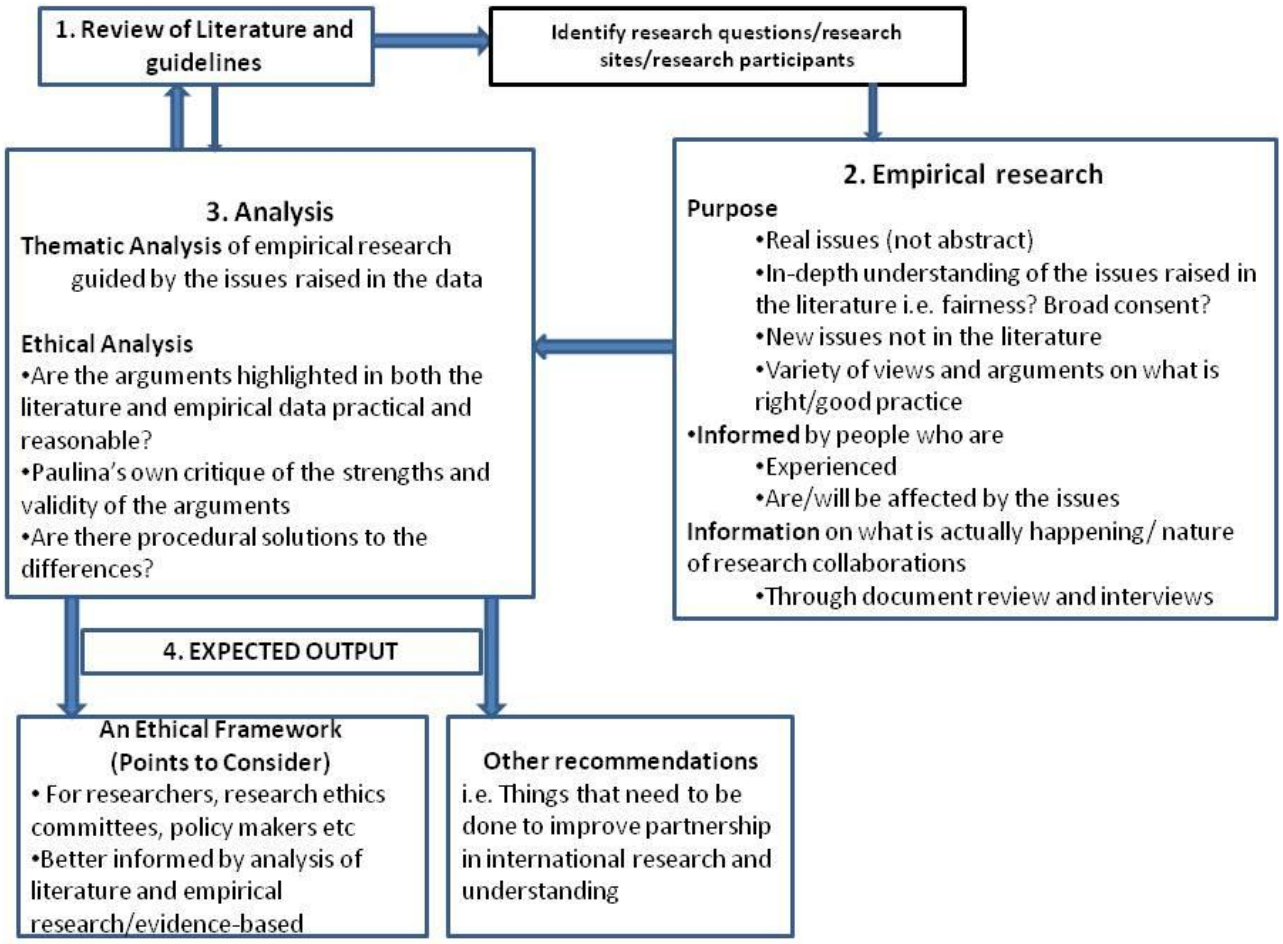

Figure 1: Schema of the empirical bio-ethics project

1. Review of literature and guidelines

To prepare for the empirical research component of this thesis, I conducted a review of relevant literature related to international collaborative research and the ethical issues arising in sample export, storage and future uses. This is discussed in Chapter 2. While the literature revealed the spectrum of perspectives that exist about sample export and storage, especially in HICs, none of the few empirical studies I identified answered the deeper questions about what the fundamental issues are from key stakeholders' perspectives. My initial analysis of the literature highlighted the main ethical issues as *consent*, *privacy*, *confidentiality and ownership* of samples.

However, this process also highlighted the lack of the necessary ethical framework – and empirical evidence – about the views of key stakeholders in SSA regarding the appropriate governance of export and long-term sample storage. This provided further justification for carrying out the empirical research.

2. Empirical research using qualitative methods

The second stage of my research was the empirical component which employed a qualitative strategy of inquiry to address my research questions –discussed in Chapter 3. The rationale for using qualitative research methods was to allow the stakeholders to express their views on what they see as the fundamental issues around sample export, storage and future issues based on their own experiences. Data were collected from three main sources: documentation (review of existing ethical guidelines, standard operating procedures, sample of consent forms, material transfer agreements), semi-structured interviews and focus group discussions, and observations.

3. Analysis

Qualitative analysis of empirical data

Data analysis was an on-going process during the course of the project. This involved a systematic coding of each of the transcripts and thematic analysis focusing on the description of the data and conceptual interpretation of the data. I followed the steps used across many different qualitative analytical traditions. I paid particular attention to: 1) the ethical issues arising in storage, export and future use of samples guided by the literature, and 2) new or different issues arising in the data.

Ethical Analysis

This process involved an on-going analysis of the various positions and arguments in both the literature and empirical data about the best practices for governing sample export, storage and future uses.

It involved (1) examining whether the arguments made are practical and reasonable 2) a critical assessment of the strengths and validity of the arguments, and 3) assessing whether there are procedural solutions to any differences highlighted in the data, for example finding a middle ground for the different positions about the validity of broad consent for future uses of stored samples.

4. Expected Outcomes

The goal of this project was to develop a framework for the ethical governance of the export, storage and future uses of human biological samples. This involves bringing together the findings of the empirical research and ethical analysis to develop 1) a list of points to consider for researchers, ethics committees, policy makers and relevant stakeholders, which are informed by the data analysis and based on good reasons and arguments and 2) further recommendations about what needs to be done to improve partnerships in international research collaborations and participants'/communities' understanding of biomedical research.

1.3. Outline of the thesis

This thesis comprises eight chapters. In this chapter, I have given an overview of the whole project, justifying its importance and how I became interested in pursuing this research subject. In the next chapter, I will present a review of relevant literature on international collaborative research in general and sample export, storage and future uses in particular. I draw this literature from philosophy, social science and general bioethics discourse and highlight the current gaps in literature that this research aims to address.

Chapter 3 describes and justifies the research design used to address the research questions for this project including the sources of data and the methodological considerations that guided the process of data collection, interpretation and writing.

Chapters 4 to 7 present my analysis of the empirical research. Chapter 4 begins with stakeholders' perspectives of the nature of scientific research collaborations and relations. I highlight the types of research projects conducted, how these are initiated and the centrality of human biological samples to these projects. Then, I discuss the current practice of sample export and storage, outlining their rationales and the destination of exported samples. The penultimate section of the chapter discusses existing institutional and national requirements for sample use and export and the gaps identified by the respondents.

In Chapter 5, I aim to get a deeper understanding of the practical ethical issues relating to researcher-participant relationships (and by extension local institution-local community relationships). Chapter 6 focuses on the practical ethical issues arising from the relationship between the host institution and external collaborating institutions.

Chapter 7 discusses stakeholders' proposed solutions and recommendations for addressing the micro and macro level issues discussed in chapters 5 and 6. It also investigates their views about what might count as best practice for international collaborative research more generally and sample export, storage and future uses in particular.

Finally, in Chapter 8 I reflect on the key findings of the empirical research and stakeholders' proposed solutions and recommendations. In relation to the literature, I critically examine and take forward stakeholders' arguments for what ought to be done in addressing the ethical issues arising from sample collection, storage and export of biological samples, in order to work towards the development of my own arguments for what should count as good ethical practice.

Chapter 2: The ethics and governance of biomedical research

2.1. Introduction

This chapter presents a review of the literature relevant to the growth of transnational scientific collaborations and the use of human biological samples, set in the general context of the ethics and governance of biomedical research. Given the huge body of literature on this topic, the aim here is not to provide a comprehensive or philosophical discussion of research ethics. Rather, the focus is on aspects of this literature relevant to transnational biomedical research and of the ethical issues arising in practice. It begins in (2.2) with the literature on key milestones in the development of ethics standards for research with humans. This background is important to understand the major ethical issues that have shaped the research ethics field and how these have evolved over the past seven decades. This is followed by a more detailed review of the literature on the ethical issues arising from research collaborations between low and middle-income countries (LMICs) and high-income countries (HICs). Within this context, in (2.3) I highlight the recent expansion in such collaborations as a direct effect of revolutionary advances in science and technology especially in the fields of genetics and genomics. Then, in (2.4) I discuss how these developments have led to new ethical challenges, particularly around the increased use of human biological samples (2.5). This sets the stage for a discussion in section (2.6) of the literature relating to sample export, storage and future uses in the context of international collaborative research and the rather limited literature on the emerging ethical issues relating to samples. The chapter ends with a summary of the knowledge gaps in the literature and a statement on the rationale for this research project.

2.2. The development of ethical standards for research with humans

For the purpose of this investigation, biomedical[5] research, is taken in broad terms, to include a range of research, including clinical trials, which aim at evaluating new treatments for both safety and efficacy, epidemiological studies, and other types of research that aim to contribute to better understanding of the causes, prevention and treatment of major diseases (WMA 2002; Collins, Green et al. 2003; Wertheimer 2011). Pursuing these scientific goals often involves research with humans.

From the beginning of the 20th century to date, there has been a large body of work – academic, policy and regulatory – carried out relating to the ethical requirements in biomedical research with humans (Jonsen 1993). The key historical events that have influenced this development include, but not limited to, the atrocities of the Nazi medical experiments during the Second World War (Mellanby 1947; Annas and Grodin 1992), the infamous Tuskegee study of the natural history of untreated syphilis among African-Americans in Alabama, United States (US) beginning in the 1940s (Jones 1981; Brawley 1998; Baker, Brawley et al. 2005), and other examples of unethical research activities, many of which were described in Henry Beecher's article on 'Ethics and Clinical Research' in 1966 (Beecher 1966). While very detailed discussions of these events would be outside the remit of this thesis, it is nonetheless important to briefly summarise the main accusations that were levelled against medical researchers during this period. They included failures to obtain the voluntary informed consent of research subjects, the inappropriate use of vulnerable populations such as prisoners and marginalised groups, the violations of participants' rights and the exposure of research subjects to unacceptable risks and harms.

[5] The terms *biomedical* and *medical* research are often used interchangeably in the literature but for the purpose of this thesis I shall use the term biomedical to place emphasis on the biological aspects of scientific research which is the focus on my research.

One of the key lessons from these historical events was that they highlighted the need for the development and implementation of appropriate ethical standards to ensure that the interest and rights of research participants are adequately protected (Simmons 1964; Beauchamp and Childress 2009).

The Nuremberg Code, which is often claimed to have marked the beginning of modern research ethics, required, amongst other things, the voluntary consent of potential research participants and for the anticipated risks of an experiment never to exceed the anticipated benefits (Simmons 1964; Annas and Grodin 1992). Principle 1 specifically stressed on the research subjects' right to 'exercise free power of choice, without … any element of force, fraud, deceit, duress, ….or coercion' (*ibid*). The provisions of the Nuremberg Code focused on protecting the human rights of the research subject, with voluntary consent as the cornerstone of ethical research (Shuster 1997). As a central theme in this thesis, consent remains one of the most contentious issues in research with humans. One of the shortfalls of the Nuremberg Code is that it left no room for research involving people with limited capacity to consent such as the mentally ill and children and was thus not generally applicable to many research projects that would count as ethically acceptable (Emanuel, Grady et al 2003).

This shortfall was recognised in the formulation of the World Medical Association (WMA)'s Declaration of Helsinki in 1964 (WMA 1964). [6] While the basic principles of this Declaration, were similar to those in the Nuremberg Code, such as respecting the rights of the research subject and minimising risks of research, the Declaration of Helsinki made exceptions in the area of consent, allowing proxy consent in therapeutic research for patients with limited capacity.

[6] The first statement on medical ethics by the WMA was in 1954 in response to growing concerns about the state of medical ethics globally. Since 1964, there have been six revisions to the Helsinki Declaration; in 1975, 1983, 1989, 1996, 2000 and 2008. Another revision was proposed in 2012, which is currently receiving public comments and recommendations.

Also, from statements on general principles to guide all types of research in the Nuremberg code, the Declaration introduced two different sections to provide clarity on the distinction between therapeutic (clinical) and non-therapeutic (non-clinical) research and the duty of physician-researchers in each context (*ibid*).

The scope of the provisions in the Declaration of Helsinki has evolved overtime, with several revisions since it was first adopted in 1964, to meet the changing demands for guidance in the evolution of biomedical research (WMA 2008). The Declaration in itself, has no legal force and only serves as a guidance document for physicians involved in medical research. However, over the decades, the general principles have informed the development of several international and national guidelines and regulations across the globe. For example, in 1982, the Council for International Organisation of Medical Sciences (CIOMS) and World Health Organization (WHO) developed the international ethical guidelines for biomedical research involving human subjects to provide guidance on how the overarching ethical principles stipulated in the Declaration of Helsinki should be effectively applied in low-income countries (CIOMS 2002). This was particularly important to take into account the cultural, socio-economic and religious differences in these settings. There are now guidelines for specific types of research, including clinical trials and drug development such as the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH/GCP 1996), epidemiological studies (CIOMS 2008) as well as the Ethical Considerations in HIV Preventive Vaccine Research (UNAIDS 2000).

Another key document that has influenced the ethics of research with humans is the Belmont report, produced by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research (Belmont report, 1979).

Drawing upon the Nuremberg Code and Declaration of Helsinki, this report proposed core principles for the ethical conduct of research with humans. These are respect for persons, beneficence and justice. Subsequently, Beauchamp and Childress developed a principles-based approach to research ethics (often referred to as principlism) which expanded the Belmont report into four moral principles: respect for autonomy, beneficence, non-maleficence and justice (Beauchamp 2004; Beauchamp and Childress 2009).

1. *Respect for persons (and autonomy)* is based on the moral imperative of respecting the rights and dignity of human beings. It requires that human beings are treated as ends in themselves and not merely as a means to an end (Beauchamp and Childress 2009; Tangwa 2009). The practical application of this principle is informed consent which requires that potential research participants are provided with adequate information about proposed research and understand that information, that they are competent to make their own decisions regarding research participation and that their decision is voluntary devoid of coercion or undue influence.

- *Beneficence and Non-maleficence:* Beneficence means doing good and implies duties to maximize the benefits of research. Non-maleficence is enshrined in the medical maxim '*primum non nocere'*, above all do no harm (Beauchamp and Childress 2009). In research ethics, these principles – beneficence and non-maleficence – guide the evaluation of the risks and benefits of research and demands that for research to be ethical the potential benefits must outweigh the potential risks (WMA 2008).

- *The principle of Justice* requires that 'equals are treated equally and un-equals unequally'(Beauchamp and Childress 2009). This means that all human beings should be treated equally, unless there is a justification for treating them differently (Tangwa 2009).

  In medical research, the principle of justice demands fairness in the selection of populations and groups for research and the equitable distribution of the burdens and benefits of research (Tangwa 2009).

Taken together, these key ethical principles have provided a framework for evaluating the scientific and ethical merits of research proposals for many decades and underpin many ethical guidelines and regulations currently in existence (CIOMS 2002; WMA 2008).

Research Oversight by Research Ethics Committees (RECs)

One of the key requirements stipulated in the Declaration of Helsinki was the appointment of independent committees for consideration, comments and guidance on research protocols (WMA 1964, Basic principle 2). In the decades since then, research ethics committees have been established across the globe and remain a key governance mechanism for human subjects' research. For example, in 1974, the US Department of Health and Human Services (DHHS) developed federal regulations for protection of human research subjects, which mandated institutional review board (IRBs) review of all federally funded research thus extending ethical responsibilities in research from individual investigators to research institutions (The Common Rule 45 CFR 46 1991). Given the financial influence of the US on research across the globe, the literature suggests that IRBs/RECs in many countries, particularly in Africa were established to meet requirements for obtaining US federal research funds and to meet the US Food and Drugs Administrations' requirements for clinical trials (Ashcroft 2003; Kass, Hyder et al. 2007; Hedgecoe 2009; Nyika, Kilama et al. 2009). According to international and national guidelines, IRBs and RECs are responsible for safeguarding the rights, safety and wellbeing of research subjects (CIOMS 2002; CIOMS 2008; WMA 2008). There are now a number of specific international and national documents to guide the composition and operations of RECs such as the WHO operational guidelines for research ethics committees (WHO 2011), amongst others. The requirement for ethics review was in recognition that other protections such as consent alone was not sufficient for the ethical conduct of research.

According to international guidelines and regulations, RECs are expected to be independent of the researcher and sponsor of the research and to act primarily in the interests of research participants *(ibid).* Their role is to establish that the potential benefits of a proposed research are reasonable to the potential benefits and to determine that appropriate measures are in place for potential participants to provide their valid consent. This requires a range of expertise in its composition, including scientific and lay perspectives (CIOMS 2002; WHO 2011). Although biomedical research is increasingly been regulated by RECs across the globe, questions remain about their actual role in human research protection (Ashcroft 2003; Garrard and Dawson 2005; Coleman and Bouesseau 2008; Nyika, Kilama et al. 2009). Some of the challenges with RECs relate to composition and competence (Nadig, Joshi et al. 2011), conflict of interest issues, especially with IRBs (Lemmens and Thompson 2001), variations in decision-making and lack of training and adequate logistics to monitor approved research in LMICs. There have been some progress to address these challenges, including funding initiatives to support continuing education of REC members and logistical support to enable these committees function efficiently (Kass, Hyder et al. 2007; Nyika, Kilama et al. 2009).

However, questions still remain about the legitimacy of RECs, especially in LMICs where there are very limited ethical and regulatory frameworks (Chima 2006; Noor 2009). With recent advances in biomedical research and the growth of scientific collaborations, are current ethics review systems still fit for purpose?

In the next section of this chapter I will review the literature on the ethical issues arising from international biomedical research and how these have contributed to further development of ethics guidance and research oversight.

2.3. Ethical challenges in international biomedical research

Towards the end of the 20th century, international biomedical research, particularly research that is sponsored by HICs and conducted in LMICs (especially in SSA) increasingly raised particular ethical concerns which have been discussed extensively in the literature (Angell 1988; Schuklenk and Ashcroft 2000; Benatar 2002; Lavery, Upshur et al. 2003). Given the emphasis on the importance of individual informed consent in much of the research ethics literature and earlier guidance, the debates on the ethical conduct of research in LMICs initially centred on cultural differences in consent requirements (Angell 1988; Christakis and Rox 1992; Ijsselmuiden and Faden 1992; Benatar and Benatar 1998). Since then there has been a growing number of empirical studies to assess the practical ethical issues arising when seeking consent in LMIC settings (Molyneux, Peshu et al. 2004; Marshall, Adebamowo et al. 2006; Marshall 2008; Bull, Farsides et al. 2012; Mandava, Pace et al. 2012; Tindana, Bull et al. 2012). Most of these studies have highlighted some of the challenges in obtaining voluntary informed consent in LMICs such as lack of research understanding, and the importance of context in determining appropriate processes for consent (Molyneux, Peshu et al. 2005; Gikonyo, Bejon et al. 2008).

In the 1990s, however, the HIV/AIDs pandemic and the expansion of clinical trials in SSA generated further debates about the ethics of research in LIMCs. This began with criticisms of the use of placebo in controlled clinical trials to test the efficacy of a short-course of zidovudine (AZT) for the prevention of perinatal (mother to child) HIV transmission. Lurie and Wolf argued that it was unethical to deny participants in LMICs the 'best proven treatment' available in HICs when conducting trials in LMIC settings (Lurie and Wolfe 1997). This sparked extensive debates about the standard of medical care that should be provided to research participants in LMICs. Much has been written on the so-called *standard of care* debate (Angell 1988; Varmus and Satcher 1997; Benatar 2000; Benatar and Singer 2000; London 2000; Tangwa 2001).

Whilst this thesis does not focus specifically on the standard of care debate, it is nevertheless worth noting that these debates contributed to a paradigm shift in international research ethics. From an initial focus on cultural differences in consent requirements, concepts such as avoiding exploitation[7], benefit-sharing, post-trial access, and responsiveness to the health needs of the host community began to shape much of the discussions on the ethics of research in LMICs (Wilmshurst 1997; Benatar 1998; Nuffield Council on Bioethics. 2002; Participants 2002; Arras 2004). Some commentators also called for research in LMICs to contribute to addressing global health inequalities (Benatar and Singer 2000). These debates also led to further revisions to international guidelines such as the Declaration of Helsinki (in 1996, 2000, 2004 and 2008) and the CIOMS guidelines (in 1996 and 2000), in an attempt to develop international ethical standards for transnational research.

However, these developments have not taken place without challenges. There is an ongoing debate about the ethical standards that should be applied when researchers from HICs conduct trials in LMIC settings (Varmus and Sarcher 1997, Angell 1997; Christakis and Rox 1992; Benatar 1998; Tangwa 2004; Petryna 2005). At one end of the spectrum is the arguement for *moral universalism,* a position that there are some core moral standards or values that are universally relevant, that is, they hold for everyone, without exceptions. Human rights for example, are often presented as moral values considered universally valid, with recent calls for a human rights framework for bioethics (UNESCO 2005). Some scholars have also cautioned against *moral imperialism* (the imposition of non-universal norms and values from the West on other cultures, populations or countries in LMICs) (Angell 1988; Benatar 1998).

[7] Alan Wertheimer defines exploitation as a transaction in which 'a person (or group) takes unfair advantage of another person (or group), resulting in an unfair distribution of benefits' (Wertheimer 2008).

At the other end of the spectrum from moral universalism is *moral relativism*, a position that moral judgments (about what counts as right or wrong, good or bad) are relative to a particular context in which research is carried out. Thus, for example, the principle of respect for persons may be interpreted according to a community's morally held views about what constitutes a person, particularly in some communalist settings that may seem to undermine individual autonomy.

Over the decades, there has been an increasing recognition that neither extreme relativism nor absolute universalism can satisfactorily address the ethical issues arising in transnational biomedical research in LMICs (Christakis and Rox 1992; Angell 1997; Benatar 2002). There is now an emerging, pragmatic agreement that a kind of middle ground between universalism and relativism should be adopted, even if not theoretically articulated, to promote the core universally accepted ethical values such as respect for human rights and dignity and protection from unnecessary risks, while respecting cultural diversity and sensitivities (Mfutso-Bengu and Taylor 2002; Nuffield Council on Bioethics. 2002; Tangwa 2004; Marshall 2005). These calls for culturally respectful ethical standards have influenced the development of ethical benchmarks for research in LMICs, which is discussed next.

Ethical Benchmarks for research in LMICs

In addition to the development of international and national guidelines, major sponsors of international research, particularly the US and UK have produced key reports to address the controversies and debates around the conduct of health-related research in LMICs.

The US National Bioethics Advisory Commission (NBAC) report and the UK Nuffield Council on Bioethics (NCB) report provide a number of recommendations on how international guidelines can be effectively applied in LMICs and what issues should be considered when research is conducted in LMICs (NBAC 2001; NCB 2002; NCB 2005).

These include the need to ensure that research is locally relevant, the importance of ethics review, providing appropriate levels of research benefits when research is over and respect for individuals (and their communities). For example, the NCB recommends that:

> *'Research must be appropriately planned, taking account of the local context, and effectively reviewed on scientific and ethical grounds. Externally sponsored research also provides the opportunity to assist developing countries to strengthen expertise in conducting and reviewing research' (*Nuffield Council on Bioethics. 2002*).*

The NBAC and NCB as well as the European Group on Ethics in Science (EGE 2003) have been highly influential and often used as a reference in the review of international research protocols.

Then in 2004, Emanuel and colleagues at the US National Institutes of Health (NIH), drawing on existing international guidelines and principles proposed an ethical framework for minimizing exploitation and promoting collaborative partnerships as necessary to the ethical justification of research in LMICs. (Emanuel, Wendler et al. 2004). This consists of eight key principles and 31 benchmarks for the planning and review of biomedical research in LMICs, outlined in Table 1.

Principles	Benchmarks
Collaborative partnerships	Develop partnerships Involve partners Respect the community's values Develop local capacity Ensure benefits to participants and communities Fair benefit-sharing
Social value	Specify beneficiaries of the research Assess the importance of research Enhance the value of research for beneficiaries Prevent supplanting extant health system
Scientific Validity	Ensure that the scientific design of the research realizes social value Ensure the feasibility of the research
Fair selection of study population	Select the study population Identify and protect vulnerable populations
Favourable risk-benefit ratio	Assess the potential risk and benefits of research Assess the risk-benefit ration
Independent review	Ensure public accountability through ethics review Ensure public accountability through transparency Ensure independence and competence of the reviews
Informed consent	Involve the community in recruitment procedures and incentives Disclose information in culturally and linguistically appropriate formats Obtain consent in culturally and linguistically appropriate formats Ensure freedom to refuse or withdraw
Respect for recruited participants and study communities	Develop and implement procedures to protect confidentiality Ensure patients know their rights Monitor and develop interventions for medical conditions arising from participation Inform participants and community of the results of the research

Table 1: Ethical principles and benchmarks for international research
(Emanuel, Wendler et al. 2004)

These benchmarks have been used to evaluate best practices in international research proposals (Emanuel, Wendler et al. 2004; Kilama 2009). Despite on-going discussions on some issues, particularly consent and benefit-sharing, there are now broad areas of agreement about what counts as good research practice globally. These include considerations of the context in which research is carried out and the need for actively involving communities in the design and conduct of research and effective oversight of research (Emanuel, Wendler et al. 2004; Newman 2006; Tindana, Singh et al. 2007).

Several authors like Benatar and Singer have also consistently drawn attention to the importance of local capacity building and for research to contribute to addressing inequities in global health (Benatar and Singer 2001; Benatar and Singer 2010).

Recently, Ijselmuiden et al have discussed the evolving issues in international research highlighting the gradual shift from issues such as cultural differences in informed consent practices towards a greater emphasis on development and social justice (Ijsselmuiden, Kass et al. 2010). These authors have also recommended greater involvement of LMICs government in financing research activities and also called on research ethics committees to reflect on these evolving issues (*ibid*).

According to the United States Office of Human Research Protections (OHRP), there are now around 1300 codes of ethics, declarations, guidelines, policies and documents established and being applied to biomedical research across the globe (OHRP 2013). While the emphasis placed on the key ethical principles in current international guidelines such as respect for persons, beneficence and justice, vary and there remain much disagreement about the meanings of key concepts, there are now major areas of agreement about what counts as good research practice. It is generally accepted that in research, all humans should be treated with respect and dignity, that the vulnerable in society should be protected from exploitation, that potential research participants should be protected from research risks and harms and that there should be fairness in the distribution of the risks and benefits of research (CIOMS 2002; WMA 2008).

What remains unclear is how much of these generally acceptable ethical standards actually translate into research practice. For example, despite the plethora of guidelines, recent advances in scientific research, particularly in the field of genetics and genomics have raised new ethical concerns which require serious attention. This is the focus of the next section of this chapter.

2.4. The growth of international scientific research collaborations

In recent years, there has been a dramatic increase in international biomedical research in Sub-Saharan Africa (SSA) involving research scientists in HICs (Costello and Zumla 2000; Parker and Bull 2009). There are several forms such scientific collaborations tend to take:

- Research that is solely sponsored, initiated and led by HICs researchers but conducted in LMICs. This type of research has sometimes been referred to as *parachute research* and considered ethically problematic because of the lack of engagement with local researchers and communities in LMICs (Costello and Zumla 2000; Jentsch and Pilley 2003).
- Research that is sponsored by HICs but initiated and led by LMICs researchers and conducted in LMICs (Nchinda 2002; Kilama, Chilengi et al. 2007)[8]. This also includes south-south collaborations (Mpendo, Mwapasa et al. 2009; Ivers, Mukherjee et al. 2010) and the recent H3 Africa initiative – discussed later in the chapter (Tan 2010).
- Research that is initiated, funded and led by LMICs, for example locally funded research by local governments and research organizations (Kilama 2009).
- International collaborative research or north-south research collaborations, which involves research that is sponsored by HICs, but jointly initiated and led by researchers in both HICs and LMICs and conducted in LMICs (Emanuel, Wendler et al. 2004; Parker and Bull 2009). In recent times many of the international research projects in SSA take this latter collaborative form, which is the main focus of this thesis.

[8]The term offshore experimentation has also been used to describe the practice of outsourcing research projects particularly clinical trials in other counties, especially in LMICs by big drug companies in HICs. The literature suggests that this practice has grown over the past 10 years. My focus in this research is not on the ethics of this practice although some of the ethical challenges around international collaborative research may be relevant to 'offshore' research projects as well. See Petryna, A. (2005). "Ethical variability: Drug development and globalizing clinical trials." American Ethnologist **32**(2): 183-197. While Petryna's work focuses on the work of contract research organizations, indeed some of the issues she raises are relevant to international collaborative research as well.

Although the number and scale of collaborative research projects increased dramatically in the late 1990s, the literature reveals the existence of research collaborations between research institutions in HICs and SSA as far back as the late 1940s. For example, Tanner et al describe a research collaboration between the Swiss Tropical Institute (STI) and the Ifakara Health and Development Centre in Tanzania dating back to 1949 (Tanner, Kitua et al. 1994). SSA research institutions such as the Kenya Medical Research Institute (KEMRI) and the Noguchi Memorial Institute for Medical Research (NMIMR) in Ghana developed out of international research collaborations that were initiated in the late 1970s.

Many of the well-established research institutions in SSA such as the KEMRI Wellcome Trust Research Programme (KWTRP) in Kenya, the Navrongo Health Research Centre (NHRC) in Ghana, the Malaria Research and Training Centre in Mali and the Medical Research Council Unit in Gambia (the UK's single largest investment in medical research in a developing country) have their foundations in collaborations involving research institutions in HICs. Much of the research conducted in these settings has been funded by external bodies in HICs (Maina-Ahlberg, Nordberg et al. 1997; Mgone 2008; Mgone and Salami 2009). These research investments have not only contributed to the development of capacity in SSA research institutions (Nchinda 2002; Gezmu, DeGruttola et al. 2011; Ali, Hyder et al. 2012) but have also led to direct health benefits such as reduction in morbidity and mortality rates and improved access to health care services in some rural populations (Lairumbi, Molyneux et al. 2008; Masiye, Kass et al. 2008; Molyneux, Mulupi et al. 2012). For example, Binka et al reported that in Northern Ghana, the rural Kassena-Nankana district, a research population, is close to achieving the Millennium Development Goals for reducing child morbidity and mortality (Binka, Bawah et al. 2007).

Many reasons have been given for this increase in international research collaborations in SSA. In what follows, I discuss the three most important, policy shifts to address global health inequalities, major funding initiatives and recent scientific advancements, especially those targeting infectious diseases.

2.4.1. Policy responses to global health inequalities and how they have influenced the growth of international research collaborations

Biomedical research is seen as key to addressing the major diseases affecting populations, especially in LMICs where the burden of disease is high. However, there have been global concerns about growing health inequities between HICs and LMICs.

In the 1990s, the Commission on Health Research and Development (COHRED 1990) estimated that less than 10% of global funding for research was spent on diseases that affect more than 90% of the world (which was coined the 10/90 gap). The commission's report 'Health Research: Essential Link to Equity in Development' anticipated four key challenges in global health: 1) high burden of infectious diseases among the poor; 2) increasing threat of HIV/AIDs, Tuberculosis, and Malaria; 3) increasing epidemics of non-communicable diseases in LMICs and 4) disparities in efficiency and equitable health services in different populations (Vidyasagar 2006).

To address these challenges, four key actions were recommended:

1. set national health research priorities,
2. create international research partnerships,
3. mobilise funding to support health research and development (R&D) and
4. establish a forum to monitor progress in health research, which resulted in the formation of the Global Health Forum for Health Research.

These calls for global action led to a growth in international research collaborations in LMICs such as the Global Alliance for TB Drug Development (TB Alliance), a partnership between public and private stakeholders, major pharmaceutical companies and universities around the world, including many institutions in SSA (www.tballiance.org).

Over a decade after the 10/90 gap was highlighted, research scientists are still worried about the wide gap between the amount of research taking place in SSA and the burden of diseases (Ramsay 2001; Kilama 2009). Notwithstanding the declines in childhood morbidity and mortality worldwide, SSA is still considered the region with the worst health indicators globally (WHO 2008). For instance, malaria remains one of the leading causes of death and illness among children, infants and young pregnant women on the continent (Chandramohan, Owusu-Agyei et al. 2005; Kilama, Chilengi et al. 2007). The efficacy of current treatment strategies such as artemisinin-based combination therapies (ACTs) are also under threat (Noedl, Se et al. 2008; Cheeseman, Miller et al. 2012; Phyo, Nkhoma et al. 2012). Despite the many important research efforts, there is currently no effective vaccine against malaria, which kills over one million children each year (Vogel 2012). Thus, scientists are currently exploring effective ways of combating the disease through more research projects and partnerships (Mons, Klasen et al. 1998; Kilama 2009) and employing advanced research methodologies to address all facets of the disease, including malaria genetic and genomic research (Doumbia, Chouong et al. 2007; MalariaGEN 2008; Parker and Bull 2009). Efforts have also been made in recent times to tackle diseases classified as neglected – not given the needed research and development (R&D) attention – in the SSA (Pecoul 2009; Chatelain and Ioset 2011), such as African trypanosomiasis (sleeping sickness) and Leishmaniasis (Pecoul 2004; Croft, Sundar et al. 2006; Modabber 2010). This has led to further growth of international research collaborations.

One example is the Drugs for Neglected Diseases Initiative (DNDi) [9] which involves collaborations with private industry, public institutions, universities, governmental and non-governmental organisations across Africa, Asia and Latin America to develop new treatments for neglected diseases.

2.4.2. Major funding initiatives and how these have led to the growth of international research collaborations

Funding agencies such as the US National Institutes of Health (NIH), the UK Wellcome Trust, WHO and the Bill and Melinda Gates Foundation (BMGF) have within the past decade devoted significantly larger research funds to targeting infectious diseases such as Malaria, Tuberculosis and HIV/AIDs. In 2003, the Grand Challenges for Global Health (GCGH) Initiative awarded 45 research grants totalling $US458 million (Cohen 2005). This is one of the biggest global health initiatives in recent times and has led to the emergence of large research consortia between investigators in HICs and LMICs. These research collaborations involve scientists from 33 countries in both HICs and LMICs working together to, among other aims; develop better understanding of diseases such as Malaria and HIV/AIDs, to discover more effective diagnostics for TB, and better treatments for neglected tropical diseases which affect the world's poor. An example is the Malaria Genome Epidemiology Network (MalariaGEN), which comprises over 30 partners, many of which are in malaria endemic countries in SSA and Asia (MalariaGEN 2008). In the same year, the European Commission established the European Developing Countries Clinical Trial Partnership (EDCTP) and committed €200 million for the development of new medicines and vaccines for Malaria, HIV/AIDs and Tuberculosis (Mgone and Salami 2009).

[9] Since 2005, the Drugs for Neglected Diseases Initiative (DNDi), an independent and not-for-profit organization has been working in partnership with major private and private organisations to research into and develop new and improved treatments for Neglected Tropical Diseases such as Chagas, Malaria, Leishmaniasis and African sleeping sickness.

Several drug trials in SSA, including candidate malaria vaccine trial initiatives such as GlaxoSmithKline's RTS,S (Agnandji, Lell et al. 2012) and GMZ2 (Belard, Issifou et al. 2011) have been supported by these funding initiatives.

Although the exact scale of investments in biomedical research in developing countries is difficult to estimate, the Global Forum for Health Research, estimated that over US$16 billion was invested in health research and development (R&D) in 2005 globally (Global Forum 2008).

In general, these increased investments in research have contributed to an increase in international research collaborations, particularly those involving researchers from HICs and SSA, and enabled scientists in LMICs to participate in cutting edge science.

However, there have also been concerns about the sustainability of global funding for R&D in LMICs, particularly those in SSA (Benatar 1998). Many worry that the current overdependence on international donor funding is unlikely to address many national health priorities (Gostin 2010). Following calls for more commitment from national governments, in 2003, the African Union agreed that each member-state should commit 1% of their national Gross Domestic Product (GDP) to research. However, as at 2011, only three SSA countries – South Africa, Malawi and Uganda had met this commitment. Reports indicate that many SSA countries currently spend less than 0.3% of their national GDP on R&D (UNESCO Science Report 2010, p280). This imbalance in national financing of health research has important implications for the conduct of international collaborative research and has led to calls for more local funding of research in LMICs (Ijsselmuiden, Kass et al. 2010; Gostin 2012).

2.4.3. Recent technological advancements and growth of international research collaborations

Another factor influencing the growth of research collaborations is the significant progress in biomedical science and technology, particularly in the field of molecular biology and genetics. The successful completion of the Human Genome Project (HGP) opened new research opportunities within HICs and north-south research collaborations. This has led to significant advances in our understanding of a wide range of human diseases from non-communicable diseases (NCDs) such as cancer, stroke and hypertension to communicable diseases such as Malaria, Tuberculosis and HIV/AIDs (www.genome.gov). These scientific developments have provided insights into the genetic makeup of individuals, families and communities which provide valuable insights into the diagnosis, prevention and treatment of many diseases (Hirschhorn 2005; Hardy and Singleton 2009).

These advances have also given rise to the establishment of various research consortia involving research scientists from both HICs and LMICs. The HAPMAP project (Consortium 2004), the MalariaGEN (2008) and the African TB consortium are examples of research consortia that have enabled SSA research scientists to collaborate with their counterparts in HICs and to apply cutting-edge methodologies to major infectious diseases such as malaria and tuberculosis.

In June 2010, the US National Institute of Health and the UK Wellcome Trust announced the Human Heredity and Health in Africa project (H3Africa), a $38 million partnership to ‘discover how genes affect the way the human body responds to environmental factors, such as diet, and how this influences the risk of disease’ (Wellcome Trust 2010).

This initiative emphasises the importance of 'science in Africa, by Africans and for Africans' and is expected to empower African scientists 'to take the lead' in scientific research on the continent (Tan 2010) and as some commentators have often put it *solve their own problems* (Benatar 2002; Binka 2005). One important aspect of the H3 Africa initiative is anticipating the ethical, social and legal aspects of genomic research in these contexts to ensure that scientists do not fall into the same pitfalls as past research (Kaplan 2011).

Taken together, these three factors – policy changes, funding initiatives, and technological developments – have driven a dramatic increase in the growth of international research collaborations. The conduct of biomedical research has thus changed dramatically, increasingly involving complex research designs and complex research relationships across continents and national borders. This presents new ethical challenges for researchers, research institutions and research ethics committees as there are also limitations with current guidelines. These challenges are discussed next.

2.5. Emerging ethical challenges in scientific collaborations

Most of the ethical challenges arising from the recent increase in scientific research collaborations relate to consent and community engagement, capacity building and benefit-sharing and the increasing use of human biological samples (Upshur, Lavery et al. 2007; Parker, Bull et al. 2009; Abou-Zeid, Silverman et al. 2010; de Vries, Bull et al. 2011).

Growing challenges with consent and community engagement

All the major research ethics guidelines, codes and regulations prescribe obtaining valid consent from prospective research participants as an important ethical requirement (CIOMS 2002; WMA2008). As discussed earlier, there are now a growing number of empirical studies from both LMICs and HICs which have highlighted the challenges with obtaining and

documenting consent in LMICs, particularly in SSA (Molyneux, Peshu et al. 2004; Tindana, Kass et al. 2006; Marshall 2008; Tekola, Bull et al. 2009; Bull, Farsides et al. 2012; Mandava, Pace et al. 2012). The literature suggests that recent advances in research have further complicated consent processes. One major challenge is how to explain the complex methodologies such as genomics in contexts with low literacy levels (Marshall, Adebamowo et al. 2006; Nyika 2009; de Vries, Bull et al. 2011; Tindana, Bull et al. 2012). A recent collaborative research by the Navrongo Health Research Centre in Northern Ghana and the Ethox Centre in the UK on seeking consent in genetic and genomic research in rural northern Ghana, highlighted limitations in current consent practices in addressing gaps in research understanding within these contexts (Tindana, Bull et al. 2012). One recommendation for addressing these challenges is exploring innovative ways of explaining complex scientific terms in lay terms to research participants, including appropriate levels of community engagement (CE) (Tindana, Singh et al. 2007).

There is a growing body of literature including empirical studies on various approaches to community engagement in global health research, highlighting both the intrinsic and instrumental values of engaging communities in research (Dickert and Sugarman 2005; Rotimi, Leppert et al. 2007; Lavery, Tindana et al. 2010; Nyika, Chilenge et al 2010; Marsh, Kamuya et al. 2011). CE is seen as an important step in respecting communities, ensuring the protection of individuals and their communities and building a trusting relationship between researchers and communities as well as facilitating the smooth conduct of research (Newman 2006; Tindana, Singh et al. 2007; Marsh, Kamuya et al. 2011). Examples of CE models include community advisory boards (CABs) (Quinn 2004; Delaney, Walton et al. 2012; Parker 2012), community *durbars* or gatherings (Tindana, Rozmovits et al. 2011), and engagement through community representatives (Marsh, Kamuya et al. 2008; Kamuya, Marsh et al. 2013).

However, as highlighted in my earlier work, community engagement is a complex concept and context specific and what constitutes effective community engagement remains a challenge (Tindana, Singh et al. 2007).

Benefit sharing and capacity building

A recurring theme in international scientific collaborations is benefit- sharing. Against the background of the huge economic disparities between HICs and LMIC collaborators, it has been argued that there should be equitable distribution of research benefits between the parties involved in designing and carrying out the research such as sponsors, researchers, participants and communities (Schulz-Baldes, Vayena et al. 2007; Upshur, Lavery et al. 2007; Emerson, Singer et al. 2011). Fairness is seen as the principal rule of engagement with each party with a fair share in what is brought to the table, and each leaving equally satisfied (Lansang and Crawley 2000). This notion requires that both parties understand and have a full knowledge of fair exchange of benefits and that the parties to the exchange decide what counts as a fair trade off.

The grey literature points to the fact that communities are often uninformed of the benefits they are entitled to or the demands they may make on the research team (Upshur, Lavery et al. 2007; Andanda 2008; Emerson, Singer et al. 2011). It is therefore not possible for research participants and their communities to decide on what constitutes a fair share of the benefits of research unless they are actively engaged in the research process (Molyneux, Mulupi et al. 2012). Further studies on what benefits of research should be shared, what fairness means and how benefits should be distributed would be desirable.

Another emerging challenge is the lack of adequate capacity in SSA research institutions to participate in cutting-edge science (Kilama 2009; Gezmu et al 2011). Over the years, some progress has been made through increased funding for post-graduate studies and building of

laboratory infrastructure in many countries (Kilama, Chilengi et al. 2007; Nashiru, Huynh et al. 2007; Malkin and Keane 2010). Also, there are several published articles indicating that despite the practical challenges, it is possible to build research capacity in LMICs including SSA (Habte 1992). Focusing on research practices around sample export, storage and future uses may provide further insights into how these engagements and negotiations can be made.

2.6. Increasing use of human biological samples for research

A key emerging ethical concern in international scientific research collaborations is the increase in the number of samples used in research. Most of the rapidly expanding biomedical research activities taking place across the globe would be impossible without access to large numbers of human biological samples, such as cells, tissues, organs, blood, and sub cellular materials such as DNA. The availability of human samples in the context of collaborative research has been central in the understanding of the nature and transmission of pandemic agents and many poverty related diseases in Africa such as malaria (MalariaGEN 2008; Sirugo, Hennig et al. 2008; Dalal, Holmes et al. 2010).

Though the collection, storage and use of human biological samples for research are increasingly common, they are not new. For several decades, various human biological samples have been collected and used for the diagnosis and treatment of diseases in local healthcare settings, and for biomedical research around the world (Blatt 2000; Nakkazi 2006; Cunningham and Dunbar 2007). Some samples have also been stored in repositories for various important public health reasons. What is new is the sheer scale of the collection, storage and use of human biological samples for research purposes.

In 1999, the US NBAC estimated that there were over 282 million human samples stored in various laboratories and tissue repositories and banks across the United States. This figure was expected to have increased by tens of millions by the end of 2009 (Crigger 2001).

Recent advances in computer technology and high-throughput DNA sequencing have also resulted in an increase in the establishment of biobanks in many HICs such as the United Kingdom (Cambon-Thomsen, Rial-Sebbag et al. 2007; Kaye 2010; Kaye 2011).

The literature suggests that while discussions about appropriate ways of governing these scientific resources only received attention relatively recently (Winickoff and Winickoff 2003; Zika, Schulte In den Baumen et al. 2008), many research institutions across the globe have amassed human biological samples collected in the course of research and diagnostic procedures for many decades (Wonkam, Muna et al. 2010). Many authors, especially scientists, have described biobanks and the collections of samples as a powerful tool for undertaking important medical research (Blatt 2000; Collins 2003; Collins, Green et al. 2003; Zika, Schulte In den Baumen et al. 2008).

The advent of new research methods such as those developed in the field of genomics has also given rise to an increase in the number of samples used for research, especially research involving LMICs. For example, in one project, over 100,000 samples have been collected across several developing countries to explore and identify critical mechanisms of protective immunity against malaria which could lead to successful malaria vaccine development (MalariaGEN 2008; Teo, Small et al. 2010). Research scientists believe that despite the complexities associated with conducting genome-wide association studies (GWAS) in African populations, which have a high level of genetic diversity, increasing sample sizes can produce fruitful results (Thye, Vannberg et al. 2010).

In the context of international collaborative research, there is also the tendency for research samples to be exported and sometimes stored in well-established laboratories in HICs (Langat 2005; de Vries, Bull et al. 2011) as well as the data derived from their analysis to be shared across research institutions. This has raised new ethical concerns that require attention.

2.7. Ethical concerns about the increased use of samples

The increase in sample collection, export and storage for long term use has raised important questions about appropriate ways to govern the use of samples, and safeguard the interests of sample donors such as research participants and their communities (Charo 2006; Cambon-Thomsen, Rial-Sebbag et al. 2007). Issues about consent, particularly the validity of broad consent and what consent should be acceptable for sample export have been highlighted in the literature (Wendler and Emanuel 2002; Emanuel, Wendler et al. 2004; Weijer and Miller 2004; Wendler and Pace 2005; Hansson, Dillner et al. 2006). These are discussed next.

2.7.1. Broad consent for sample storage and future uses

As discussed earlier, the research potential of stored samples has increased dramatically, and provides opportunities for several studies including genetic studies (with a potential for stigmatization) to be carried out (Ashcroft 2000; Wendler and Emanuel 2002; de Vries, Jallow et al. 2012). For many international research collaborations, samples may be split and stored both locally and in overseas laboratories depending on the nature of the research. A common practice is stripping samples of identifiers to preserve privacy and confidentiality during the research process. This is seen as one way of protecting the privacy and confidentiality of research participants, who are the donors of these samples (Blatt 2000).

In HICs, public views and perceptions of research with stored samples are increasingly being reported and contributing to the development of regulatory frameworks (Wendler and Emanuel 2002; Pace, Grady et al. 2006; Gibbons and Kaye 2007; Steinsbekk, Ursin et al. 2011). However, there is lack of clarity over appropriate governance of human samples, and issues of ownership and property rights over human tissues/samples have not been adequately addressed (Charo 2006; Andanda 2008).

A recent case involving the Havasupai Indian tribe and the Arizona State University, a renowned university illustrates what can go wrong if the appropriate protection mechanisms are not established for the reuse of archived samples (Mello and Wolf 2010). While the tribe willingly donated blood samples for studies on Type 2 diabetes in the late 1980s, research scientists used these samples for subsequent genetic studies without appropriate consent (Lunshof and Chadwick 2011). Despite these controversies and apparent limitations of current guidelines, there is still no consensus on the appropriate consent that is required for future research uses of samples (Salvaterra et al 2008). Table 2 gives an overview of the different types of concepts for consent for human biological samples in the literature.

Specific informed consent	Allows the use of biological samples and associated data only in immediate research: forbids any future research that is not foreseen at the time of the original consent
Partially restricted consent	Allows the use of biological samples and associated data in specific immediate research and future research directly or indirectly associated with them.
Generic /Broad Consent	Allows the use of biological samples and associated data in specific immediate research and future research of any kind at anytime, but with ethics approval and opportunity for participants to withdraw consent.
Multi-layered consent	Requires several options to be explained to the research subjects I in a detailed form such as what to opt in and out.
Blanket consent	Allows the use of biological samples and associated data for future research of any kind at anytime

Table 2: Key concepts for consent for use of human biological samples in research
(from Salvaterra et al 2008, p309)

In the biobank literature, there is a growing scholarship in HICs on the concept of broad consent for future uses of samples (Wendler and Pace 2005; Hansson, Dillner et al. 2006; Wendler 2006; Upshur, Lavery et al. 2007; Kaye 2010; Petrini 2010; Karlsen, Solbakk et al. 2011; Sheehan 2011; Steinsbekk, Ursin et al. 2011). The current practice is a one-time individual consent with a statement on future uses of samples and approval by local ethics committees as the best model for managing the use of samples in research. (Wendler and Emanuel 2002; Hansson, Dillner et al. 2006; Wendler 2006).

However, there is currently very limited discussion in SSA on what the key elements of broad consent should be for it to be valid and adequate for future uses of samples. In the context of sample export and long-term storage in LIMICs, the literature highlights growing concerns that current informed consent practices do not address issues about ownership and local control of exported samples (Upshur, Lavery et al. 2007). As a result there have been proposals for appropriate engagement with relevant communities from which samples will be exported as a necessary additional requirement (Upshur, Lavery et al. 2007).

For example, the ethics committee of the Medicines Sans Frontiers (MSF) have recommended that local communities should be actively engaged in issues related to future uses of samples (Schopper, Upshur et al. 2009). How this process of engagement should be done in practice remains unclear. Given the lack of consensus in the literature on appropriate consent processes for future uses of samples, particularly the paucity of information from SSA, it is important to elicit the views and perspectives of key stakeholders in SSA on what might count as good ethical practice.

2.7.2. Public concerns about sample export from Africa to HICs

The increased collection and export of samples has also led to growing discussions and some controversies in international research collaborations. In 2006 a Ugandan newspaper reported that about 80% of human biological samples collected in the context of research had been exported (Nakkazi 2006). The justification given for exporting samples to laboratories in HICs include: (1) the lack of capacity and the necessary technology and laboratory infrastructure to process and securely store samples and large datasets and (2) to facilitate centralized analysis and standardize quality control, especially in multi-country and multi-centre trials (Upshur, Lavery et al. 2007).

More recently, controversies surrounding sample export in international collaborative research have generated discussions about how this further widens the health and economic disparities between HICs and LMICs (Upshur, Lavery et al. 2007). In one case, local Kenyan scientists protested against their foreign collaborators from Oxford University for patenting an HIV vaccine development process without giving them sufficient acknowledgement (Andanda 2008). In another controversial case, a Kenyan researcher accused foreign researchers from Oxford University of 'stealing' blood and tissue materials from a Nairobi orphanage laboratory (Daily Nation 2002)[10].

Controversies such as these have the potential of creating tensions between researchers, local institutions and research communities, and hindering the scientific research process. However, they also highlight the growing recognition of the importance of having clear and workable frameworks for collaborative research. The Kenyan case, for example, highlighted the lack of clear frameworks governing sample export and the need for prior research agreements between

[10] Although some of these claims could not be substantiated, they highlight the concerns that may arise from the use of samples in research without an appropriate collaboration or ethical framework.

collaborating partners to ensure that each partner receives a fair share of the research benefits (Upshur, Lavery et al 2007).

What is not clear is whether these controversies are all about sample export or there are other underlying issues such as ownership, local control and fairness that need to be recognised. Does it really matter where samples are exported to? For example, is it more problematic to export samples from Ghana to the United Kingdom than to South Africa or Mali? Are there issues about sample export that are of concern to local researchers, local ethics committees and local communities? How do communities feel about their samples moving across country borders and to what extent should communities be involved in deliberations around sample use, storage and future uses in scientific research?

2.7.3. Cultural and social beliefs about blood samples

One of the most salient aspects of biomedical research is blood taking. As discussed earlier, access to human biological samples such as blood is essential to much of the biomedical research needed to address the global burden of disease. Published articles dating back to the early 1960s reveal tensions between medical researchers and researched communities about the purpose of blood-taking in medical research.

Writing about the Kaguru kin of East Africa, Beidelman refers to the physiological concept of blood among the Kagurus and how that influences their perception of medical research in general (Beidelman 1963). He highlights how medical researchers have often been referred to as ‘blood stealing strangers’ across the region. There is evidence to suggest that while most communities across the region appreciate the benefits that they derive from participating in research activities, they also view these institutions as people who collect their blood and sell to their foreign collaborators (Fairhead et al 2006; Molyneux et al 2005; Kingori et al 2010).

For example, Fairhead and Leach describe Gambian participants' pervasive view of the MRC as an institution that offers good, free medication to participants, but also 'steals blood' (Fairhead, Leach et al. 2006). Empirical studies by Molyneux et al have also highlighted a range of concerns expressed by local communities in a Kenyan Coast about blood taking including misunderstanding what the blood is used for and concerns that the blood collected in the context of research will be used for 'other things' such as being sold for profit (Molyneux, Peshu et al. 2004; Molyneux, Peshu et al. 2005).

As Rosnow and Fine have suggested, rumours can be viewed as 'a form of individual and collective information-seeking when a formal information gap exists' (Rosnow 1988). They could also be attributed to incomplete information or mistrust of the official sources of information (Rosnow and Fine 1976). For example, the literature suggests that there is confusion among research participants and communities about the purpose of taking blood samples for research and concerns about the rationales for exporting such samples for research purposes (Upshur, Lavery et al. 2007).

Geissler and Pool have also suggested that rumours about blood use in research reveal local communities' responses to research and the more general relationships of dependence and inequality on which these are based (Geissler and Pool 2006). This should be taken seriously. It also calls for greater clarity on the underlying concerns about sample export. Upshur et al have also suggested that if these issues matter to research participants and their communities, then they must be given an appropriate place in determinations of whether a proposed research is ethical or not (Upshur, Lavery et al. 2007). As Fairhead et al and other commentators have also argued, rumours and suspicions about the purpose of blood in research should not be taken for granted but rather, require serious attention in determining acceptable research practices. (Fairhead, Leach et al. 2006; Geissler and Pool 2006).

This underscores the importance of open dialogue with communities around the export and long-term storages of sample to make research in LMICs 'sustainable and politically legitimate' (*ibid*). What is still not very clear is how to determine what really matters to research participants and their communities regarding these research practices and how these cultural concerns should be taken into account in the development of governance mechanisms. This requires further investigation to inform best practice.

2.7.4. Limited guidance on sample export, storage and future uses

Despite the rapid growth in the use of samples, there is currently lack of guidance on the best way to address the ethical issues that arise in the export, long-term storage and reuse of samples. While guidelines from both HICs and LMICs endorse the need for informed consent from participants, they are unclear on the necessity of documenting and justifying or of explaining the potential cultural significance of sample export (Upshur, Lavery et al. 2007). Especially in the context of international collaborative research and long-term overseas sample storage, there is little guidance on what the best practices are in engaging local communities around these issues. This needs further exploration.

There is an urgent need for effective governance mechanisms for the export, storage and future uses of human biological samples, especially in the context of SSA. In recent times, there have been efforts to provide guidance on how these ethical issues arising from the use of human biological samples in research should be addressed. As shown in Table 3, in HICs such as the UK and US, there are a number of guidelines and policy statements aimed at clarifying researchers' obligations with regards to these research practices (Human Tissue Act 2004; MRC Ethics Series 2001). While some SSA countries have begun to establish similar national guidelines and policies, there is still lack of clarity on many of the issues arising in practice such as those around sample export.

Country/International bodies	*Laws, Guidelines, regulations*	*Guidance on informed consent for storage and future uses*	*Guidance on sample export*
World Health Organization	Guideline for Obtaining Informed Consent for the Procurement and use of Human Tissues, Cells and Fluids in Research (2003)	Specific informed consent Partial restricted consent Broad consent	*None*
Council for International Organization of Medical Sciences (CIOMS)	International Ethical Guidelines for Biomedical Research Involving Human Subjects (2002) International Guidelines for Ethical Review of Epidemiological Studies (2009)	Specific informed consent Broad consent	*None* *None*
Human Genome Organization (HUGO)	Statement for DNA Sampling	Broad consent	*None*
United Kingdom	Human Tissues Act (2004) Human Tissues and Biological Samples for Use in Research –Medical Research Council (2001)	Broad consent	Advice to refer to appropriate national guidelines
United States National Bioethics Advisory commission (NBAC)	Research Involving Human Biological Materials: Ethical issues and Policy guidelines	Multi-layered consent	*None*
Gambia	Medical Research Council (UK) The Gambia – Guidelines of the National DNA bank (2001)	*None*	*None*
Ghana	*None*	*None*	*None*
Kenya	National Council for Science and Technology –Guidelines for ethical conduct of Biomedical Research Involving Human Subjects in Kenya (2004) Kenya National Guidelines for Research and Development of HIV/AIDs vaccines, page 44 (2005)	Broad/generic consent	Explicit consent
South Africa	Medical research Council-Guidelines for Ethics in Medical Research	None	None
Sudan	Federal Ministry of Health –Human Organs and Tissues transplant Legislation, Chapter 2, Article 3 and 4 (1978)	Informed consent	None
Zimbabwe	Medical Research Council –Ethical Guidelines on the Collection of Blood Samples for Research (1999)	Informed consent	None

Table 3: List of international and national guidelines and regulations adapted from the international guidance list compiled by the US Office for Human Research Protection (OHRP)

2.8. The need for more empirical research to inform guidelines and practice

With the growing number of biomedical research activities in SSA, the literature highlights tensions around the export and long-term storage of samples (Upshur, Lavery et al. 2007; Andanda 2008). These tensions need to be addressed to move both the science and ethics of biomedical research forward. As the literature suggests, while there is a growing body of scholarship in HICs on public perspectives regarding the use of their samples, little is known about the perspectives of key stakeholders in LMICs. This requires further evidence-based research to get a deeper understanding of the key ethical issues arising from sample export, storage and future uses.

Despite the growing scholarship in HICs on participants' perspectives on the ethical issues arising in long-term storage and future uses of samples, at the beginning of my research for this thesis – in 2009 – I found only three empirical studies from LMICs, specifically in SSA. In a study of two ethics review committees in Kenya, Langat reported that 25 per cent of protocols reviewed stated there was a need for the storage and reuse of samples, however, only half actually informed participants of this need. The author concluded that investigators do not recognise 'the need to seek consent for storage, reuse and exportation of samples' (Langat 2005). This study did not seek the views of investigators on why they do not consider it important to inform participants about the potential export and long-term storage of their samples.

In a survey of participants in a malaria clinical trial in Uganda, Wendler *et al*. found that most participants were willing to permit sample export and storage and were willing to waive additional consent for future research, provided the study was approved by an ethics review committee. However, respondents expressed a desire to be informed about the sorts of studies stored samples would be used for (Wendler and Pace 2005).

In 2010, a survey of patients in Egypt found that most patients (62%) preferred to have their samples exported to other Arab countries compared to Europe and USA (Abou-Zeid, Silverman et al. 2010). Since 2009, there have been calls for more empirical studies to understand the perspectives of research participants in LMICs, including SSA. Recently, Igbe and Adebamowo reported that research participants were generally supportive of biobanks on condition that the right structures are in place to prevent unethical research practices (Igbe et al 2012). In another study among participants in a TB research in South Africa, van Schalkwky et al reported a wide and complex range of views on sample storage and reuse but a general support for uses of their samples if it is for a 'good-course' (van Schalkwyk et al 2012). These authors have also called for further research in other contexts to inform research practices.

While these empirical studies indicate that there is likely to be a range of perspectives in SSA about sample storage and reuse, none of these studies have answered the deeper questions about what the underlying issues are from various stakeholders' perspectives including researchers, fieldworkers and members of research ethics committees. As a result, Upshur et al and Abou-Zeid et al have all called for further qualitative studies to understand the underlying issues behind these responses and how they might be addressed in the context of scientific research collaborations (Upshur, Lavery et al. 2007; Abou-Zeid, Silverman et al. 2010).

The empirical literature also suggests the urgent need for further research to examine researchers' perspectives of the consent process for sample export, and the extent to which key stakeholders in Africa understand the rationales for the collection, export, storage and the unforeseen future uses of human biological samples (Upshur, Lavery et al. 2007). Studying the perspectives of relevant key stakeholders in research such as researchers, fieldworkers, ethics committees, research participants and community representatives could shed light on the real ethical challenges arising from these research practices.

This could also help identify possible solutions that could feed into institutional policies and guidelines on research involving human samples.

Against this background, the aim of my project is to explore key stakeholders' perspectives of and responses to the ethical issues around the export and long-term storage of human biological samples from Africa. The primary research question is: what are the ethical issues arising in sample export, storage and future uses, in the context of international collaborative biomedical research involving African research institutions with a long-term (over twenty years) relationship with a host community? Specifically my aim is to address the following questions:

- What are the ethical issues arising in the export and long-term storage of human biological samples?
- How do key stakeholders understand the rationale for sample export and long-term storage as well as future use?
- How should communities be involved in the deliberations around the export and storage of human samples?
- What needs to be put in place to address the practical ethical challenges arising from sample export, long-term storage and future uses?

The goal is to contribute to this debate and to the development of good practice and governance mechanisms. In the next Chapter, I describe and discuss the methodology and research methods used to address these research questions.

CHAPTER 3: Research Design

3.1. Introduction

In Chapter 2, I highlighted the fact that only a limited number of empirical studies have investigated stakeholders' perspectives on the ethical issues around sample export, storage and future uses. I also noted that there is currently a lack of guidance on the best way to address the ethical issues that arise in these research practices. Especially in the context of international collaborative research and long-term sample storage, there is also little guidance on what the best practices are for engaging local communities around these issues. Against this background, my primary aim in this research was to contribute to an empirically-informed understanding of the ethical issues arising in the export, storage and future uses of human biological samples in sub-Saharan Africa (SSA). Specifically, I aimed to address the following research questions:

1. What are the key ethical issues that arise in the export and long-term storage of human biological samples?
2. How do key stakeholders understand the rationale for sample export and long-term storage as well as future use?
3. How should host research communities be involved in the deliberations around the export and storage of human samples?
4. What needs to be put in place to address the practical ethical challenges arising from sample export and long-term storage and future uses?

In this chapter, I outline the research design used to address these research questions including the research methods, context, sources of data and the methodological considerations that guided the process of data collection, interpretation and writing. I begin by describing the rationale for selecting the two research settings and the context in which this research was conducted.

3.2. Research settings and context

The research was conducted in two host research sites in Sub-Saharan Africa: Navrongo in Ghana which hosts the Navrongo Health Research Centre (NHRC) and Kilifi in Kenya, which hosts the Kenya Medical Research Institute (KEMRI)/Wellcome Trust programme (KWTRP). These two research institutions were purposively selected because they are both involved in major research activities involving international collaborations. They both have a research connection with the Oxford University. They both run a longitudinal health and demographic surveillance system (HDSS) and they both have had a research relationship with the host community for over twenty years. Conducting my research within these contexts provided a great opportunity to address my research questions.

3.2.1. Ghana, the Kassena-Nankana Districts and the Navrongo Health Research Centre (NHRC).

Ghana, formally known as the Gold Coast, was the first country in Africa to gain independence from British colonial rule in 1957 (Ghana. 1957; Bourret 1960). With a population of 24.6 million (Ghana Population and Housing Census 2010), Ghana is situated in West Africa and bordered by three francophone countries; Burkina Faso to the North, Togo to the East and Ivory Coast to the West. It is described as one of the most stable countries in SSA with six successful democratic elections since 1992 and the fastest growing economy in the region. In 2010, the World Bank rebased Ghana from a low-income country to a lower-middle-income country as a result of its recent economic growth and discovery of oil in commercial quantities (World Bank 2010).

Health and biomedical research in Ghana is currently organised under three main governmental agencies; the Centre for Scientific and Industrial Research (CSIR), the Universities and the Ghana Health Service with affiliation with the Ministry of Health. The Ghana Health Service (GHS) is the largest autonomous national body responsible for implementing all national health policies in the country. The NHRC – my research site in Ghana – is one of the three research centres of the GHS. There are also a number of non-governmental organisations (NGOs) involved in health-related research in the country. Estimated health and economic indicators for the country in 2011 are as shown in table 4.

	Estimated figures in 2011
Population	24,965,816
Health Indicators	
Neonatal mortality rate/1000 live births	50
Infant mortality rate/1000 live births	50
Under-5 mortality rate/1000 live births	80
Maternal mortality rate /100,000	163
Life expectancy at birth (males in years)	59.6
Life expectancy at birth (females in years)	62.3
Economic Indicators	
Income Level	Lower-middle Income
Gross Domestic Product	39.20 Billion
GDP growth	14.3%
People living below the poverty line	28.5%
Research and Development Budget	0.3% of GDP

Table 4: Key national health and economic indicators: Ghana (Ghana DHS 2008; World Bank 2012).

There are currently eight independent institutional research ethics committees in Ghana and no national ethical guidelines, although most of these RECs have institutional standard operating procedures for the ethics review of research projects.

The Kassena-Nankana Districts (KNDs)

The Map of Ghana and the location of the Kassena-Nankana Districts originally presented here cannot be made freely available via ORA because of copyright reasons. The map was sourced at *Oduro A R et al. Int. J. Epidemiol. 2012;41:968-976.*

The Kassena-Nankana East district (KNED) and the Kassen-Nankana West district (KNWD) are two of the administrative districts in the Upper East region of Ghana, which have hosted biomedical research in Ghana. They are situated in the north, close to the border with Burkina Faso and cover a land area of 1675 square kms. Both districts have an estimated population of 151,000 (Oduro, Wak et al. 2012). There are two main ethnic groups in these districts, the Kassenas and the Nankanis and a minority Buli. These ethnic groups share a traditional rural agrarian culture and tradition, but they have different languages. They live in scattered settlements of mud houses and the majority of the population depends on subsistence farming. Literacy rates are currently estimated at 57%. The districts are divided into ten (10) paramouncies which are headed by a traditional paramount Chief and a council of elders. The districts are currently served by one district hospital, health centres and private clinics. Current key health and economic indicators for the districts are as shown in Table 5 on the next page.

Kassena-Nankana Districts	Estimated figures in 2011
Population	151,000
Health Indicators	
Neonatal mortality rate/1000 live births	13.4
Infant mortality rate/1000 live births	32.1
Under-5 mortality rate/1000 live births	60.8
Life expectancy at birth (males in years)	56.4
Life expectancy at birth (females in years)	67.0

Source: (Oduro, Wak et al. 2012)

Table 5: District health indicators - Kassena-Nankana districts.

The Navrongo Health Research Centre (NHRC)

The Navrongo Health Research Centre is located in Navrongo, the capital of the Kassena-Nankana East district. It started as a field site for a Vitamin A Supplementation Trial (VAST) in 1988 and has grown into an international Centre of research excellence (Ross 1993). The VAST project was a collaboration between the Ghana Ministry of Health, the University of Science and Technology and the London School for Hygiene and Tropical Medicine (Oduro, Wak et al. 2012). Since then, the Centre has collaborated with major research institutions within the country such as the Noguchi Memorial Institute for Medical Research (NMIMR) and external collaborators in the United Kingdom, United States and West Europe.

In 1993, the Centre established a demographic surveillance system (DSS) to support the evaluation of a study on permetrine (an insecticide) impregnated bednets. This study demonstrated that sleeping under a treated bednet was associated with a 17% reduction in all cause morbidity and mortality in children (Binka, Mensah et al. 1997). Over the years, the DSS platform has been used to provide a baseline for many of the research studies in the district (Oduro, Wak et al. 2012).

The majority of the Centre's research has been in communicable diseases such as malaria, HIV/AIDS, diarrhoea, meningitis and lymphatic filariasis (Chandramohan, Owusu-Agyei et al. 2005). The Centre has also conducted both exploratory and intervention studies. A number of the findings of these studies have been adopted into national policy in Ghana and in the international health community. These include the routine administration of Vitamin A to infants (Ross 1993), the use of impregnated bed nets for malaria control (Binka, Mensah et al. 1997) and the community-based approach to health delivery and provision of family planning services (Nazzar, Adongo et al. 1995; Debpuur, Phillips et al. 2002; Oduro, Wak et al. 2012).

Although the NHRC is part of the Ghana Health Service, its research activities are funded by external sources, such as the NIH, the Rockefeller foundation, United States Agency for International Development (USAID) the Department for International Development (DFID), the Bill and Melinda Gates Foundation and the Wold Health Organization (WHO). About 80% of NHRC's research is conducted in collaboration with partners outside of Ghana. Through these collaborative efforts, the NHRC has managed to strengthen its human and infrastructure capacity which has put the Centre in a position to contribute to cutting-edge health research activities with their research partners in HICs. Despite these improvements, a great number of samples from medical research are sent to laboratories in Accra (Noguchi Memorial Institute for Medical Research) and foreign laboratories in South Africa, Europe and the United States for analysis and storage for future research.

Figure 2: Picture of the main entrance to the NHRC and a typical KND compound

Empirical and practical ethics projects in Navrongo

For the past twenty years, the NHRC has reached out widely in the two Kassena-Nankana districts, and most residents of these districts have participated in at least one of the Centre's research projects. The NHRC has a strong system for engaging the local community in its research activities. Utilizing traditional communication strategies, the NHRC's community engagement (CE) process begins with a community entry process with meetings with traditional authorities, followed by community durbars (gathering), targeted meetings with households and then the individual consent process (Tindana, Rozmovits et al. 2011).

To ensure that its research activities are addressing local health needs and are culturally acceptable, the NHRC has carried out a number of studies to examine the informed consent process in this rural African setting. In an earlier study, together with colleagues, I carried out a study on the informed consent process and the role of key stakeholders such as chiefs in this process (Tindana, Kass et al. 2006). The study observed that trust in researchers and perceived benefits of the research were major factors in research participation. The study concluded that in settings where participants assume few risks in research, there is the need for research ethics committees to be vigilant to ensure that the trust that participants place in researchers is not exploited.

Oduro et al also studied the parental informed consent process for a malaria prevalence study in this area and found that comprehension of the consent process was significant among parents and that benefits from research in the form of medical care was the major motivating factor for participation. The team concluded that the practice of informed consent in this setting was fairly effective (Oduro, Aborigo et al. 2008). Both studies have recommended more empirical work to evaluate the existing practice of informed consent in this setting to identify innovative ways for improvement.

In 2009, the NHRC also conducted a case study to describe community engagement (CE) practices associated with research projects and to determine what makes these practices effective, or not, from the perspective of multiple stakeholders (Tindana, Rozmovits et al. 2011). This was in response to the increasing recognition that CE is an important ethical requirement for research in developing countries (Newman 2006; Tindana, Singh et al. 2007; Upshur, Lavery et al. 2007) and calls for some guidance for effective CE. In collaboration with the Ethox Centre, University of Oxford, another study explored consent issues in genomic research, using a case control study of the Malaria Epidemiology Network (MalariaGEN) as a case study (Tindana, Bull et al. 2012). However, no study has specifically looked at the ethical issues arising from sample export, storage and future uses at Navrongo.

3.2.2. Kenya, Kilifi District and the KEMRI/Wellcome Trust Research Programme (KWTRP)

Kenya is one of the five independent nations of East Africa. Kenya gained independence from British colonial rule in 1963. It is located in the eastern part of Sub-Saharan Africa and has a population of 38.6 million. Kenya is bordered to the South by Tanzania, to the West by Uganda and the North by Sudan, Ethiopia and Somalia.

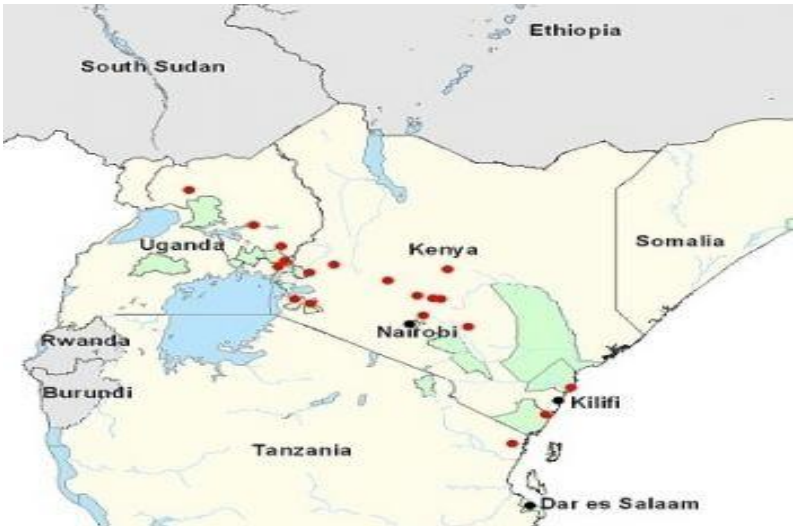

Figure 3: Maps of Kenya and Kilifi District. Source: http://www.kemri- wellcome.org

The Kenya Medical Research Institute (KEMRI) is a parastatal organisation under the Kenyan Ministry of Public Health and Sanitation (MoPHS) and is the largest governmental research institution in Kenya. It was established in 1979 with the mandate – among others – to carry out research in human health in Kenya (www.kemri.org). One of its ten semi-autonomous research centres is located in Kilifi on the Kenyan Coast. Current key health and economic indicators for Kenya are as shown in table 6 below:

	Estimated figures in 2011
Population	41,609,728
Health Indicators	
Neonatal mortality rate/1000 live births	31
Infant mortality rate/1000 live births	52
Under-5 mortality rate/1000 live births	74
Life expectancy at birth (males in years)	58.9
Life expectancy at birth (females in years)	60.1
Economic Indicators	
Income Level	Low Income
Gross Domestic Product	33.36 Billion
GDP growth	4.3%
People living below the poverty line	50%
Research and Development Budget	0.3%

Table 6: Key national health and economic indicators: Kenya (KNBS, 2012; World Bank 2012).

Kilifi district

Kilifi district is situated 60km north of Mombasa. The district covers an estimated area of 891 km with a population of about 260,000 (Scott, Bauni et al. 2012). Residents are mainly Mijikenda, with the main tribes as Giriama, Chonyi and Kauma. It has been described as one of the poorest districts in Kenya with low levels of literacy (Molyneux, Peshu et al. 2004). The majority of the population in this district depend on subsistence farming and the literacy rate is estimated at 69%. The district is served by one District hospital, one health centre, 12 dispensaries and 23 private clinics. The KEMRI Wellcome Trust Research Programme is the main research institution and largest employer in Kilifi district. Table 7 presents an overview of current health indicators for the population under the demographic and health surveillance in the Kilifi district.

	Estimated figures in 2011
Population	261,191
Health Indicators	
Neonatal mortality rate/1000 live births	17.1
Infant mortality rate/1000 live births	32.1
Under-5 mortality rate/1000 live births	41.0
Life expectancy at birth (males in years)	69.5
Life expectancy at birth (females in years)	75.4

(Source: Scott et al 2012)

Table 7: Key health indicators: Kilifi district

The KEMRI Wellcome Trust Research programme

The KEMRI Wellcome Trust Research Programme (KWTRP) is physically located in two sites in Kenya: the capital city Nairobi and Kilifi district on the Kenyan Coast. Kilifi is the programme's main base. In Kilifi, the programme is part of the Centre for Geographic Research Medicine, Coast; which is one of the largest of the ten research centres of the Kenya Medical research Institute (KEMRI).

The KWTRP was established in 1989 as a partnership between the Kenyan Government, KEMRI and the UK Wellcome Trust (www.kemri-wellcome.org/home). In 2012, the programme was involved in over 80 international research collaborations, with the research agenda falling under five major disciplines: Clinical sciences; Epidemiology and Demography; Pathogen Biology, Public Health, and Health Systems, Social and Behavioural Research (HSSR). KWTRP had a staff strength of about 800 in 2012 across both the Kilifi and Nairobi sites, of whom, 108 were scientific staff (90 Kenyans and 18 expatriates). The KWTRP receives 70% of its core funding, and a large proportion of its additional funds, from the UK Wellcome Trust (www.kemri-wellcome.org/research).

Figure 4: Picture of the main building of the KWTRP

Similar to the NHRC in Ghana, the KWTRP runs a demographic and health surveillance system (HDSS) and is a member of the INDEPTH network (Bangha, Diagne et al. 2010). This system was first set up as a longitudinal clinical surveillance in the 1990s to evaluate the impact of insecticide-treated bednets on malaria morbidity and mortality (Nevill, Some et al. 1996; Scott, Bauni et al. 2012).

Since then, this platform has provided a sampling frame for most of the biomedical research projects within the KWTRP and also functions as a demographic surveillance system (Scott, Bauni et al. 2012).

Empirical and practical ethics projects in Kilifi

A key feature of the KWTRP's research activities is its comprehensive programme-wide and study-specific community engagement practices, which have been studied, described and discussed in detail elsewhere (Marsh, Kamuya et al. 2008; Marsh, Kamuya et al. 2010; Boga, Davies et al. 2011; Marsh, Kamuya et al. 2011). Research elements of the community engagement activities fall under the HSSR group mentioned above.

The community engagement research has built on and taken forwards earlier research on informed consent, including understanding (Molyneux, Peshu et al. 2004), and trust (Molyneux, Peshu et al. 2005). Related and more recent research focuses on benefits and payments for research participants (Molyneux, Mulupi et al. 2012), and the role of fieldworkers and implications for ethical practice (Kamuya et al. 2013). While most of these studies have provided a rich description and insight into the local community's views on these issues including challenges with implementing effective guidelines and procedures, no study has specifically explored stakeholders' views on sample export, long-term storage and future uses. This background research and interest provided an excellent opportunity and context to undertake my own empirical research. Unlike Navrongo, where I was more of an insider, I was exploring the issues as an outsider in Kilifi. As I will discuss later, these positions played an important part in the research process, which I now turn to.

3.3. Methodology and research methods

"Not everything that can be counted counts, and not everything that counts can be counted"
Albert Einstein.

To date, most of the empirical studies on the export, storage and reuse of human biological samples have used quantitative survey methods. As discussed in the previous chapter, while these studies have provided some evidence of the range of views, they have not adequately addressed the underlying issues arising from the export and long-term storage of samples in the African context. They have also not helped us to understand the values that are most important to stakeholders. For example, what are the key concerns behind participants' preferences for export of their samples to other Arab countries and not the United States and Europe, as reported in the study by Abou-Zeid et al? (Abou-Zeid, Silverman et al. 2010). Why do researchers not see it necessary to inform research participants about sample export, as shown in Langat's study? How do we reconcile the inconsistencies in Wendler et al's study which shows that while research participants are in favour of sample export without further consent, they still want to be informed about the types of studies exported samples will be used for? Furthermore, the perspectives of other key stakeholders such as researchers, members of ethics committees and lay communities, which are important for determining the best governance mechanisms for sample storage and export, are missing in these published studies, as shown below. Table 8 summarises the few empirical studies I identified in the literature and the methods used.

Study/Country	*Focus of study*	*Method used*	*Target interviewees*	*What is missing*
Langat et al 2005 Kenya	Views on storage, export and reuse of samples	Review of research protocols	Ethics protocols	Perspectives of key stakeholders through qualitative enquiry
Wendler et al 2006/ Uganda	Views on storage and export of samples	Survey/ quantitative	Research participants	Perspectives of researchers and RECs through qualitative enquiry
Abou-zeid et 2010/ Egypt	Views on storage and export of samples	Survey/quantitative	Patients	Perspectives of researchers and RECs through qualitative enquiry
Igbe and Adebamowo 2012/ Nigeria	Perspectives on biobanks	Qualitative interviews	Research participants	Perspectives of researchers, research ethics committees
van Schalkwyk et al 2012/ South Africa	Views on sample storage and re-use	Qualitative interviews	Research participants	Perspectives of researchers, research ethics committees

Table 8: Empirical studies in Africa on Sample Export, Long-Term Storage and Reuses

This gap in the literature calls for a mode of enquiry that will help reveal some insights and meanings that remain unanswered through these survey methods. This research project therefore aimed to combine an exploration of key stakeholders' perspectives of and responses to the ethical issues around the export and long-term storage of human biological samples from Africa with an ethical analysis of the issues informed by this empirical data.

To answer the research questions – listed above – required a qualitative research approach. Although there is no single definition of qualitative research, several authors have discussed the defining characteristics of qualitative research; highlighting its interpretive and naturalistic approach to its subject matter (Butterfield 1989; Ritchie and Spencer 1993; 1994; Denzin and Lincoln 2000; Mays and Pope 2000). Qualitative research also emphasises the importance of context and of understanding the world as socially constructed (Baum 1995; Creswell 2003). This contrasts with quantitative research, which is based on positivism, an epistemological position which assumes that "phenomena can be reduced to their constituent parts, measured and the causal relationships deduced" (Baum 1995).

Table 9 highlights some of the key differences between qualitative and quantitative research highlighted in the literature, although many social scientists have pointed to the important overlaps and complementarities between these two approaches (Pope and Mays 1995; Baum 2004).

	Qualitative Research	**Quantitative research**
Purpose	To illuminate meaning and understanding	To increase knowledge and find universal laws and generalizations
Framing	Concerns understanding phenomena	Focus on behaviour, not context
Rationale for planning	Research planned to investigate phenomena	Research planned to text hypothesis
Techniques	Ethnography, case study, phenomenology	Uses measuring techniques
Rigour	Through discussion of bias and constraints	Statistical analysis and techniques or establishing validity and reliability
Evaluation	Evaluated by questions and related to meanings and understanding	Evaluated by questions referring to reliability and duplication

Table 9: Qualitative and Quantitative approaches to social research

A qualitative approach emphasises qualities of entities – the processes and meanings that occur naturally. "it studies phenomena in the environments in which they naturally occur and uses social actors' meanings to understand the studied phenomena" (Denzin and Lincoln 2000, p3).

In order to explore in depth the range of key stakeholders' perspectives of sample export, storage and future uses in the context of international research collaborations, I adopted a primarily interpretive framework to my qualitative work. In this approach,

> "individuals seek understanding of the world in which they live and work. They develop subjective meanings of their experiences –meanings directed towards certain objects or things. These meanings are varied and multiple, leading the researcher to look for the complexity of views rather than narrow meanings into a few categories or ideas. The goal of research, then, is to rely as much as possible on the participants' views of the situation" (Creswell 2003, p9).

Using this approach encouraged me in my project to do what Bryman refers to as "seeing through the eyes of the people" I was studying (Bryman 2007), that is, aim to get a deeper understanding of what the real issues are from those who experience and are affected by these research practices. However, my research also had a very practical goal of identifying what needs to be put in place to address the practical ethical challenges identified. Drawing insights from Creswell's interpretation of pragmatism (Creswell 2003; Creswell 2007), I adopted a pragmatic approach to address my research questions. In this approach individual researchers have a "freedom of choice and are free to choose the methods, techniques, and procedures of research that best meet their needs and purposes" (Creswell 2013, p28). These two perspectives influenced my methods (reviews, interviews, observations) and analytical strategy, as described in greater detail below.

3.4. The Research Process

Fieldwork for this project was carried out in two phases; *a scoping visit* to each of the research sites and a *data collection* and analysis phase.

3.4.1. Phase One: Scoping visits to research sites

Phase 1 of this project involved two scoping visits; first to Kilifi, Kenya in March 2010 and the second to Navrongo, Ghana in May 2010. These visits provided the opportunity to engage with the host research institutions and to collect important contextual information for the description of the project and on the approach to data collection. These initial field visits gave me the opportunity to better understand the structure of the local community, and the biomedical research projects taking place at these sites, particularly in Kilifi, which I was less familiar with. It served as a form of engagement process prior to the actual commencement of my research project. I also used the visits to identify potential research projects to target for the interviews and key informants who would speak to the issues.

The researchers I interacted with reaffirmed the importance of carrying out the proposed research and made suggestions to further strengthen the project such as reconsidering appropriate ways of eliciting the views of community representatives and the practical challenges and concerns around interviewing biomedical research participants. There were also suggestions to include questions around pathogen samples that may be extracted from human biological samples.

3.4.2. Selection of key stakeholders for the interviews

The potential interviewees were purposively selected using the following criteria (Ritchie and Spencer 1993; Mays and Pope 1995). Five categories of stakeholders were targeted: 1. Research scientists who design the research projects and their assistants; 2. fieldworkers who obtain consent and collect samples, 3. Cross-study key informants such as laboratory staff who manage the samples, 4. Research ethics committees who review research projects and 5. Community representatives to provide community views on the issues.

1. *Research scientists and research assistants:* Three main research projects were purposively selected from the list of all active studies to ensure that there was: a) some similarity and therefore comparability across the two sites, and b) that there was as much diversity as possible in the studies within each site, so that as wide a range of project types as possible was included. These projects were: 1. the MalariaGEN project, a genomic study on susceptibility to malaria (MalariaGEN 2008) 2. the Rotavirus/RSV projects (Armah, Hoshino et al. 2010) and 3. a Cerebrospinal/pneumococcal vaccine trial. These projects involve international collaborations and the collection, export and storage of samples. The principal investigators and other key research staff (co-investigators, research assistants) were purposively selected for interview.

2. *Fieldworkers* play an important role in the research process. They are typically members of the local community and are generally responsible for recruiting research participants (including obtaining consent and collecting samples) and for conducting follow-ups during the course of research (Kamuya, Theobald et al. 2013). They are therefore an important interface between the research institution and the local community and their views about the ethical issues arising in practice were deemed important. I was therefore careful to include a range of fieldworkers in my sample; given potentially invaluable insights.

3. *Cross-study key informants:* During the initial interviews with research scientists, it became apparent that many of the issues raised were not limited to individual research projects but rather related to the general practice of sample management at the institutional level. There was therefore the need to identify other key research actors within the institution who would provide insights into how samples are handled locally. The Directors of the two institutions and the laboratory managers were thus approached for interviews. In Kilifi, through discussions with my supervisor and insights from the first sets of interviews, I also interviewed the Head of Clinical Trials, the Head of Training, the Community Liaison Officer and a member of Consent and Capacity Committee (CCC).

4. *Research ethics committees*: Given that the research questions in this project arose from concerns in the review process (see Chapter 1, 1.2), I held interviews with members of the RECs in both institutions. I wanted to understand their views on how wide-spread concerns about approvals for sample export and storage are and how decisions about what counts as ethical practice are made. All members of the NHRC institutional review board (IRB) and the KEMRI ethics review committee (ERC) in Nairobi were selected for interview. The assistant ERC administrator in Nairobi facilitated the initial contacts with the KEMRI REC members.

5. *Community representatives;* One of the objectives of this project was to elicit local communities' views on research involving human samples. This meant interviewing members of the community who are informed and have experienced these research practices. Initially, research participants themselves were targeted but following discussions with the principal investigators of the projects, concerns were raised about how informed participants are, the sensitive nature of sample export and the potential for interviews to create unnecessary tensions and anxieties for the participants. A decision was therefore made to speak to a sample of community representatives. In Navrongo, a group of assemblymen (who are typically elected by the local community and a traditional chief who was also a member of the IRB) were purposively selected for the interviews. In Kilifi, given the wide range of perspectives that were already included in the study, including the opportunity to interview the institution's community facilitators, the plan was to conduct these interviews with the KEMRI community representatives (KCRs). The intention had been in Kilifi to interview KCRs last of all, and to focus on the assumptions or issues raised in interviews with other stakeholders (for example about what the biggest local concerns might be about archiving or export). However, at the end of the interviews with the fieldworkers and community facilitators, I decided in consultation with my supervisors, that I had obtained a rich enough range of data on a range of actors' perspectives, with valuable insights into community views from fieldworkers, and that interviews with the KCRs were no longer necessary for this particular study.

3.4.3. Phase Two: Data collection using qualitative research methods

Qualitative research typically uses multiple methods such as interviews with key informants, observation of a social phenomenon and documentation (Ritchie and Spencer 1993). The empirical research for this project involved three main methods; document review, semi-structured interviews, focus group discussions and observations. Known as data triangulation, the use of these multiple methods aims at enhancing the validity and reliability of the research findings (Breitmayer, Ayres et al. 1993; Adami and Kiger 2005).

Document review: I conducted a review of existing guidelines, institutional policies on sample export, storage and future uses as well as consent forms from current and past projects. The aim of this review was to understand the extent to which sample export, storage and future uses are accounted for in institutional policies and whether information on these research practices are featured in consent processes. My analysis of the documents also helped frame the questions for the interviews. For example the presence or absence of information about sample export and storage in consent forms led me to ask further questions on the relevance of this information for consent to be valid.

Semi-structured interviews: These interviews were aimed at soliciting the views and perceptions of key stakeholders on the practical ethical issues arising from the collection, export and use of human biological samples. Guided by the objectives of this research, a semi-structured interview guide was developed for each of the stakeholder groups. The guide was piloted with five researchers during my scoping visit to Navrongo. Although the interview guides were developed to cover the main themes of the research, the actual interviews and discussions were responsive and sometimes ranged beyond these. The themes explored in these interviews included understanding and perceptions of guidelines for long-term storage and export of samples, rationales for long-term storage and export of samples, perceptions of the

importance of human tissues to community members, risks/benefits of long-term storage and exporting tissues, and recommendations for change in guidelines and practice. Follow-up questions depended on the interviewees' responses to earlier questions. As is typical of qualitative designs, the tools were used flexibly, allowing the flow of the interview to be guided by the responses of the interviewees, although at the end, it was ensured that most of the questions on the guide were discussed.

Focus group discussions: A focus group is defined as an in-depth, open-ended group discussion which can last for 1-2 hours (Burgess and Bryman 1999). It is used to explore a specific set of issues on a predefined and limited topic. Such groups typically consist of between five and eight participants and a facilitator. This method was deemed appropriate for soliciting host communities' collective views about sample export, storage and future uses. This method was useful for exploring common perceptions, experiences and understandings of these research practices through the eyes and experiences of fieldworkers, community facilitators and community representatives.

Observations: The purpose of observation in this research was to corroborate and expand on the data obtained through the semi-structured interviews. This was particularly important in the Kilifi context, which I was less familiar with. The five weeks I stayed in Kilifi enabled me to observe the way the institution works, interact with key staff and also understand the institution's broader approach to consent, community engagement and capacity building. Within the five weeks, several specific activities included the following:

- I observed a scientific coordinating committee review meeting, which reviews the scientific merits of research proposals. This process was particularly valuable as it demonstrated the institution's negotiating power in research collaborations.

- I also took a tour of the institutions' laboratory to get firsthand information on how samples are stored and the existing capacity of the institution. It was also an opportunity to verify some of data highlighted in the semi-structured interviews about laboratory tours that are offered to community representatives as part of the KWTRP's community engagement strategy.
- The ethics review committee in Nairobi declined my request to observe their review meeting due to issues around the confidentiality of research projects.

Phase 2 of the empirical research project: The data collection stage

Data Collection in Kilifi, Kenya

Data collection in Kenya was carried out over a period of five weeks from 18th October 2010 to 18th November 2010. This involved conducting interviews, document review, observing a Scientific Coordinating Committee (SCC) meeting and a tour of the research laboratory in Kilifi. I obtained and reviewed key documents that were relevant to my project; the KEMRI Scientific Steering Committee (SSC) Guidelines for exportation and storage of human blood and other biological samples for research, KEMRI research guidelines, the consent form template and the KEMRI's standard operating procedures for research and related activities.

I conducted 25 semi-structured face-to-face interviews with researchers and cross-study participants (see table below), at the KWTRP in Kilifi and with members of the KEMRI ethics review committee in Nairobi. I also conducted 3 focus group discussions with community facilitators and fieldworkers in Kilifi. The list of interviewees and the dates the interviews were conducted are as shown in Appendix 4.

Research Participants	*Data collection methods*	*Number of interviews/ group discussions*
Researchers/Research assistants	Semi-structured interviews	12 (8 men and 4 women)
Cross study key informants (Clinical trials coordinator, lab manager, community liaison, training coordinator and)	Semi-structured interviews	5 (4 men, 1 woman)
Community facilitators	Focus group discussions	1 (5 men and 1 woman)
Fieldworkers	Focus groups discussions	2 Groups
Ethics committee	Semi-structured interviews	8 (5 men and 3 women)
Total number of interviews		**28 (25 IDIs and 3 FGDs)**

Table 10: Study sample in Kilifi and Nairobi, Kenya

Data Collection in Navrongo, Ghana

From 14th December 2010 to 2nd February 2011, I conducted interviews in Ghana with scientists, members of the NHRC institutional review board (IRB), and fieldworkers of three main research projects. Mirroring those in Kilifi, the main methods for this research were document review, in depth interviews and focus group discussions.

19 face-to-face semi-structured interviews and 3 focus group discussions were conducted in Ghana. These included 8 interviews with study-specific investigators, 3 with research assistants, 6 interviews with members of the NHRC Institutional review board (IRB), 1 with the Director of NHRC and 1 with a community representative. The group discussions were with fieldworkers of The MalariaGEN project and Meningitis projects and 1 with community representatives. The list with the characteristics of the Navrongo interviewees is as shown in Appendix 4b.

Research Participants	*Data collection methods*	*Number of interviews/ group discussions*
Researchers/Research Assistants	Semi-structured interviews	12 (10 men and 2 women)
Community representatives	Semi-structured interview Focus group discussions	1(man) 1 group (6 men)
Fieldworkers	Focus groups discussions	2 Groups
Research Ethics committee	Semi-structured interviews	6 (4 men and 2 women)
Total number of interviews		22 (19 IDIs and 3 FGDs)

Table 11: Study sample in Navrongo

The consent forms, draft interview guide and a lay summary of the project were sent in advance to all interviewees to facilitate the actual interviews and discussions. Written consent was obtained from each of the participants before each interview. The individual interviews lasted between 45 minutes and 1.25 hours while the focus group discussions with the community facilitators and fieldworkers lasted for approximately 2 hours. All the interviews were conducted in English except group discussions with the community representatives in Navrongo which were conducted in the local language (Kasem). All interviews were audio-recorded, except with two interviewees who declined to be audio-recorded (I researcher in Kilifi and 1 member of the ethics committee in Nairobi). Detailed field notes were also taken during the interviews to facilitate the data analysis and write-up.

A total of 44 interviews (25 in Kilifi and 19 in Navrongo) and six focus group discussions (3 in Kilifi and 3 in Navrongo) were conducted.

3.5. Data Management and Analysis

Regarding my analytical strategy, I followed the steps used across many different qualitative analytical traditions. I began by familiarising myself with the data set, making summaries and notes of recurring issues and themes or surprising findings. Then, I developed themes based on a combination of my research questions, the key points raised in the literature, the questions in my research tools and the points that emerged ‘in vivo’, or through the interviews and

observations. Thus, data analysis was an iterative process during the course of the project. Following the five pilot interviews conducted with researchers in Navrongo in May 2010, I conducted a preliminary exploratory analysis (Miles and Huberman 1994). This involved systematic coding, that is, labelling chucks of interview extracts with words and phrases that capture the meaning of the data, using OpenCode software. A sample of these coded transcripts were shared and discussed with my supervisors in Oxford focusing on the appropriateness of my selected codes and emergent themes as well as possible codes I had missed. This initial process of data analysis was critical in shaping and situating later data collection stages in Kilifi in October/November 2010 and in Navrongo in December/January 2011.

During the main data collection stage, I developed weekly progress reports summarising the main issues highlighted in the interviews conducted during the week based on my field notes and reflections of the research process. These were discussed with my supervisors, in person with Dr. Sassy Molyneux in Kilifi and over the phone with Prof. Mike Parker and Dr. Susan Bull in Oxford. This process was to ensure transparency and rigour in the research process (Mays and Pope 1995). The discussion was also important in reframing some of the questions and for planning subsequent interviews. Tables summarising the key points in these interviews were also developed to facilitate the writing up at a later stage. Once all the scheduled interviews were completed for both study sites, further data analysis was carried out in Oxford over a period of six months starting in March 2011.

3.5.1. Data analysis

All the forty-eight (48) audio-recorded individual interviews and six (6) focus group discussions were transcribed by trained transcribers in Oxford, Kilifi and Navrongo. Two (2) of the interviews which were not audio-recorded were summarized into a table, highlighting the key points raised by the interviewees.

I verified all of the transcribed interviews through listening to the audiotapes and comparing these with transcripts to check for corrections and filling in any gaps. This repeated process enabled me to familiarize myself with the data and to make notes of important themes arising from the interviews. The verified transcripts were then imported into Nvivo version 8 to facilitate the analysis process.

The analysis first focused on the Navrongo data set. Each transcript was read thoroughly (line by line) and systematically coded. The codes used were guided by the objectives of the study and mostly selected directly from the interview transcripts. Some codes were descriptive such as *types of samples, destination of exported samples, types of study/project, ethics review* while others were conceptual such as. *consent, fairness, trust, luck, agreements, integrity, (in Nvivo, these open codes are known as the free nodes).* The various codes were constantly reviewed and compared and similar codes were further collated into various categories (organised hierarchically under tree nodes in Nvivo) such as. *nature of research collaborations, informed consent, fairness/justice, governance, capacity building and trust relationships*.

This *thematic* analysis focused on an in-depth description and conceptual interpretation of the entire data set (Boyatzis 1998; Fereday and Mair-Cochrane 2006). Using both deductive and inductive analytic strategies, I paid particular attention to the a prior ethical issues in storage and export of samples highlighted in the literature, and new or different issues arising from the data while looking out for patterns across the entire data set. A list of themes were generated and circulated to my supervisors, together with a sample of the interview transcripts, who independently reviewed them and gave comments and suggestions for further analysis. As the data analysis progressed, I printed a coding summary report from Nvivo 8 (QSR 2009) and reviewed the codes and categories, deleted those I found inappropriate or vague, renamed some and reapplied these to subsequent transcripts.

Following further discussions with my supervisors, the Kilifi data were analysed using the same coding scheme as the Navrongo data but also looking out for new issues specific to Kilifi and similarities and differences between Kilifi and Navrongo. I referred to some of the coded transcripts from Navrongo to shed light on what could be accounting for the differences between the two research institutions. For example, I observed that although both institutions were established around the same period (in 1989); there were striking differences in the growth of these institutions in terms of personnel and laboratory capacity to conduct analysis locally. Furthermore, although most of the concerns and challenges, such as fears and anxieties around sample export, were similar across the two sites, Kilifi was a step ahead in terms of implementing strategies for addressing them, for example through demystifying the uses of blood samples by providing a tour of the research laboratories.

Reflective notes (memos) about some of the interesting issues emerging from the data were also written alongside the coding process. These were my reflections on what the interviews were highlighting, especially about what was my sense of what my interviewees considered to be most important issues that were of concern to them. Efforts were also made to highlight variations across the various stakeholder interviews. Similarities and differences in perspectives from the various stakeholders were consciously identified. These reflective notes also provided a structure for the writing up the findings report for the entire data set.

Ethical analysis: While my research project is primarily empirically driven, I do in my final chapter, move from developing an account of what *is* to say something about what *ought* to be the case. There is currently little consensus in the literature on integrating empirical data with ethical analysis, thus moving from the empirical account of my data to a normative claim about how things ought to be, proved a challenge.

Given the exploratory nature of the research topic, my project is empirically driven, that is the recommendations and normative claims I make at the end are largely grounded in critical reflection on the issues that stakeholders have raised as most important and the arguments they make for possible solutions. Apart from the practical recommendations made by the various stakeholders, for capacity building and ethics guidelines, there were consistent calls for trust-building in research collaborations at the micro and the macro-levels. Taking this forward, I critically analysed stakeholders' arguments for taking virtues such as trustworthiness seriously against generally accepted principles of ethics and ethical theories. I then developed my own arguments for what should count as good ethical practice in the export, storage and future uses of human biological samples. This is discussed in Chapter 8 of the thesis.

3.5.2. Presentation of the results and development of thesis structure

To facilitate the write-up, I developed a report on the research findings for each of the two study sites summarising the main themes drawn from the data. These reports were structured to address the key objectives of the research, which can be grouped under three main categories, (Ritchie and Spencer 1994):

- *Contextual:* Identify the form and nature of international research collaborations and describe current practices in sample collection, export and storage.
- *Diagnostic:* Understand the key ethical issues arising in practice and the views, beliefs and concerns of key stakeholders including consent issues, fairness and justice issues.
- *Strategic:* Identify new theories, strategies, policies and actions to address the ethical issues arising in practice, and stakeholders' arguments /recommendations for what forms of governance ought to be put in place.

Following the completion of the analysis process, the two research reports were developed into four main empirical chapters (4-7).

- In Chapter 4, I present data on the nature of research collaborations at the KWTRP and NHRC, current practices in sample collection, storage, export and plans for their future uses. I also discuss existing policies and governance mechanisms at the institutions based on the document reviews and interviews.
- Chapter 5 discusses the issues arising from the research institutions' interactions with the local community, which I refer to as micro-level issues
- Chapter 6 focuses on those arising from the institutions' interactions with external collaborating institutions. I refer to these as macro-level issues.
- Chapter 7 addresses stakeholders' perspectives and recommendations on the governance of sample export and storage and their future uses.
- Chapter 8. Here, I critically reflect on the analysis in chapters 4-7 and explore their implications for good ethical practice.

3. 6. Ethical considerations

Ethics approvals: This research was reviewed and approved by the following ethics committees: the Oxford Tropical Research Ethics Committee (Ref: OXTREC 11.10), the Navrongo Health Research Centre Institutional Review Board (Ref: NHRCIRB092) and the KEMRI/National Ethical Review Committee (Ref: SCC 1818). In addition, it was reviewed and approved by the KEMRI Scientific Steering Committee (SSC 1818) and the Kilifi/Wellcome Trust Scientific Coordinating Committee (SCC).

Written consent was obtained from all the stakeholders I interviewed. The consent forms, with an email introducing myself, were initially sent to all potential interviewees, except the community representatives and fieldworkers.

The form spelt out the purpose of the research, why research is important, how long the interview will take and anticipated outcomes for improving research practice. Only one REC member in Nairobi declined to be interviewed. In Navrongo, I had an interesting discussion with some of the principal investigators who indicated that they could not decline their consent because of the working relationship I had with them. Even when I assured them that I would not take any offence if they refused participation, one jokingly added that *'I know you need this information for your PhD so how can I refuse?* This highlights the influence of relationships in consent processes, a theme which is discussed later in the thesis.

I also requested for permission to audio-tape the interviews. Two of the stakeholders in Kenya declined for their interviews to be audio-taped. One explained that he did not feel comfortable having his voice, which he referred to as a type of 'sample' being stored in a recorder and transported to Oxford for analysis. This was not anticipated and it goes to highlight the need, as a researcher, to be prepared to address respondents' concerns about the research process, and the relevance beyond biological samples of some of the issues raised in this thesis.

Confidentiality: All participants were assured of confidentiality. Thus, in the presentation of the data, verbatim quotes have been anonymised and assigned unique code numbers – odd numbers representing male respondents and even numbers for females, for example NREC07 represents a male member of the ethics review committee in Navrongo. The audio-tapes are also currently stored securely in locked cabinets with access limited to me and my supervisors. They are currently stored indefinitely but a decision would be made at the end of my DPhil studies on how and when they should be destroyed.

Feedback of findings to stakeholders: In November 2012, I travelled back to Navrongo, Ghana to present findings of my research to the stakeholders I interviewed. This process was very useful as it allowed me to discuss the findings of my research and also to test the practicality of

feeding back research findings to participants. Present at this session were senior staff of the Navrongo Health Research Centre and some members of the NHRC IRB. The discussions suggested that the ethical challenges I had identified through my research were still relevant and needed practical solutions. Staff of NHRC requested that I present the Centre with a set of practical recommendations on how to address the key issues, particularly on how other research institutions have handled these issues to inform the establishment of institutional guidelines for sample storage, sample export and data-sharing. A formal dissemination session is planned for the Kilifi research site in 2013.

Reflexivity: Acknowledging my position and some methodological challenges

One of the key aspects of qualitative research is reflexivity, broadly defined as the analytic attention to the researcher's role in the research process and an acknowledgment of the impact this has on the meaning and context of the experience under investigation (Gouldner 1971; Horsburgh 2003). Reflexivity is generally recognised as an important way of enhancing credibility in qualitative research (Horsburgh 2003; Cohen and Crabtree 2008). As I described in Chapter 1 (1.2), I have worked in the Navrongo research context and been a member of the NHRC REC for over ten years. I therefore had personal experiences with the ethical challenges I was exploring in this research. Total objectivity was therefore not achievable during the research process, particularly in the Navrongo context. However, this prior experience and knowledge of the context served as strength and a challenge to the research process.

A key strength is that knowing the context allowed me to probe further during my interviews and to present interviewees with alternative views. The aim here was to arrive at carefully thought-through recommendations for addressing the issues arising in practice and to add richness to the data.

It also facilitated my analysis of the strengths and arguments respondents made on practical recommendations for addressing the ethical challenges. However, I made a conscious effort to not allow my prior assumptions to influence the research process. This meant detaching or putting aside my REC role during the research process, what some authors have referred to as 'bracketing' (Ahern 1999). Constant feedback and discussions with my supervisors in-between the data collection stage also assisted in sustaining some objectivity in the research process and ensuring that the actual experiences and perceptions of the stakeholders were reflected in the analysis and interpretation of the data.

My previous REC role also posed a number of challenges. First, it was important to win the trust of the stakeholders, particularly researchers and laboratory mangers and to assure them that my research was not aimed at identifying loopholes or 'unethical' practices in their research. This required approaching the interview process as 'a reciprocal sharing of knowledge' where I considered the stakeholders I interviewed as collaborators in the research project, working together to identify and address the ethical challenges arising in practice (Bergum 2002; Evans et al 2004). This approach allowed the stakeholders to open up and discuss their views and sometimes personal experiences with me.

I also gathered from some of the interviews I conducted in Navrongo, particularly those with researchers and fieldworkers that, they saw my project as an opportunity for them to 'let out' the struggles and grievances they had between and within the research teams. While this facilitated the research process by providing more data, it also meant that there was an expectation that these grievances would be taken forward with the management of the Centre. I handled this issue by reassuring the interviewees that although this project was primarily an academic exercise, recommendations from the overall analysis of the research will be shared with the management and staff of the institution to improve practice.

3.7. Conclusions

The aim of this research was to contribute to an empirically-informed understanding of the ethical issues arising from sample export, storage and future uses in the context of international collaborative research. Specifically, I was interested in getting evidence and developing a better understanding of stakeholders' perspectives of and responses to the key ethical issues arising in practice and their proposed recommendations for what should count as best ethical practice. To do this required a qualitative research strategy that allowed people who are informed and/or affected by these issues to share their experiences and propose practical solutions. In this chapter, I have described the research design employed in this research and highlighted the fact that the research strategy I used falls within the remit of empirical ethics. I combined the collection and analysis of empirical data through qualitative research with normative analysis to inform a number of recommendations for best practice.

As I discussed in Chapter 1, my research is a form of 'empirical bioethics' a research strategy that aims to combine the collection and analysis of empirical data – in my case through qualitative research – with ethical analysis. Like many other scholars I believe that empirical research has an important role in normative analysis. Firstly, the ethical questions I am interested in are related to practical problems in research practice; the collection, storage, export and use of samples. Thus it was important to understand the current and changing practices around these research practices, the actual ethical issues arising in practice and the views, beliefs and concerns of key stakeholders who are informed and affected by these issues such as researchers, fieldworkers, members of ethics committees and community representatives.

It was also important to elicit these stakeholders' views on what ought to be done to address the issues arising in practice. However, I also recognised that it was not enough to just describe stakeholders' views about the ethical dimensions of these practices and what they propose as solutions, but also important to attempt to analyse the empirical data with an eye to their relevance for best practices.

In the next four chapters, I will present and discuss my analysis of this empirical data.

Chapter 4: Current and changing practices in sample use, storage and export

4.1. Introduction

In Chapter 2, I highlighted the tensions around the export and potential future uses of human biological samples in international research collaborations. While there is a growing literature in High-Income-Countries (HICs) on participants' perspectives regarding the use of their samples, little is known about the perspectives of stakeholders in Sub-Saharan Africa (SSA). Similarly, the literature points to a lack of clear guidance on the best way to address the ethical issues arising in practice. This background suggested the need for an empirical study to explore stakeholders' perspective on and responses to the ethical issues arising from sample export, storage and future uses.

In this chapter, I report on findings of this research, providing an overview of current and changing practices in sample use, export and long-term storage at the KEMRI/Wellcome Trust research programme (KWTRP) and the Navrongo Health Research Centre (NHRC). This chapter is contextual and aims at situating the ethical issues – discussed in chapters 5 and 6 – within a specific research context. I present stakeholders' views on the nature of scientific research collaborations, highlighting the types of research projects conducted, how these are initiated and the centrality of human biological samples. I then discuss current practices of sample export and storage, outlining their rationales and destination. The penultimate section of the chapter discusses existing institutional requirements for sample use and export and the gaps identified by the interviewees. The chapter concludes with a general summary discussion.

4.2. The nature of international research collaborations

> "The very existence of the KEMRI/Wellcome trust programme in Kilifi is international in nature" (Kilifi: CSK0I).

As discussed in Chapter 2, most of the well-established health research institutions in SSA including the KWTRP in Kenya and the NHRC in Ghana trace their genesis to international research collaborations. Both institutions came into existence in 1989. The KWTRP was an agreement between the University of Oxford, the UK Wellcome Trust and the government of Kenya, while the NHRC started as a field site for a Vitamin A Supplementation trial (VAST), a research collaboration between the London School of Hygiene and Tropical Medicine and the Ghana Ministry of Health. The majority of the research projects carried out in these institutions have involved major research institutions in the United States, United Kingdom and other counties in Europe. Some projects involve other African research institutions in Tanzania, Mali and South Africa.

Types of collaborative research projects conducted

In line with the significant growth of research collaborations across SSA, the number of collaborative projects conducted by KWTRP and NHRC has also increased. For example, six clinical trials were conducted in Navrongo between 2000 and 2010, as compared in four in 1990-2000. These involve multi-centre trials on Malaria, HIV, Human Rotavirus and other infectious diseases; basic science research, epidemiology, human genetics/genomics, pathogen genomics, and clinical (drugs/vaccine) trials. Both institutions are also part of research consortia such as the Malaria Epidemiology Network (MalariaGEN). KWTRP's research activities are bigger and broader than those of Navrongo and also involve preclinical studies.

KPTRP is also involved in large cohort studies on HIV funded by the International AIDs Vaccine Initiative (AIVI), and in GlaxoSmithKline (GSK)'s phase 3 RTSS candidate malaria vaccine trial, involving eleven sites in three countries (Agnandji, Lell et al. 2012).

As would be expected, most of these projects are externally funded although the RECs in Nairobi and Navrongo reported that they do review locally funded research projects such as health systems research and social science projects.

> "The nature of research done in KEMRI is always almost 80% of international collaborations and 20% which are locally driven or with funding from the government or research funding institutions in the country. But the majority of these, the research taking place in Kenya is of an international or collaboration or consortia nature" (Nairobi: ERC00).

My interviews also suggest an increasing trend toward research collaborations as a means of attracting competitive research funding:

> "Virtually all of them are with international collaborators because currently....to get funding for the kind of studies we undertake we have to be working with collaborators in a kind of consortia" (Navrongo: RES17).

Rationales for scientific research collaborations

There are several compelling reasons for establishing scientific research collaborations. According to researchers I interviewed, a key motive is the desire to bring together the strengths of various partners to achieve common research goals. The main strengths of these African research institutions are their field sites and 'disease' populations which provide easy access to research participants, communities and samples. As discussed in Chapter 3 (p47), both Navrongo and Kilifi have longitudinal health and demographic surveillance systems (HDSS) which facilitate the conduct of clinical trials. The HDSS database maintains vital information on all individuals and households in the district which facilitates an optimal selection of participants for randomized trials, easy tracking of study subjects for samples and data and the follow-up of study participants.

External collaborators, on the other hand, often have the resources such as funds and more advanced equipment needed to facilitate sample and data analysis, as suggested below:

> "We have the field site, we are good at field operations and we have the scientists who can contribute to the science that is rolled out. For them [external collaborators], they have more sophisticated labs and they are also into the sciences. So once we all bring our strengths onto the table; it is not like master servant relationship but a discussion of equals" (Navrongo: RES17).

> "They [external collaborators] also had the technology that we wanted to transfer, so there were reasons of mutual interest, of technology transfer, and a feeling of being part of a network organisation" (Kilifi: RES07).

The above quotes also underscore African researchers' expectations of equal partnership based on the importance of each partner's contributions to achieve the research objectives. But this raises questions about what counts as equal partnership and how this can be achieved in the real sense. I classify these as macro-level issues, discussed later in Chapter 6.

Another motivation for involvement in scientific collaborations is the opportunity for African researchers to participate in cutting-edge science that has public health relevance to the local population. As explained by this researcher in Navrongo:

> "In service delivery, that is the mantra now. You need evidence to be able to come out with policies that really work but what has been a major challenge in our environment has been that, a lot of the policies that we tend to formulate have come from research that has been done elsewhere and not actually based on research that has been done in-country or on the continent and basically that has been my motivation" (Navrongo: RES21).

Interviewees in Kilifi shared a similar view:

> "As a program we want to be seen that we remain objective to our cause and not necessarily attracted by money or resources that might come from 3rd parties, so I think the important thing is if the collaboration is coming up, the context that it is coming has to be centred on solving and addressing the public health need of Kenya" (Kilifi: CSKI01).

Consequently, most of the scientific research projects at KWTRP and NHRC focus on malaria, pneumonia, diarrhoeal diseases, and HIV/AIDs, which are major diseases affecting the local population.

Research collaborations also provide opportunities for building/strengthening local personnel and infrastructure capacity. In Kilifi for example, KWTRP has developed a cadre of local Kenyan scientists who are leading big scientific research projects and being recognised internationally[11]. According to researchers, this has been achieved through efforts by the institution to focus on local capacity-strengthening:

> "... you have seen the facilities that are being built over the last twenty years,.....we have tried very hard to build up capacity to do as much of the work as possible here" (Kilifi: RES13).

Although NHRC researchers highlighted their struggles with strengthening local capacity, they suggested that the institution can also boast of a team of scientists (epidemiologists, clinicians, entomologists, pharmacologists, microbiologists, statisticians) who are currently leading the scientific agenda of the institution.

What counts as a good scientific research collaboration?

According to interviewees, scientific research collaborations are either initiated at the institutional level or by individual investigators, through their interactions with people at conferences, networking meetings and/or personal contacts. Regardless of how these collaborations are formed, researchers' accounts suggest there are key guiding principles underpinning these collaborations. Interestingly, the principles discussed here are largely shared across Kilifi and Navrongo. As a researcher in Kilifi explains:

> "I think there has been a diversity of experience, we cherish very much collaborations that are based on trust and mutual respect so collaborations that start from the outside with the collaborators recognizing that we are partners, we need each other to do what we have to do and no one should dictate or override the interest of the other, that I think works very well and so from the start we have that understanding, and it works very well" (Kilifi: RES13, Expatriate).

[11] In 2010, Dr. Abdulsalam Mohamed Noor won the 2009 African Union National Young Scientist Award. Dr. Samuel Kariuki received the 2012 Royal Society Pfizer Award, Vincent Okungu, a Health Economist also won the 2012 Emerging Voices for Global Health (EV4GH) competition.

Researchers perceive *trust*, *mutual respect*, *partnership*, *understanding* and *mutual interest* as fundamental to successful research collaborations. They reported that they are also inclined to collaborate with people they have worked with before and are assured of their track record and reputation:

> "I would say that the collaborations have all gone well in the spirit of science because there is a mutual respect and the issues that we discuss are professional and scientific so there is very little room for grey areas so it is pretty much spelt out what is expected of the collaborator from the onset so that either you are leading the study, you are collecting data, you are helping to analyse it or to run maybe certain samples or certain investigations in the study process so these are usually pretty much spelt out from the onset (Navrongo: RES21).

Some researchers at KWTRP also emphasised that collaborations are often based on the principle of 'meritocracy' (RES13)**.** They expect high quality research proposals which allow local control of the research process, and would often reject agreements that are not favourable. This highlights the importance of having strong local negotiating power:

> "There are examples in which we have declined opportunities for collaboration that have come up for the reason that we were unsure that we were going to be in a sense in control of what was going on ... I think we averted what could have been difficulties amongst collaborations" (Kilifi: RES07, Expatriate).

My observation at a scientific coordinating committee (SCC) meeting in Kilifi confirmed the above assertion. Most researchers attributed KWTRP's negotiating power to several factors including; having core funding from a major international funder, working with the right people, negotiating the key deliverables right from the beginning and having clear agreements on various aspects of the research process including how research samples are managed within the collaboration. These are discussed later in Chapter 6 (p151).

Generally, stakeholders' accounts suggest that how research collaborations are negotiated for and agreed upon from the outset determines the management of research samples. I now turn attention to the central role of human biological samples in collaborative research projects in Kilifi and Navrongo.

4.3. The scientific value of human biological samples

An important feature of the research activities in Kilifi and Navrongo is the use of human biological samples such as blood and its derivatives (serum, DNA). My findings highlight the importance of human biological samples and tissues in scientific research. As illustrated in the quotes below, researchers and RECs reiterated that many research projects would be impossible without access to samples:

> "Because that really is central to their studies, you need samples, you need blood samples, you need urine, you need saliva, you need all these kind of samples to carry out research" (Nairobi: REC11).

> "I think all the clinical trials need to assess some end points and those end points basically involve the taking of biological samples and for the malarial studies, the most important thing that they sought to establish was whether there were malaria parasites so that one was basic microscopy, blood slides were taken which were processed locally (Navrongo: RES11).

Other researchers explained that while it is possible to use alternatives such as tissue culture and mouse models for some research projects; there are limitations and in most cases they cannot find substitutes for human samples. These quotes represent a common view researchers expressed about the nature of *techno-science* and the central role of blood samples.

> "There are certain situations where you can advance science by taking alternative sample types, so like oral fluid as opposed to blood sample but there are questions about the immunology of an infectious disease, particularly cellular immunological work that could not be possible without collecting a blood sample. So certain sciences I think to do with immunology, basic science would quickly meet with limits to moving forward if you couldn't collect a blood sample" (Kilifi: RES07, Expatriate).

> "blood can tell us a lot about their genetic background, it can tell us a lot about the drugs or the products or the medicinal products that we may wish to study and so I think that blood is important because it's sort of getting the human being and opening the map that's one window into the human being that we have" (Kilifi: CSk01).

Although other types of human biological samples are used in research, such as urine and stool, blood is the most common. Respondents suggested that:

> "...blood samples are the easiest samples to get and the reason you need quite a bit of blood is that blood has different components and then you have cells, white blood cells that are harbouring , hopefully the immune response or the answer to the possible immune response that can then be mimicked by a vaccine" (Kilifi: RES05, Expatriate).

> "Yes for blood blots you just take a drop, or a drop of blood for the blots. We also take finger prick samples that we usually will spin for serum or plasma; this is for immunological assay, so we take about 0.5 to 1ml of blood from the finger. For the drug study, for example ...what we are doing there is taking blood blots again because we are looking at a study to determine when somebody has failed and follow up with parasitological analysis and so we collect blood smears" (Navrongo: RES07)

For many of these research projects, samples are mostly collected in the communities and within the research clinics at the district hospitals. These are then transported to the research laboratories for storage and analysis. Although samples have an inherent scientific value, processing, storing and analysing these samples in order to maximize this value comes at a cost; trained personnel and good laboratory infrastructure, such as space, fridges and freezers and efficient electric power supply, are necessary. With the recent advances in science and technology, particularly in molecular biology and genetics, sophisticated analysis techniques such as high throughput genotyping, region specific or whole genome sequencing are possible. However, these techniques are only valuable if samples are properly handled and processed downstream (in the field).

In Kilifi, there were indications in both m*y* own observations and interviewees' accounts of continuing improvements of local laboratory infrastructure and capacity. Consequently, interviewees reported that the institution has the capacity to conduct most (about 80%) of necessary analyses locally. The following quote illustrates a widely held opinion about the institution's ability to be self-reliant:

> "We type for CR1 polymorphism, so probably ten different strong candidate genes that we're specifically interested in. We can do all of that here using our own equipment and having trained staff, lab technicians and doctoral students, post docs to do all of that work. So we do it all here. We can extract the DNA, we do the typing and we do the analysis here….so I mean you've been here obviously, seen the facilities that are being built over the last twenty years, so I think we have tried very hard to build up capacity to do as much of the work as possible here" (Kilifi: RES13).

The story in Navrongo is quite different. Although there have been some efforts to strengthen local capacity, the Centre still lacks some basic laboratory infrastructure to carry out local analysis, such as Polymerase Chain Reaction (PCR)[12] a technique which is currently considered the norm in most laboratories across the world. Despite these differences in capacity, sample export is still practiced across the two research sites for various scientific reasons, which I discuss next.

4.4. Rationale for sample export

In addition to the collection of samples, sample export is also an important aspect of international research collaborations. The REC in Nairobi reported that about 75% of the analysis needed for the clinical trials taking place in Kenya, is conducted in overseas collaborating laboratories. Figures for Ghana could not be established in my interviews. Interviewees gave three main types of reasons for sample export in international research collaborations. Two of these are related to the current lack of local capacity, the third related to the importance of consistent approaches to processing and management for effective analysis.

Lack of local capacity

The first capacity-related reason for sample export was as follows: despite the efforts made over the years (and on-going) to strengthen local research capacity at these research sites, researchers and RECs I interviewed see facilities as inadequate to handle some of the analyses needed for some research projects. This is particularly the case for those that require more sophisticated analysis such as whole genome sequencing and certain antibody assays. This has necessitated the export of samples to other laboratories abroad that have specific capacity in these areas, as the following responses suggest:

[12] This was the case at the time of conducting the interviews in 2010. At the time of writing up this thesis in 2012, the Centre had acquired a PCR and strengthened various aspects of its laboratory infrastructure including a new laboratoty under construction.

> "But when it comes to more high throughput and much higher density typing, like whole genome, genome-wide typing then we don't have the capacity to do that here" (Kilifi: RES13).

> "We don't have all equipment, for example for now in this centre we don't have an immunology lab so most of the immunology activities, immunological analysis, have to be done elsewhere. Similarly the molecular aspect of the work is not done locally and so we have to do it elsewhere" (Navrongo: RES07).

A second capacity-related reason for export is that some research projects require specific analysis that can only be done in a few places in HICs, where such specific expertise exists. In most cases, these technologies are so highly specialized that they are not easily transferable. Indeed, because of their restricted use it is prudent to outsource such work rather than investing in establishing the technology locally, as suggested below:

> "We just don't have the technology and there are extremely specific tests that can only be done at very few centres throughout the world" (Kilifi: CK07).

Requirement for uniformed analysis

The third reason for sample export identified by interviewees is to facilitate uniform analysis, particularly in multicentre trials. Researchers were of the view that such uniform analysis could also minimise errors that are likely to occur if samples are analysed by different people in several different settings:

> ".. ideally we would want it done in one lab for standardization purposes and the reason we're sending it to Belgium is that GSK has a lab where they have standardized this assay so they're able to process the samples. So if you have all the samples done in one lab if there's an error it will be a standard error across all the samples and therefore your results would not be skewed. However, if you do it here and here and here you're not able to say the difference. Maybe there was a small difference in how this assay was done, the equipment, the reagents, just those small things that make a difference in the final result and that is the reason why it's all been done in one place" (Kilifi: RES02).

Although much of the current literature on sample export happens in the context of research consortia focusing on genetic/genomic research, my data suggest that in practice this trend features in other types of research as well for some of the same reasons highlighted above.

While some researchers in Kilifi envisaged that as KWTRP continues to strengthen its local capacity, sample export is becoming increasingly uncommon, and that this trend looks likely to continue, others maintained that advances in science and technology will continue to require analysis necessitating sample export.

Destination of exported samples

Study responses suggested that the destination of exported samples is determined by the nature of the research collaboration and the agreement of the parties involved. Some of these decisions are made at the outset of the project while others are made during the research. Most receiving laboratories are in HICs where the required expertise currently exists:

> "Those laboratories can be in Asia, Africa, Europe or United States but it is always determined by the nature of the collaboration or who the collaborating centres are and where the centres of analysis were predetermined at the beginning of the protocol development. So that determines where the analysis takes place" (Kilifi: REC00).

According to study interviewees, in choosing the destination of exported samples, what really matters is where samples can be analysed in the quickest and cheapest way**.** Some researchers were of the view that in the very near future, scientists would rather send samples to emerging economies such as China because of the technological capacity available in that country.

> Respondent: "And so probably if you looked ten years from now I don't think anyone would be sending samples to Oxford or to the Sanger. Everywhere in the world will be sending the samples to Beijing and waiting for the results to come back from Beijing" (Kilifi: RES013).
>
> Interviewer: Oh really? Why Beijing?
>
> Respondent: "Because that's where they're building the most huge genome resource unit, it's almost a city dedicated to doing genetic typing ... it's a bit odd that people are worried about where the typing gets done, so long as the capacity is there to interpret the information that's a much more important thing than it is to have the capacity to actually do the typing. If I want a full blood count it's entirely political if I build a bio mechanism to do it here or whether I send it to Nairobi to do or whether I can send it to Beijing to have the full blood count done. If I want to get the results back as quickly as possible, the quickest way and the cheapest way possible then to me it doesn't really matter where it's done so long as I get the results" (RES013).

Interviewees' general perception of sample export and its destination and the matters arising from this practice is discussed in more detail in Chapter 6 (p135). In the next section, I discuss stakeholders' perspectives on the rationales for sample storage and future uses.

4.5. Scientific reasons for storing samples

There is a growing recognition of the scientific value of stored human biological samples. Sample storage is therefore a common trend in most research projects in Kilifi and Navrongo. The RECs I interviewed reported that almost every scientific research protocol recently reviewed include requests for long-term sample storage, that is beyond the duration of the current study.

Study responses suggested that a vast majority of the samples collected in the context of research are stored locally. For example, the KWTRP has the capacity to store very large quantities of samples. According to the laboratory manager, samples have been stored since the establishment of the institution over twenty years ago and there are over a million samples currently stored in the laboratories in Kilifi alone.

During my field visit to Kilifi, I was given a tour of the laboratories and observed several huge freezers containing research samples, labelled and dated. Some of these stored samples, mostly blood and its derivatives, were collected in 1990. My estimation is that the KWTRP laboratory facilities are about three times that of NHRC.

Most researchers I interviewed explained that in practice, samples are not deliberately sent abroad for long-term storage. Rather, aliquots of samples may be sent to research labs for specific analysis, as discussed earlier, (see p88). Long-term overseas sample storage could however take place when samples are left over after the initial analysis.

These then could potentially be used for addressing research questions that may or may not involve the institution that originally collected the samples. Some researchers explained that because samples are often exported for very specific purposes, they are often used up during the analysis process or destroyed as per an approved protocol. In the case of scientific research consortia, long-term storage is an integral part of the research process to address a range of broad scientific questions. It is these kinds of projects that would often include information about sample storage on consent forms. There are also specific research projects that require the storage of samples overseas. For example, multicentre trials may require sample storage in a centralised laboratory outside the country from where the samples were collected such as. South Africa for samples collected for the RTSs project in Kilifi.

> "And the blood is for two purposes. One is for safety and that is processed locally and then we separate the sample into serum which we export to Belgium for immunological assays. But we also do collect slides and filter paper and these are for the assessment of malaria for which we ship at least 50% of those samples to South Africa as an archive" (Kilifi: RES04).

> "Some are stored externally; there are some that are duplicated so we have some here and some there. Not many stay here for long storage because of all the problems with storage. But many times they will be here for a while until they are needed for certain specific study before they move but when they move out usually they tend to stay there" (Navrongo; RES017).

While most interviewees indicated that local storage of samples is desirable, they also acknowledged that maintaining this infrastructure comes at a cost; as discussed earlier it requires appropriate local infrastructure such as storage facilities and stable power supply. Power outages, a common phenomenon in Navrongo, could also affect the quality of stored samples and in one case in NHRC; a fire outbreak necessitated the storage of research samples in another institution within the country. Table 12 on the next page outlines the types of samples involved in research projects and the destination of exported samples. It is interesting to note that, by contrast with Navrongo, Kilifi also receives samples from other African countries such as Tanzania for analysis.

Kilifi:

Type of samples collected	Types of samples stored	Types of samples exported	Destination of exported samples
Serum, Blood and blood products, parasite RNA, post mortem tissues, nasal serum, DNA, throat swabs	DNA, RNA, serum, blood blots on filter paper	Human and parasite DNA, RNA, blood serum, blood blots on filter paper, blood plasma	Oxford, London, UK, NIH, USA, Atlanta, Bangkok, Australia, Germany, South Africa

Type of samples received	Source
Serum, Blood and blood products, parasite	Tanzania, Uganda

Navrongo:

Type of samples collected	Types of samples stored	Types of samples exported	Destination of exported samples
Whole blood (serum, plasma, blots) DNA, parasite DNA, stool, throat swab	DNA, RNA, serum, blood blots on filter paper	Human and parasite DNA, RNA, stool, blood serum, blood blots on filter paper, blood plasma	CDC, NIH, USA, Oxford, UK, Basel, Switzerland Noguchi, Ghana

Table 12: Overview of human biological samples and their destinations

The main justification for sample storage is for future research use. Interviewees explained that storing samples will provide great opportunities for researchers to conduct future analysis and generate new knowledge at a lower cost without 'bleeding' research participants:

> ".. for quite a long time they have done malaria studies in several cohorts over the years, longitudinal cohorts; so all the plasma samples from those cohorts are still available and now that malaria has rapidly declined it is possible to actually look back at those plasma samples and see how immunity or antibody responses change over time with declining transmission. So they are very valuable samples, so we don't tend to throw things out" (Kilifi: RES04).

4.6. Existing governance mechanisms for sample export, storage and future uses

A key objective of this project was to examine and critically review existing governance structures for sample use, export and storage. Research governance is the development of standards and mechanisms for the proper management and monitoring of research and where necessary allows sanctions to be brought in cases of research misconduct (Kaye 2011).

These mechanisms are important for promoting good research practices, ensuring ethical and lawful research and promoting public confidence and trust. According to interviewees in my project these are values that both KWTRP and NHRC strive to maintain in their research activities. However, the literature points to a general lack of clear and transparent governance mechanisms in sub-Saharan Africa (SSA). I was therefore interested in understanding what mechanisms relating to sample collection, export and storage currently exist in Kilifi and Navrongo, and what are the challenges with implementation.

4.6.1. Institutional requirements and approvals for sample export

In Kilifi, there are three layers of approvals. First, requests for samples to be exported are reviewed internally by the scientific coordinating committee (SCC) in Kilifi, followed by a scientific steering committee (SSC) at KEMRI in Nairobi and then, finally, ethics clearance from the REC in Nairobi.

> "..for each export you are doing, even if it's the same study, if you have to export sample, even ten times, each time you are exporting you must have a license to export otherwise it won't go" (Kilifi: RES09, Expatriate).

All requests for sample export must be justified and clearly stated in the research protocol; and approval is given for specific analysis that cannot be done locally. This requirement is, however, a recent development. It follows a controversy over the export of samples from Kenya by foreign collaborators in early 2000:

> "…in a children's home in Nairobi that caters for HIV infected children, a newspaper reported that children were bled and that some [samples] were taken to the UK. And one of the local scientists complained that the people who were using the samples were never in the protocol and he was a PI and never got to use [the samples], papers were published without him. So after that [controversy] is actually when Kenya started introducing a requirement for a licence to export samples" (Kilifi: RES09).

During the visit to the REC office in Nairobi, the secretariat took me through a request for sample export form that researchers are required to fill, as well as an authorisation form giving the final approval for sample export (see appendix 5).

> "You can see first of all there's the form that you fill, you see the project title, you see the affiliations, you see the PIs, you see the other investigators, then there's part B, there's specimen details, details of exportation, you describe the specimens that are going to be exported, the research lab, the results, regular typing, and these are all the things that we put in our database" (Kilifi: REC02).

An additional requirement for sample export is that samples have to be accompanied by a local Kenyan scientist to provide opportunities for developing local capacity and to sustain the research collaboration:

> " ..for tests that can be done locally, we are not allowed to send them and its great, one thing is it encourages us to build capacity to do these things and as an offshoot you then create jobs and offer opportunities" (Kilifi: RES02).

In the case of Navrongo, interviewees mentioned different requirements including approvals from the local REC and the Ministry of Health as well as immigration control requirements.

> "In Ghana, you would need to clearly indicate that they are for scientific research and they have no commercial value and that is what would allow the customs exercise and preventive services to allow the samples to be exported. I think it is the protocol that stipulates the whole study design and that is submitted to the ethics review committees and that also spells out the arrangements for material transfers and other things" (Navrongo: RES13).

The NHRC has an institutional review board (IRB) that reviews research protocols for their scientific and ethical merits and grants approvals for protocols that meet these requirements. Although there are no specific requirements for sample export and storage, at the time of conducting these interviews (in Dec 2010), the NHRC IRB has recently instituted a new requirement for projects to submit Material Transfer Agreements (MTAs) and for the return of unused samples to Navrongo after the analysis. An IRB member explained that these new guidelines have become necessary because of increasing local concerns around the fate of exported samples:

> "We didn't have that in the last operations but the last revisions that we made, we added that to our standard operating procedures which are available to the research officers and other researchers so they know that in the event that they need to transport samples; there should be MTAs with the sponsor wherever they are taking the samples to" (Navrongo, REC03).

While most researchers were generally satisfied with these institutional requirements, they suggested that more should be done to streamline these review processes to avoid delays in reviews and approvals. According to a REC in Nairobi, despite the fact that most research protocols include requests for samples to be stored, actual requests for the reuse of these stored samples are rare. He expressed the view that either samples are being reused without REC approval, which is difficult to verify or scientists are yet to make use of these stored samples.

> "They're supposed to come back to the REC to get authority to do any other research which they may think is useful. But I, I haven't seen that being done, I haven't seen any requests so far of any institution or any scientist asking for permission" (Nairobi: REC09).

Strikingly, although researchers and IRB/RECs extensively discussed the institutional procedures that have been established for sample export, group discussions with fieldworkers, community facilitators and community representatives suggested that they were unaware of these structures and processes beyond the collection stage including how they are analysed, where they are exported to, and how and where they are stored. This raises the question of transparency in the research process and the policies governing them within the institution.

Another important requirement is obtaining participants' consent for sample export. This is however a recent practice. Interviewees in Kilifi reported that most research projects requiring sample export seek participants' informed consent. This process is well known by fieldworkers because they are directly involved in administering consent forms to research participants. They explained that this information is often translated into the local language justifying the "transport" of samples abroad:

> "In such case that their blood has to be transported, you have to explain further why, most importantly, when the study involves blood. You have to say that (statement in Kiswahili) exactly. Some of the test cannot be done here locally so we have to transport the samples for further tests. So you only have to explain a bit more" (Kilifi: FW01).

This suggests an improvement in the system from what Langat described in a 2005 study reporting that 25% of research projects failed to inform research participants about sample export (Langat 2005). Notwithstanding these improvements, interviews with researchers suggest that at the national level, not much has changed in establishing policies for managing sample export. They highlighted the urgent need for clear national policies and guidelines specifically for the export of samples.

In Navrongo, interviewees reported that explicit requests for sample export are not part of the consent process for most NHRC research projects, although information about the collaborative nature of research projects is usually provided.

> ".. the consent forms provide information that the sample that has been collected is going to be used by the team involved in the project and this includes the external collaborators so it is not very clearly stated that this sample would be shipped to a laboratory outside the site… [but] the participants also deserve the right to know that the samples would be analyzed either locally or externally [without] necessarily telling them the specific laboratory" (Navrongo, RES13).

One researcher and a REC member explained that sample export is not discussed with participants because of the expectation that all aspects of the research would be carried out locally. Sample export arises when the Centre fails to build the required capacity for local analysis.

> "In terms of exporting no but we tell you that we are going to take your blood, we are going to do one, two, three four, but we don't talk about export of blood because we always have the hope that we should be able to do some of these things once we build up the capacity" (Navrongo, RES07).

> "It may be a legitimate issue in some researches that immediately it is not possible to define where the samples would be sent to for the further analysis but you know very well that you will not be able to do it in country. So in those situations it may not be possible to specify that the samples would be sent to this country for further analysis, that I think is a possibility in some settings" (Navrongo: REC01).

For some international research consortia whose primary aim also involves sample export, there is an expectation that sample export will clearly feature on the consent forms; however I did not come across a single consent form in Navrongo explicitly seeking participants' consent for sample export. Whether this is a necessary requirement for ethical research with human participants is arguable and will be explored in more detail in Chapter 7.

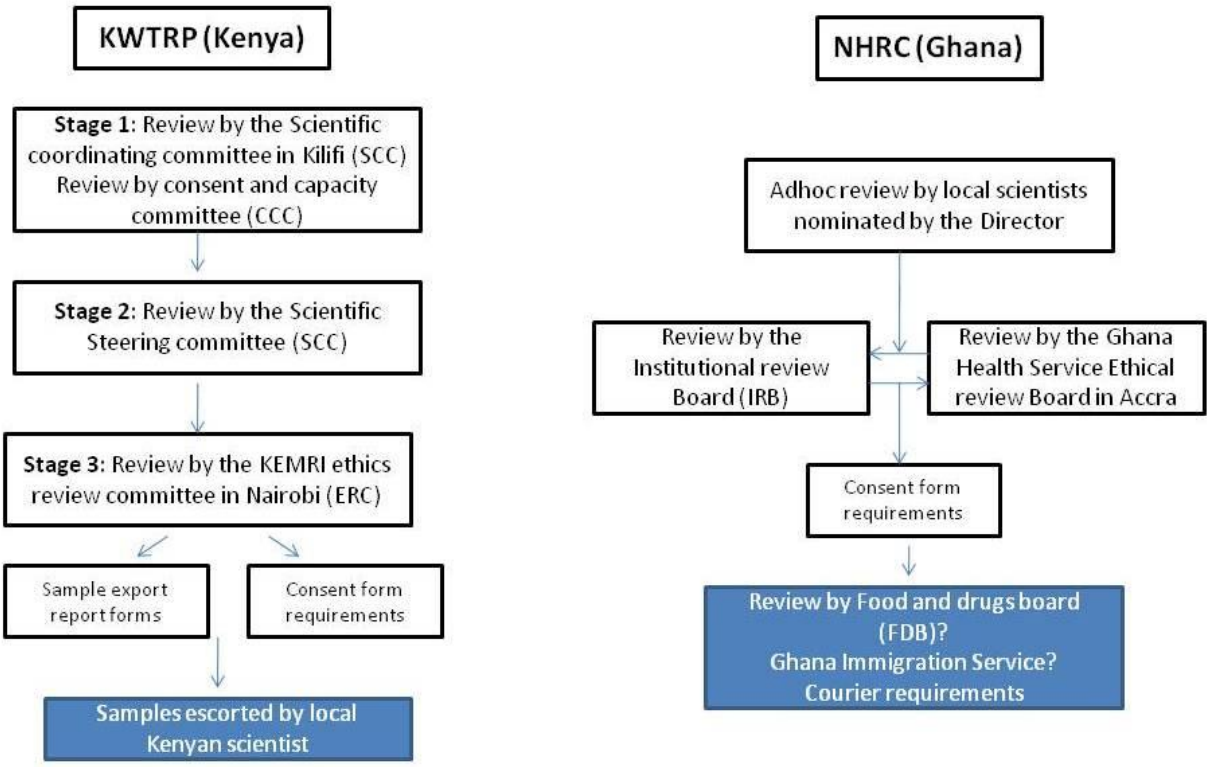

Figure 5: Review processes and procedures in Kilifi and Navrongo.

4.6.2. Sample storage and requirements for future uses

While institutional policies for sample export and storage were evident in Kilifi, they were absent in Navrongo, apart from the requirements for informed consent. Researchers only reported some internal procedures and agreements within specific research projects on how samples should be stored and how these should be accessed.

In the wider literature, there is a growing scholarship on the concept of broad consent for future uses of samples (Wendler and Pace 2005; Hansson, Dillner et al. 2006; Wendler 2006; Upshur, Lavery et al. 2007; Kaye 2010; Petrini 2010; Karlsen, Solbakk et al. 2011; Sheehan 2011; Steinsbekk, Ursin et al. 2011). Until recently, consent forms did not include information about storage of samples and possible future uses. However, with advances in research, a growing recognition of stored samples as a resource and global debates on ownership of samples and informed consent issues, this information is now included on consent forms. Although some of these forms specify the area of research to be conducted in the future, such as genetic studies, most consent forms only state that samples will be used for "future research purposes" [*excerpt from consent form: Navrongo*].

Also, although most projects do not indicate the number of years samples will be stored for and where they would be stored, a few of the consent forms I reviewed indicated a storage length of ten years. Some forms also include a statement that the approval of the local REC will be sought for future uses of the samples, while others do not. To address the lack of uniformity in these practices, researchers at both KWTRP and NHRC have called for appropriate national and institutional governance mechanisms. I will discuss this later in Chapter 7.

4.7. Conclusions

The aim of this chapter has been to provide an account of the current and changing practices of sample use, export and storage at KWTRP and NHRC. It was important to get a clear sense of the nature of the research collaborations in these research institutions and why research samples are central to the research projects taking place at these institutions. Both institutions have been involved in several international research collaborations for over twenty years.

The data also highlights the motivation for scientific research collaborations such as the desire to participate in cutting-edge science and the opportunity for capacity building. According to interviewees, the guiding principles for a successful collaboration include mutual trust, respect and equal partnership.

The data also suggest that the nature of the research collaborations at these research institutions largely determines how research samples are eventually managed; collected, stored, exported and re-used. Stakeholders argue that there are compelling scientific reasons for collecting, storing and exporting human biological samples. These include the lack of local facilities to process these samples and the need for uniformity of analysis and quality control. Despite reports in the literature about the lack of governance structures in most African institutions for sample use and export, I found some important institutional guidelines and procedures at these two institutions, such as requirements for scientific and ethics review, informed consent and MTAs.

These mechanisms place the primary responsibility on local researchers to ensure that they have all the right approvals for their research and that their research activities are conducted to the highest ethical and scientific standards. Awareness of these processes is however limited to researchers and IRB/RECs, which may create challenges for other staff of the institutions, such as fieldworkers. This calls for more transparency in the research process.

It was interesting to note that these perspectives reflect both the experiences and expectations of the various interviewees. In most cases, it was difficult to separate their expectations from what actually happens on the ground. For example, when local researchers spoke about the importance of equal partnerships, it was not clear if this is achievable in practice. I will return to this issue in Chapter 6.

In this chapter, I have also noted that despite the compelling scientific reasons for sample use, storage and export, study interviewees raised a number of ethical challenges that arise in practice. The quantity and frequency of samples involved in a particular research project as well as the location of the sample collection also present specific practical ethical challenges for some of my interviewees.

In the next two chapters, I will be exploring these practical ethical challenges. Chapter 5 focuses on the micro-level issues arising from researcher-participant relationships and by extension institutional-community relationships, drawing on local perspectives and experiences with consent processes and general understanding and perception of scientific research. Chapter 6 examines the macro-level issues with a focus on matters arising from institutional relationships such as capacity building, justice and fairness issues in relation to international research collaborations.

Chapter 5: Practical ethical issues at the micro-level: consent, trust and local relationships

5. 1. Introduction

In the preceding chapter, I presented data on the current and changing practices around the use, export and storage of human biological samples in Kilifi and Navrongo. Drawing on the perspectives of the various stakeholders interviewed, I gave an overview of the nature of research collaborations at these two institutions and showed how human biological samples are managed in specific projects. Despite the existence of what stakeholders considered to be compelling reasons for sample use, storage and export, and the existence of local structures governing these practices, such as consent forms and ethics committees, they also raised several ethical and practical concerns arising from researchers' interactions with local participants and the wider community and some macro-level issues related to institutional relationships.

In this chapter, I aim to get a deeper understanding of the practical ethical issues relating to researcher-participant relationships (and by extension local institution-local community relationships). I begin by examining stakeholders' perspectives, attitudes and experiences with current practices of obtaining consent during the recruitment of research participants with a focus on the collection and use of human biological samples. I focus particularly on the challenges with obtaining valid consent and the local factors that impede this process. I then go on to examine the cultural sensitivities around the use of blood samples in detail providing examples to illustrate how these issues are perceived by various stakeholders.

5. 2. Challenges with seeking consent for scientific research

Most interviewees in this study highlighted consent as a key ethical issue arising in the scientific research projects taking place in Kilifi and Navrongo. Valid consent is an important ethical requirement for research involving human participants. It is the application of the principle of autonomy and perceived as a way to respect and protect the research participants' self-determination, dignity and well-being (Beauchamp and Childress 2009). These requirements for consent are stipulated in several international and national guidelines and regulations governing research with human participants, which also guide the ethics review process. For consent to be valid, it must be informed, voluntary and given by a competent person (CIOMS 2002; WMA 2008).

The basic elements of consent is that potential research participants are provided with adequate information about important aspects of a proposed study and that they fully understand what they are consenting to. Generally, stakeholders' responses in Kilifi and Navrongo suggest that achieving this objective can be challenging in practice and these challenges can be experienced at two levels: 1. Determining how much information should be provided and 2. The extent to which participants are interested in and/or have the capacity to comprehend the information provided.

These responses are not surprising or unique to Kilifi and Navrongo. Indeed, several published articles have highlighted the challenges with obtaining and documenting consent in both High-income countries (HICs) and Low and middle-income countries (LMICs) (Molyneux, Peshu et al. 2004; Diallo, Doumbo et al. 2005; Doumbo 2005).

In the context of Kilifi and Navrongo, a number of empirical studies have highlighted challenges related to low levels of understanding, therapeutic misconception, trust and specific challenges with contextualising international requirements for consent (Molyneux, Peshu et al. 2004; Molyneux, Peshu et al. 2005; Molyneux, Wassenaar et al. 2005; Marsh, Kamuya et al. 2008; Kamuya, Marsh et al. 2011). There have also been experiential reports and further empirical studies aimed at addressing some of these challenges such as the relatively important role of community engagement in scientific research (Gikonyo, Bejon et al. 2008; Marsh, Kamuya et al. 2008; Boga, Davies et al. 2011). This also reflects the wider literature and other empirical studies across the globe addressing the subject of voluntary consent (Parker 2004; Dawson and Kass 2005; Boddington, Curren et al. 2011; Bull, Farsides et al. 2012).

In my research, although there was a general agreement that researchers have a duty to ensure that these basic elements of consent are met, most interviewees highlighted the challenges involved in practice. These challenges range from a misunderstanding of scientific research more generally to specific issues related to the use and export of samples.

5.2.1. General research understanding

Although the focus of my study was to examine the issues arising specifically around sample use and export, stakeholders' accounts suggest that seeking consent in these resource-constrained settings is still a major challenge more generally and the ethical issues highlighted in the literature are still relevant today. According to interviewees, this has been complicated further by recent advances in research methodologies such as those used in genetic and genomic research, coupled with low levels of literacy in these research communities which make determining the validity of consent complex.

The quote below from a researcher in Kilifi illustrates the general sentiments about obtaining consent in this growing era of genetic and genomic research:

> "It's unrealistic on an individual level for people to really understand the finer points of the research that's being done, particularly in a place like this where there's a lot of research being done and they're all quite complicated things that require a deep, in the sense an understanding of biology and inheritance of genetics. It's quite impossible for an individual with relatively low levels of education to be able to understand every aspect of it" (Kilifi: RES13).

A research assistant in Navrongo adds that:

> "When you are consenting, most of them normally just accept to participate in the study without .. fully understanding" (Navrongo: RA02).

Previous studies have suggested some complications arising out of the ambiguity of the meaning of the word for 'research' itself (Marsh et al 2011). In my interviews, it became clear that several factors may impede participants' understanding of research. They include the difficulties associated with explaining complex scientific terms in lay local languages, for example, what it means to sequence genes (or genomes) and how to translate that into the local language of the research participants, as required by guidelines and regulations. Tailoring these consent requirements to the local context remains a challenge:

> " ..there are always issues about contextualising the processes of obtaining consent in the local situation and taking into consideration the language barriers, taking into consideration the issues about translation, sometimes information is lost in translation" (Nairobi, REC00).

> "..but there are some challenges. Maybe some words, being translated into local language becomes a bit hard. Like translating the word "confidentiality" which when you translate into local languages like "siri", it raises some concerns in the community. "siri" is like something which is hidden so it does not come out that it is just confidentiality but they think that there is something which is being hidden from them" (Kilifi: FW01).

As indicated by the quotes above, while the idea of translating consent forms into the local language is perceived as a way of ensuring research understanding, significant detail may be lost in the process, and attempts to translate concepts that are central to valid consent by drawing on similar terminology in the local language such as the case of confidentiality in Kenya may create silent suspicion among individuals and the community at large.

A researcher in Navrongo also admits that, there are difficulties with getting appropriate local terminologies to explain specific scientific procedures:

> "Sometimes, there are issues with genome-wide studies, genetics studies, and other areas, in terms of the local language how we translate those things is a big problem and that, I think that poses ethical issues because we want to convey a message to the people but the terminology is not there for you to give exactly what you need to pass on" (Navrongo: RES07).

What is also highlighted in stakeholders' responses are the ethical dilemmas that researchers face with striking a balance between meeting international consent requirements, respecting the rights of the participants and ensuring the scientific conduct of research. They suggest that even with the best intentions and efforts from researchers to follow the fundamental requirements of consent, there are pragmatic challenges with actually 'doing ethics' in these settings.

5.2.2. (Mis) understandings around the use of biological samples in research

In the context of scientific research involving human biological samples, RECs in Nairobi and Navrongo emphasised that, as part of meeting the fundamental requirements for consent, potential participants should be informed and understand 'exactly what is going to happen to [their samples].

The following quote from a REC member in Nairobi illustrates the main elements expected in a valid consent process:

> "As you know the consent, even for taking samples alone is required from every participant and it is a duty, we expect the researcher or investigator to explain in sufficient detail to the subject the purpose of taking the samples, if there are any benefits, if there are any risks and what is going to be done to the sample, what it is going to be used for. … in its methodology explain how they will go about using the samples and what it is supposed to be used for. If for example it is research on malaria we expect that it will be used only for malaria. So as a REC we would be concerned that the subject knows exactly what is going to happen to the sample" (Nairobi, REC11).

In practice, meeting these expectations of local RECs can sometimes be extremely difficult. It is apparent from the data that researchers are sometimes unable to demonstrate to potential research participants 'exactly' what scientific processes are involved in their research, which contributes to the lack of sufficient research understanding:

> "..if it were possible for researchers to demonstrate somehow the whole process from taking samples from a person to really finding out what parasite is in that person's blood that is causing the person to come down with malaria and at the end what becomes of that 5ml of blood that they have collected, then it may be possible for the community to see. But nobody knows what really happens with that quantity of blood that is taken, so it is difficult to understand that this blood that is taken although it's 5ml this is how it is going to be treated and at the end of the day this is what is left and this is what we do with what is left" (Navrongo: REC01).

> "…without belittling people it can be a very difficult thing to [explain] why you want to collect a blood sample to look at rising levels of specific antibody to an infectious disease. If somebody has no comprehension of what an immune response is, what antibodies are, to put that across such that people really comprehend why you're doing it and to link that to the research objectives I think is an extremely difficult task" (Kilifi: RES07).

As a result of these difficulties, some background information that should be the foundation of the information provided in a consent form is not communicated to research participants, which could lead to a general misunderstanding of scientific research. And for many people who have not had any scientific training, a more typical foundation is the more familiar (and more immediately necessary/needed/prioritised) information about clinical care that is not part of research.

Interviewees indicated that there is often a misunderstanding about the rationale for collecting samples for research purposes within the community, especially from children who are well. They suggest that while there may be a general acceptance of the need to draw blood from sick children in research, akin to clinical diagnostic practices, the rationale for collecting samples from healthy volunteers in the community is often not well understood.

As a REC member in Navrongo explains:

> "If you are going to treat the person and you take somebody's blood, in their minds, they think you are just going to see what is in the blood but when you are going to conduct research with it, that gives something different. 'There is nothing wrong with my blood and you are taking it" (Navrongo: REC05).

To some extent, this response also relates to the notion of therapeutic misconception, inaccurately attributing therapeutic intent to research procedures, which has been extensively discussed in the bioethics literature and highlighted in previous studies conducted in Kilifi and Navrongo (Appelbaum 2004; Molyneux et al 2005; Tindana et al 2006). Although this was not a major theme in my study, largely because interviewees were not asked specifically about it and most of them did not mention it in their narratives, there were some indications that this was a challenge in these settings and may undermine valid consent if not practically dealt with during participant recruitment and through broader community engagement.

Overall, researchers suggested that with the evolving nature of scientific research, it is impossible to expect that potential research participants would be given all of the relevant information (as discussed earlier), and for them to comprehend it all during the consent process and make their own 'value judgements' regarding their participation. For example, these responses hint at the inadequacy of information likely to be provided given the complexity of the topic and the time spent during the consent process:

> "People's capacity to decide some of the finer points that we've just been talking about on the basis of a brief consent form, it's just nonsensical to expect that a woman in a village who's been visited and given a bit of information by a fieldworker could make any sort of value judgement about any of the sorts of things we're just discussing" (Kilifi, RES13, Expatriate).

The general feeling is that fully informed consent –in its strictest sense of understanding every detail – is unattainable in these contexts and could be affected by low-levels of literacy and complications with translating scientific terminologies, which supports other studies on seeking consent in LMICs, reported in the literature.

While these responses might sound like an exaggeration of the effect of illiteracy and low access to formal education on research understanding (Nyika 2009), they highlight the need for a re-examination of the depth of scientific information researchers must provide under the various elements of the consent document that is considered adequate for valid consent.

Interestingly, the difficulty with understanding the scientific methodologies (and rationale for sample use) involved in some of the research projects in Kilifi and Navrongo is not just limited to the non-literate participants in the community. As illustrated by a REC member in Navrongo below, other staff of the institution and REC members, with no biomedical background sometimes find it difficult to comprehend how samples are analysed:

> "I mean even for some of us as scientist who are not biomedically oriented who don't know how these samples are really processed once they get into the lab. It's difficult to imagine why you would collect 5mls of blood from say 2000 children in an area and I mean if people do a quick addition or multiplication 5ml, 5ml times 2000 that amounts to something and that may be why people say that we collect the samples to sell because if you collect small, small, small from 2000 children it amounts to a lot of blood" (Navrongo: REC01) .[13]

All these responses point to a recognition that seeking valid consent in these contexts is challenging and has been further complicated by the growing practice of sample collection and use in scientific research.

[13] I also struggled initially to make sense of some of the scientific terminologies the researchers I interviewed used in their responses. I had the opportunity to take part in a laboratory tour and extraction of DNA at the Wellcome Trust Centre for Human Genetics in Oxford during my DPhil studies. This experience made me to appreciate the complex nature of sample analysis which might make informed consent a challenge.

5.2.3. Uncertain future uses of samples

Another issue raised in the data is the uncertainty of future uses of samples and its implications for obtaining valid consent. Over the past two decades, advances in computing and software development have revolutionized research laboratory infrastructure; scientists now have an incredible capacity to store vast amounts of samples and track individual samples in the apparent maze. This has given an unprecedented research value to stored human biological samples. Samples provide opportunities for future related studies especially long term genetic and other health-related research studies.

It is however common for consent forms to include clauses requesting research participants to consent for samples to be stored for future research purposes. This recent approach to consent has arisen because of the challenges researchers have encountered with using archived samples for research that was not covered by the consent obtained at the time of the sample collection. However, the evolution of this scientific field makes it difficult to clearly and specifically determine the nature of possible future uses of these samples. As a REC member in Nairobi explains:

> "I would say the consenting process is difficult because to be able to tell the person who is providing the sample all the possible research questions that it's going to answer at the time of collection is not possible and also as technology is advancing, even if one had intended to do an analysis using a particular kind of machine or a particular kind of process one maybe able to get more information than originally intended just by using a more sophisticated technology" (Nairobi: REC00).

Therefore, broad consent is an approach that has been adopted to accommodate future research. Consent generally requires the full disclosure of information about all key aspects of the research and that participants understand what they are authorizing. However, in broad consent, researchers may not be in a position to disclose information about what future research could be carried out, which makes the consent process challenging. In essence, participants are asked

to grant permission to 'the unknown' which raises concerns about the validity of consent. There were varied responses to the question of the validity of broad consent. Some of my interviewees argued that since the requirements of full disclosure cannot be assured in broad consent, this cannot be considered as valid consent:

> "This is certainly not valid. What is the consent all about? That you have explained the purpose of the research to the person, the risks and benefits of the research to the individual and s/he has granted consent. Now these are things that you do not know so how can that be valid? So you don't know the risks involved in using those future samples for any other type of research? How can that be consenting to something that I don't know. Certainly, people cannot behave that way. We have seen it in a couple of consent forms and this IRB has really been critical about that" (Navrongo: REC03).

While this strong view was uncommon, many interviewees expressed a sense of 'fear of the unknown' suggesting a limit to what future research could be conducted with stored samples:

> "In my experience with the IRB what we have tended to do is to say future related research, so if you are collecting the samples for malaria research, that future research should be malaria related, it cannot be HIV or something that has nothing to do with the initial purpose for which the samples were collected" (Navrongo: REC01).

Others, particularly researchers, highlighted the challenges involved in making broad consent valid. A researcher in Navrongo explained that:

> "…. the issue of abuse, you cannot rule that out because some scientist may go beyond the bounds and want to do other things that initially were not disclosed to the study participant even though the consent form, they say, these aspects would not be included in whatever analysis they are going to do" (Navrongo: RES013).

The uncertainties associated with future uses of samples generate special concerns. Most interviewees, especially REC members, suggested that these concerns arise because of the fear that samples may be used in specific studies such as genetics that have the potential to reveal information that may harm or stigmatize participants and their families or the wider community:

> "This of course for us triggers off issues like genetic studies that would expose or would bring in issues of confidentiality to people who were never participants. For example if my blood was taken and even if I consented to its use I may have consented to its use for a specific purpose but in genetic studies it may involve people who were not participants in the first" (Kilifi: REC02).

> "You know that genetic research has raised several ethical issues because it has conflicts with religion and it has conflict with culture so it is something that globally, there is no uniform position as to its acceptability so when you are talking about genetic research, then you really have to be cautious because it is not everyone who would accept because of the potential of stereotyping or labelling that can come out of genetic research and that if taken negatively, you can really hurt a whole race and not only a given population because it can be used negatively and that is why genetic research is in much disrepute" (Navrongo: REC13).

In general, the above quotes highlight the specific concerns that people may have about participating in future genetic studies that may have implications for them and their community. These issues relate to research findings that participants consider confidential and/ or raising potential issues around stigma, which support other views in the literature highlighting the ethical issues arising from genetic/genomic studies (de Vries, Jallow et al. 2012). Responses from this study suggest that there are local concerns arising from these studies that need to be recognised and discussed in order to foster a broad consensus approach for genetic and genomic research in Africa.

The data also suggest that participants may be sensitive about possible uses of their samples for other sensitive research, particularly diseases that are potentially stigmatizing in certain cultures such as HIV/AIDs research.

> "..some would also attribute it to other analysis. You are going to take their blood to do analysis on further things to probe further for whether they are HIV positive. They have other diseases that one should not know" (Navrongo: CR01).

A common response across the two sites was the need to protect the interests and rights of the research participants and their community by requiring that future uses of samples are related to the initial study they consented to. This will be discussed in more detail in Chapter 7.

5.3. Specific concerns about sample export

Study interviewees also raised specific issues related to sample export. Most interviewees, especially fieldworkers and community representatives were of the view that it should be a moral requirement to provide potential participants with information about sample export:

> "Ethically, in research, everything should be explained to the participants so it is their right to know that their samples are being transported but also again, we should make sure that the information we give them is good information. We should explain all the processes on the consent and if they understand, then they agree that we do that" (Kilifi: FW01).

> ".. it is important for participants to know.. it is may be an omission on the part of investigators that they don't include it .. but I think that the individuals should be made aware that their samples may be taken out to be analysed and it should be part of the consent forms" (Navrongo: RES021).

However, others, especially researchers and REC members, raised some skepticism about making this a requirement. They caution that this might further complicate current consent practices if the process is not conducted appropriately. Thus, while there is a general desire to respect participants' right to adequate information about sample export, there is also a sense that this needs to be considered carefully. As suggested by a REC member, the issues around consent for sample export are complex:

> "Now, the complication is also with the details of this analysis, and how much of the detail of the analysis is necessary and relevant information to the research participant. When you say that you are taking blood samples, eventually what is sent outside is not what we took. There in an attempt to explain these fine, I think we may even be making things rather too difficult for the participant to understand" (Navrongo: REC01).

This raises the question of how much detail should be provided to participants and how such attempts might further complicate the informed consent process, which links directly with the issue of research understanding discussed earlier.

Another potential challenge with seeking consent for sample export is how that might affect the scientific conduct of the research itself. The worry here is that if the analysis of samples can only be done outside the country and research participants refuse to have their sample exported, then the analysis required of such samples cannot be carried out. There is therefore a tension between respecting research participants' autonomy in the consent process and generating scientific knowledge through research. To resolve this quandary, most international guidelines such as Declaration of Helsinki stipulate that the 'needs of society should never trump those of the participant'(WMA 2008). However, the researchers I interviewed emphasised the need to find a balance between justifying the scientific aspect of the research and meeting these requirements for informed consent. These responses are not suggestive that information about sample export to participants is not important but rather the worry here is that obtaining valid consent which requires the competence, full disclosure and understanding of the research could be unattainable in this context because of the complex nature of scientific research. Researchers are worried that science will suffer unnecessarily in an attempt to meet some of these basic elements of informed consent:

> "..if I was asked where, where would you prefer your blood test to be typed and whatever I would say I'd like it to be done by the people who've taken the sample or whatever. But in the bigger picture, if there are rationales and reasons for doing it in different ways then it is almost impossible to get the individual concerned to make that sort of decision or to work, to formulate that sort of conclusion" (Kilifi: RES13).

As highlighted by other authors in the literature, there is also the danger of half knowing, when attempting to explain complex terminologies to large groups of people (Marsh, Kamuya et al. 2010). Thus, study responses suggest that other mechanisms for communicating these scientific procedures to research participants, beyond the individual consent process, may be warranted. These are discussed later in Chapter 7.

5.4. Sensitivities around use of blood samples

Data from this study reveal that although other human biological samples are involved in research, there are specific community apprehensions about the use of blood samples in research. Seeking consent for blood sampling is therefore a major concern, as narrated by researchers in Navrongo:

> "It's not been easy getting consent to take blood samples from participants and so after explaining deeply about what we are doing, one always has to be careful to protect the blood and to make sure that it's used for what it has been collected for. Participants always have concerns about what the blood will be used for, the effect it will have on them, not even thinking about what other things the blood can reveal about them. Most of the time the concern is about the effect of the amount of blood taken on their physical wellbeing at the time" (Navrongo: RES08).

Interestingly, while previous studies have documented these challenges around the use of blood in research (Molyneux et al 2004; 2005), my interviewees found the same even years later. Most interviewees were of the view that the lack of understanding and feedback about the rationale for sample use in research, discussed above, has contributed to rumours and apprehensions in the community about 'selling of blood' in both Kilifi and Navrongo and about 'devil-worshiping' specifically in Kilifi:

> "…generally [people] have apprehensions about bloodletting and we have had a few occasions where people have had to complain that we collect blood and we sell it because they don't understand. … So there is a big apprehension in some of the communities about taking the blood, in fact some of them call it bottles of blood" (Navrongo: RES07).

> "…they have a feeling that you have this snake logos on your car, maybe you are devil worshippers, maybe you are drinking the blood, maybe you are taking little aliquots of blood and mixing them, and a making a bit pint and selling it, you know those sorts of things which are common everywhere" (Kilifi: Kenyan: RES04).

What are these specific concerns about the use of blood in research and what could be accounting for these local concerns? According to interviewees, blood is of concern to people for several reasons. First of all, blood sampling involves a painful process, especially those that involve venous blood. According to some researchers and fieldworkers, mothers of potential research participants often express particular concerns about the collection of 'so many blood draws' from babies who are already ill. Therefore, while participants do not raise any issues during the consent process at the recruitment stage, they tend to become more anxious during the course of the study when they are faced with the reality of actually giving several blood samples:

> "I think in some of the consent forms it is included that the blood may be exported outside for further tests, and usually during consent no issues are raised and usually the community members don't ask anything about why their samples are going to be exported. It's only when there are so many blood draws that, especially for children that mothers become apprehensive" (Navrongo: RES08).

Participants may also have concerns about the consequence of actually giving blood, what it will be used for and the implication for them individually and for the wider community. Although it was not clear if these sensitivities are particularly about the uses of blood in research specifically or on more general clinical uses, interviewees reported several instances where there was suspicion from community members about what researchers use their blood for:

> "...blood is sacrilege for some people and their major concerns are where the blood is going, what is done with this blood and they think it is for devil worship because this thing is not usual so these questions are expected when you are in a public forum or community meeting you would get such a reaction. What about the blood? What is happening to this blood"? (Kilifi, CSKI03).

> "I mean there were several complaints and reactions. Some were saying that they don't know that we were actually going to do with the blood, some were saying that we are going to sell their blood and some were not also happy with the kids crying when they are taking the samples so they withdraw and don't want to be part of it" (Navrongo: RA 01).

Interviewees' accounts of the rumours surrounding the uses of blood samples relate to three types of concerns: one, that too much blood is being taken, two, that blood is being sold and three, that blood could be used for other spiritual activities such as devil-worship.

1. Too much blood collected for research

There is a general apprehension that the amount of blood being taken for research purposes is too much and could possibly harm donors individually, especially for children:

> "I think what the mothers seem to imply is that if you take blood out of my child my child gets weak. And that makes sense. If you're cut and you bleed a significant amount you get weak. So for them they can't correlate how much is too much blood to make my child feel weak. And also it's distressing to them that their child is being bled" (Kilifi, RES04).

The above quote illustrates a common view that research participants are unable to comprehend what it means to collect a certain amount of blood from a person for research. Specifically, there are apprehensions about what it means to take 5ml or 10ml of blood from sick children and the possibility that this might make the child sicker. As a community key informant in Navrongo explains:

> "I don't know whether it is misinformation about why the blood sample is taken and why we take only 5ml? They are still scared of the 5ml blood that is taken and so some will tell you that "I don't have that much" (Navrongo: CKI01).

This is further complicated by the fact that local words for 'anaemia' literally means 'not enough blood'. Thus it is difficult for a mother to comprehend why researchers would want to take more blood from her child who has anaemia.

2. Concerns about blood selling

Secondly, there are rumours within the community that blood samples collected in the context of research are often sold to 'outsiders' for money. Fieldworkers specifically reported that some participants and community members have personally expressed these concerns to them.

They attribute this to a general misunderstanding of what it means to "transport' blood samples overseas:

> "There is a whole mix up between misconception and then maybe misinterpretation because when they hear the word "transport", that notion that all the blood samples are transported separately is not in their mind. They think that all the blood is put together and put in the ship so there is that feeling that if this blood is transported and maybe they think that it is put into buckets,.. so there is that feeling that they are doing something else dubious about this blood because transporting to them and even to me might mean many things packed together to outside countries" (Kilifi: FW 01).

As suggested above, even fieldworkers themselves do not sometimes comprehend complex sample export processes. They reported that even when they explain the scientific rationale for sample export, such as the lack of equipment locally to process the samples, most participants would often raise queries.

> "they think that the blood is going to be sold and even after you explain to them that the test cannot be done here, they have questions "why is it not been done here?" and if it is about the equipment, maybe you don't have the equipment, "why, this is a big organization can't we get the equipment to test the blood here?" "why should the blood be transported abroad", they have questions on the blood transportation" (Kilifi: FW 01).

In both Kilifi and in Navrongo, fieldworkers and a community representative reported that the practice of "buying blood' for blood transfusions in clinical settings has also fuelled the rumours about selling of blood.

As a community representative explains:

> "The ignorant ones try to educate the people that they were taking the blood sample to sell because when people go to the hospital and they say you are short of blood, they say look for people to give you blood if not you buy at the blood bank, so the first idea that came to them was that probably that was [the NHRC's] way of taking blood from the people to go and sell to patients at the hospital" (Navrongo: CR03).

Consequently, fieldworkers in Navrongo reported that some mothers of study participants have approached them to ask if blood that had been collected from their children during the course of a research project could be given back to them for transfusion.

Another community representative in Navrongo suggested that from a community point of view, what accounts for the apparent wealth and growth of the research institution and staff is the blood that is collected from the community:

> "There is this fear that you are drawing blood for other things. For the rituals, here, they don't easily say it. Rather, they attribute it to the selling of blood. We come to collect their blood for sale and buy our cars in the research. So they think that it is because we sell their blood; that is why we are getting these things. We collect their blood that would help us to get these cars that we are driving; so unless you take your time to explain to their understanding, it is difficult" (Navrongo: CR01).

According to this respondent, this belief about blood selling is so ingrained in some parts of the community that researchers have to always prepare adequately to address it when approaching individuals in these areas:

> "We actually encounter many challenges and we have some particular zones within the district that … you have to prepare yourself well before you can approach an individual because it involves blood" (Navrongo: CKI01).

Group discussions with NHRC fieldworkers confirmed this allegation. They shared experiences of being driven away from a community meeting because of these misunderstandings about blood use in research:

> "We went to Manyoro (community)…. and they drove us away. They said no, they don't need us again. We have been taking their children's blood to go and sell and buy some nice cars so that day, honestly, we didn't get anything. We just had to come back" (Navrongo: FW01).

3. Devil-worshiping

Almost every respondent in Kilifi and some REC members in Nairobi reported the general perception among members of the community that KEMRI was involved in devil-worshiping. They explained that these views are largely related to two factors; historical events and the snake logo on the institution's vehicles:

> "…people consider KEMRI [to be] related to devil worship organization and the issues of blood came as a result of that. It is a devil worship organization because it takes blood and then the blood is fed to the devils. So in fact they think that if it is transported, it is not here. Is it really transported abroad or is it given to the devils at KEMRI" (Kilifi, FW01).

Although interviewees spoke positively about several community engagement strategies that have been adopted by KWTRP to address this misconception, such as giving tours to community leaders around the research laboratories, this issue has persisted. Some fieldworkers explained that the removal of the snake logo from the institution's vehicles made some members of the community even more suspicious:

> "…even after the logo had been removed, that created another issue like you said they are not devils and now you have removed them to blindfold us but you should have left them there so that they educate the community. So it is a whole lot of issues surrounding the snake logo; understanding and education" (Kilifi: FW01).

The above quote demonstrates that although community sensitization and education is important in improving understanding of research, these local rumours may not just be about lack of understanding as perceived by some interviewees. Rather, there may be more underlying issues such as trust and people's special attachment to blood which cannot necessarily be addressed by providing more information about the research.

The following quotes attempt to connect these rumours to historical accounts:

> "…there's that connection with the past where people generally were used for other people's financial gain. It's all connected to the way people have been treated in the past and that maybe it's difficult, it's very difficult to disconnect it" (Kilifi: RES03).

> "I think traditionally blood is life and traditionally there are attachments and stories linked to blood. Especially when it comes to research it goes back to our great grandfathers who attributed blood to the initial white men who used to come and steal blood and just run away so when you talk about blood it triggers many memories and that's why you have to be very careful" (Kilifi: CFs).

The concerns raised here support other claims in the literature linking historical accounts with people's perception of medical research in general and the local community's pervasive view of some research institutions in Africa as 'blood-stealing' organizations (Pool and Geissler 2005; Fairhead, Leach et al. 2006). Some of these scholars have suggested that rumours about blood use in research reveal local communities' responses to research and the more 'general relationships of dependence and inequality on which this is based'.

This raises issues of equity and benefit-sharing as ethical concerns, which require serious attention in determining whether research is ethical or not.

A call for equity in the distribution of benefits?

These community views may not be farfetched. In comparison to workers of the few other establishments within the Kassena-Nankana Districts, mostly government agencies, the staff at the NHRC are economically better off because they are more likely to own a house, motorbike or a car. These perceptions also support work by other scholars highlighting rumours in Africa linking blood and the wealth of an individual (Barber 1982; White 1994).

In Kilifi, community facilitators shared a similar sentiment:

> "…most of those who are asking or querying that procedure are asking why we should export samples and they end up benefiting some individuals who have never set foot in our country and yet they get PhDs and the person who has agreed to give the sample is left out, because it is voluntary. There are people who end up upgrading their CV's and receiving big salaries and living comfortable lives, so there is that debate" (Kilifi: CFs).

Although the views of actual research participants were not sought to support these claims (a limitation of this current study), these responses are an indication that local communities are recognising the potential benefits of research and the general inequalities in the distribution of these benefits.

5.5. Motivation for research participation

Interestingly, despite the challenges highlighted above about the perceived misunderstanding of research, the validity of consent, and the rumours about other possible uses of blood samples, the data suggest that most members of the local community are still willing to participate in research projects conducted by the KWTRP and the NHRC. It is worth noting that not all participants believe in these rumours or have concerns about the issues discussed above.

While some attribute the motivation for research participation to the perceived benefits of research, others highlighted the trust-relationship between the local community and the institution.

5.5.1. Perceived benefits of research participation

According to research assistants and fieldworkers involved in directly seeking consent from research participants, one factor motivating research participation is participants' perception that research provides health benefits:

> " honestly speaking at the beginning I don't think they understand that well and whatever causes them to get into studies for most of them, a large percentage of them is the benefits" (Kilifi: RA02, F).

> "Many did not understand, they think if their kids are recruited then it relieves them from financial burdens taking care of the children because all the children were insured, their parents were insured so because of that some of the parents because of poverty really did not think seriously before giving their consent" (Navrongo: RA 01, M).

These responses support previous empirical studies in Kilifi and Navrongo linking research participation to the ancillary health care provided by research projects (Tindana et al 2006; Molyneux et al, 2005). However, it also brings the validity of consent in these settings into question. Is it ever possible to obtain voluntary and informed consent from research settings where the options for potential participants are generally constrained, with limited access to affordable and quality health care? Reports of consent refusals in these settings suggest that participants are able to say 'no' to research (Molyneux et al 2005). On the other hand, many are likely to have their choices influenced by their interest in – and indeed often great need – for basic health care.

Study responses from community facilitators and fieldworkers, who come from and live in these communities, suggest that while there is a general appreciation of these health benefits, the community expects more from research institutions. For example, the following quotes indicate the expectation that research institutions with a long-term (over twenty-years for both KWTRP and NHRC) research relationship with the local community should contribute to improvements in the lives of people in the community through non-research related developmental projects, such as schools:

> "It's true that in this community when you go out, people will say, this organization has been here for 20 years but they have got nothing here to show that they have been here, why don't you put up something maybe a class room or a building or something which we can easily say okay, KEMRI was here ten years, but you find you people you come in, take samples, you vanish, you will never come give us feedback, after 10 years you are back asking for more" (Kilifi: CFs).

> "We should be prepared to assist them if there is the need. You are a human being and you see your fellow human being is suffering and then willingly, if you get the information, the leadership should go there and give some assistance. Like schools in the communities, we can offer them some things. We just pick some exercise books and go to the community and say that "okay, because we have been doing research with you for these number of years, the kids are ours too. Let's give them these exercise books or the poor but brilliant students should be given some support" (Navrongo: CKI01).

While these narratives appeal to the moral responsibly of all moral agents to help those in need, they are also equating the responsibilities of these local research institutions with companies who are required to make contributions to develop local communities as part of their corporate responsibility. The assumption here is that there are potential financial profits to be made from research projects and thus the need to give back to the community. But do researchers have the same moral obligations to local communities as business companies? This is a question that requires further exploration and one to which I return to in Chapter 8.

5.5.2. The role of trust relationships

Almost every respondent (researchers, research assistants, fieldworkers, community facilitators and members of the ethics committee) mentioned the importance of trust in the relationships between the local institutions and the community. According to these responses, the KWTRP and NHRC have been able to build and maintain a trustworthy relationship with the community through their research activities, the engagement processes and by recruiting people from the community:

> "At the moment, that concern [around sample export] does not arise because they are confident that the institution would not engage in allowing their collaborators to use it in a way that would be demeaning so I think that the trust is there that once we are fronting for whatever collaborating institutions there are, they trust that the samples would be analysed in an ethical manner" (Navrongo: RES013).

Most were of the view that because of the trust-relationship between the local community and the research institution, the latter has the responsibility to ensure that samples that are entrusted to their care are used for the intended purposes. They also believe that the interests of the community will be best served if the samples are stored as close to the community as possible.

According to study responses, sustaining the trust that the community has placed in the institution would also require that researchers live up to the expectation of them and ensure that future uses of samples do not expose the community to harm. Respondents highlighted the integrity of researchers as an important issue to promote an honest research environment.

> "So I think a lot of the burden is on scientists to have high integrity in terms of the collaborative work that they do. I don't think that any amount or level of policing will solve the problem if scientists on their own do not decide that look, this is what I have committed myself to do with this sample and I am not going to step outside that. But as long as scientists are willing to use all kinds of means to discover things this issue would continue to be there. The attraction of just having samples at your disposal that you can use and just play with and see if you can come out with something is very high, except if you as an individual decide that look by my professional integrity or whatever, this is not what I have been given these samples to do with and I will not go beyond what I have been given the samples to do" (Navrongo: REC01).

Previous studies conducted in Kilifi and Navrongo have also suggested that local research institutions such as the NHRC have concretized this trust-relationship with the local community through the provision of health benefits (Tindana, Rozmovits et al. 2011). Thus, while trust may play an important role in research participation, participants and communities often perceive some benefits arising from research for them individually and also for the wider community.

5.6. Is voluntary research participation possible in resource-constrained settings?

The question remains; amid all the factors influencing research participation highlighted above, can voluntary consent be achieved in resource-constrained settings like Kilifi and Navrongo, especially in the face of advanced research methodologies such as genetics and genomics?

Most research ethics guidelines emphasise the need for consent to be given freely and voluntarily. However, in the context of scientific research, especially in LMICs, several commentators have claimed that meeting this basic element of consent is often impossible because of high illiteracy rates, poverty levels and high disease burden in these settings (Christakis and Rox 1992). To some extent challenges with research understanding is also true in marginalized communities in HICs (Snowdown et al 1997; Featherstone et al, 2002; Robinson et al 2004). While my study supports many of these claims, it is difficult to conclude that voluntary consent is unattainable in Kilifi and Navrongo. Nevertheless, there are several practical and ethical challenges that may undermine valid consent, that needs to be taken into account. For example, previous studies in Kilifi and my own work in Navrongo have shown that participants are often informed and do understand that they could refuse participation, however factors such as the relationship they have with research staff and trust often make it difficult for them to refuse (Molyneux et al 2005; Tindana et al 2006).

In Navrongo participants expressed views that suggested that although they were aware that their participation was voluntary, they felt they could or did not want to refuse because of the health benefits they could receive from participating (Tindana, Bull et al. 2012).

> "They told me it was voluntary and that I could refuse but how could I refuse when it was going to help me"? (Navrongo: Mother of research participant) (Tindana, Bull et al. 2012).

In Kilifi, recent studies by Kamuya and Molyneux report that 'silent refusals' is often used by 'participants who feel unable to say no directly' (Kamuya et al 2013). In Navrongo, clinical trials with repeated blood draws experienced a high attrition rate during follow-ups. This was reportedly as a result of participants' inability to say no at the outset, but refusing to adhere to study protocol over the course of the trial (personal communication with meningitis vaccine trial team). These behaviours could also be a strategy by participants to ensure that they get the study benefits but minimise the disadvantages associated with the study (Kamuya et al, 2013).

What I can draw from this current study is that seeking voluntary consent for sample collection and export in settings such as Kilifi and Navrongo is complex. Because there are reports of refusals to consent in these settings as well as participants withdrawing from studies they feel uncomfortable with, people are apparently able to make choices when it comes to research participation. There are also variable refusal rates for different studies which suggest an element of choice. Indeed, as other authors have also suggested it would be wrong to assume that lack of research understanding in these settings undermines competence (Gerrard and Dawson, 2004; Nyika 2009). On the other hand, there are also some 'constraining factors' such as perceived and expected as well as real health benefits, and the trust-relationships people have with research staff, that may influence people's decision to participate, even when they have concerns about uses of human samples in research.

5.7. Conclusions

In this chapter, I have examined stakeholders' perspectives of the micro-level ethical issues arising from sample use, storage and future uses. Most of my interviewees have suggested that seeking valid consent is a major ethical issue arising from these research practices. While there was a general agreement that researchers have a duty to ensure that the basic elements of consent - information, understanding and voluntariness- are met, most interviewees highlighted the challenges involved in practice. These range from a misunderstanding of scientific research more generally to specific issues related to use of blood samples in specific research projects and the export of samples.

Most interviewees reported that there is some misunderstanding about the actual uses of samples in research. This perceived lack of understanding of scientific research is affected by the low literacy rates in these settings and the complexities associated with some research projects such as genetic and genomic research and the many other factors noted above.

It is worth noting that these challenges are not unique to these settings. Indeed, several empirical studies conducted in both Kilifi and Navrongo – and internationally – highlighting the challenges of research understanding (Molyneux, Peshu et al. 2004; Mandava, Pace et al. 2012). What this research adds is that advances in the scientific methods used for research and the increasing collection, storage and export of samples have further complicated the process of seeking valid consent in these settings. Meeting the fundamental requirements for valid consent, such as understanding and the provision of adequate information about important aspects of a scientific research remains a challenge in both Kilifi and Navrongo. There are challenges with how much information about specific research projects should be provided to research participants and concerns around how such attempts may further complicate current practices of informed consent.

While most interviewees were of the view that community engagement activities have improved research literacy in these communities, they also suggest that participants' understanding of the rationale for sample use, especially blood and the scientific justification for sample export remains a challenge.

There is also lack of consensus in the literature about the validity of broad consent and thus not surprisingly this topic generated varied responses in this study. A widely accepted view in the literature is that this approach to consent could be acceptable, provided that the 'future' research is reviewed and approved by a REC and participants are given the opportunity to withdraw at any time (Kaye 2010). This is what is currently guiding current practices of seeking informed consent for storage and future uses of samples in Kilifi and Navrongo. Responses from researchers in this study suggest that because research participants are often not in the position to fully understand scientific research, decisions about future uses of samples should be delegated to the local REC. This generally supports the literature on the governance of biobanks and this line of thinking also supports views by other scholars who have argued that this broad approach to informed consent meets the criteria for 'informed consent' (Petrini 2010; Sheehan 2011; Sheehan 2011). The point made in these articles is that where research participants are able to reasonably make autonomous decisions to waive further consent for future uses of their samples, then this could be regarded as legitimate.

Other empirical studies have also reported that most participants were willing to permit sample export and storage and were willing to waive this additional consent for subsequent research, provided the study was approved by an ethics review committee (Wendler and Emanuel 2002).

The assumption is that RECs are better informed to make these decisions but as the data indicates, there are concerns that some REC members may not also understand the scientific aspects of research. This has implications for determining the composition and training of RECs in Africa and elsewhere.

I also found that although interviewees raised concerns about the uses of human samples generally, the use of blood samples was often usually the main concern. These concerns relate to apprehensions about the amount and frequencies of blood draws involved in specific studies, rumours about selling of blood and community perceptions about devil-worship.

Interestingly, most interviewees believe that the lack of understanding and feedback on the uses of samples in scientific research is what is fuelling these rumours. It was striking however that although both Kilifi and Navrongo have very strong community engagement strategies aimed at enhancing research understanding and addressing local community concerns, some of these concerns and rumours persist. While the responses from this research do not undermine these engagement strategies, they also raise questions about the inequities and complexities in power-relations, and the underlying issues around blood, such as, the special meanings people attach to blood samples and the fear that its use could potentially harm them as individuals or the community as a whole. Interviewees cited such studies as genetics research in general and HIV/AIDs in particular, which the community might find sensitive. This is not to suggest that they are against these types of research projects but there are concerns about how information obtained from these studies may potentially be stigmatising to individuals and the wider community. These concerns need to be taken seriously when formulating policies on sample and data sharing.

Stakeholders have suggested possible solutions to addressing these issues, which will be discussed in more detail in Chapter 7.

Interestingly, a few researchers (three) were of the view that some of the specific concerns around sample export have been overblown. They expressed the view that some of the issues that arise in sample export have much to do with histories of bad collaborations, and ideas of exploitation, both of scientists and of populations. Researchers and REC members reported that there are now strict rules and regulations governing the conduct of research to prevent malpractice and that researchers are now more accountable. According to these interviewees, what ought to be done needs to be taken into perspective and guidelines and processes that are put in place should take into consideration the specifics of different types of research projects.

Despite difficulties in research understanding and rumours about uses of blood, it was apparent that the community has a generally positive appreciation of the work of these two institutions in Kilifi and Navrongo and many community members are still willing to participate in research. Most interviewees attributed this to perceived and expected health benefits of research participation and the trust-relationship that exists between the institution and the local community. The ethical concerns arising specifically around the use of blood samples in research should however not been taken for granted. The community's trust in the research institution brings with it the belief that such institutions have a responsibility to ensure that samples that are entrusted in their care are not used in ways that may harm the community. This supports a recent study in Nigeria on biobanking which reported that participants are generally supportive of sample storage and future uses on condition that 'there are guarantees to prevent unethical research being conducted on their specimens and those running the biobanks are ethical, trustworthy and competent" (Igbe and Adebamowo 2012).

My data also suggest that there are specific issues arising at the level of institutional relationships. In the next chapter, I will examine these macro-level issues with a focus on capacity building, justice and fairness in relation to international research collaborations.

Chapter 6: Practical ethical issues at the macro-level: Local control, justice and fairness in institutional relationships

6.1. Introduction

The past two decades have witnessed increases in the number of scientific research collaborations in Sub-Saharan Africa (SSA) involving scientists from High Income Countries (HICs[14]). In my literature review, I highlighted a host of ethical concerns, identified in this literature – such as the potential for exploitation – that characterised some of these collaborations, especially during the HIV/AIDs pandemic in the 1990s and the subsequent expansion of clinical trials in SSA (Tangwa 1999; Benatar 2000; Benatar 2000; Benatar and Fleischer 2000; Benatar and Singer 2000; Ballantyne 2005). I also suggested that, over the years, there has been a growing recognition of the importance of collaborative relationships which are mutually beneficial (Habte 1992; Pincock 2008; Wonkam, Muna et al. 2010). In Chapter 4, my analysis illustrated the compelling reasons for research collaborations, the central role of human biological samples and the scientific rationale for sample export and storage. However, while there was a general appreciation of the important opportunities that these collaborations have provided to local African research institutions such as the KEMRI Wellcome Trust Research Programme (KWTRP) in Kilifi, Kenya and the Navrongo Health Research Centre (NHRC) in Navrongo, Ghana, interviewees also raised several practical ethical issues arising at the micro and macro-levels, which raised some concerns about this. The preceding chapter (Chapter 5) discussed the micro-level issues, paying attention to local relationships and interactions between the host institution and the community. This chapter will focus on the macro-level issues and the matters arising from institutional relationships.

[14] Although the terms north-south and developed-developing are commonly used to describe the relationship between rich countries of the United States, Canada and much of Europe (United Kingdom) and the rest of the world in Asia and Africa, I chose to use the terms High-income countries (HICs) and low and middle-income countries (LMICs) to highlight the inequalities between the two..

The chapter begins with an exploration of stakeholders' perceptions of international research collaborations in general and goes on to focus on issues around local control of samples, justice and fairness in institutional relationships, capacity building and the role of trust relationships. The chapter ends with an exploration of whether it is ever possible to attain fair scientific collaborations between unequal partners, and if so what the conditions for this possibility might be.

6.2. General perceptions of international research collaborations

Many of the scientific research collaborations between research institutions in SSA and their partners in HICs have been described in the past as semi-colonial and exploitative in nature with HICs controlling much of the scientific process (Binka 2005). Some authors and commentators have described a trend of 'parachute research' where western researchers go into an African country, collect biological samples and fly out of the country without engaging with local researchers and communities (Costello and Zumla 2000). Data from my research suggest that this has not been the case in Kilifi and Navrongo. There is also a changing trend across the region with international research moving more towards research partnerships that, in some cases are seen as mutually beneficial. As these researchers in Kilifi and Navrongo explain:

> "The perception is that we collect samples, give it to some clever people to do things with at the other end. But the way we try to reverse that collaboratively, particularly through the MalariaGEN network is to use the network to train up our own staff. So I think it's not something that happens overnight…. If we were writing a new proposal today it would be potentially quite different from what we were doing ten years ago. .. we've moved a hundred years in the last ten years in terms of capacity" (Kilifi: RES13).

> "…as the years went by, these [issues] have sort of diminished in importance. The issues of whether you are capable of doing it, whether you are a good collaborator, whether you have the capacity to carry out this research. That has gradually improved" (Navrongo: RES21).

These responses highlight the growing scientific capacity of some of the well-established research institutions in Africa. As discussed in Chapter 4, both KWTRP and NHRC have their genesis in international research collaborations as well as a long-term relationship (over twenty-years) with local communities. Most researchers suggested that the scientific projects being conducted in these settings are being responsive to the health needs of the local population and addressing relevant health problems such as malaria, tuberculosis, meningitis and HIV/AIDs. Against this backdrop, my data suggest that the ethical issues and specifically the challenges that arise with sample use and export are largely those related to the relationship between the collaborating institutions and the nature of these collaborations; how these are negotiated at the project's inception and how they are managed during the course of the research. The responses and experiences expressed in my interviews for this study vary between the institutions involved, the funding mechanism and the type of project. Thus, even within the same institution, some collaborative research projects are perceived as mutually beneficial while others are not. For example projects that were initiated and controlled locally and that are adequately funded were largely perceived positively.

In the context of projects involving sample collection, export and storage, most researchers especially those in Kilifi regarded themselves as more than 'sample providers' in their research collaborations. They highlighted the capacity developed over the years and the efforts made to initiate projects locally. Although they also highlighted areas that needed improvement such as better access to funding, local commitment to conduct the projects successfully, as well as potential ethical issues likely to arise in practice, they were generally positive about these collaborations:

> "…certainly from our programme ..we never export samples to people who just write to us and say 'can you send us 300 serum because we're really interested in this?'. That's the kind of collaboration we would never enter into. We're not interested in being sample providers, we're interested in working with partners to do something which we think is important and that's the absolute criteria" (Kilifi: RES13).

Arguably, KWTRP may be among the few institutions in Africa capable of making these choices regarding research collaborations. As will be discussed in a later section, the KWTRP has strong financial backing from the Wellcome Trust which has contributed to strengthening its local capacity and negotiating power. By contrast, the NHRC has no core funding for research and capacity development, and therefore tends to have a weaker influence on the nature and spirit of her research collaborations. In my interviews with them, NHRC researchers alluded to a lack of biomedical research infrastructure and the need for capacity building as a core element of research collaboration. However, they painted a rather grim picture of some of their collaborators in this regard. As we shall see later, however, these concerns were mainly with collaborators within Ghana rather than with collaborators from HICs. They suggested that, while there is a general desire for local researchers to play leadership roles in collaborations involving HICs, there are often limitations in practice:

> "You find highly trained people working in the South and developing countries but they've just been relegated to just collecting samples which would be shipped but I mean some of those people could actually do most of the work, it should be a partnership. I mean we know that the burden of disease is greater here so we need to do a lot more research in this part of the world, so it's in our interest to do the research so it helps us. So that's one of the things driving us into continuing to do research" (Navrongo: RES03).

This response also suggests that even when some local researchers are dissatisfied with the nature of the collaboration, they are willing to engage in projects because of the opportunity it provides to address the burden of diseases locally. Thus, while researchers in the KWTRP felt that they could confidently decline partnerships they found unfavourable, NHRC researchers suggested that they have limited options and sometimes need to weigh the consequences of

insisting on fair collaborations and losing the opportunity to carry out important research projects that may benefit the local population. This is one example of how some of the micro-level issues discussed in Chapter 5 – meeting local participants' expectations – influences researchers' decisions at the macro-level:

> "If you want to look at some of those issues then your people will continue to suffer. The people in Britain don't have malaria, so if somebody comes from Britain and wants to help us to deal with malaria I would entertain him. We end up picking up the crumbs from the table because we don't have too many options, we don't have the funds and without those crumbs we probably can't do anything anyway" (Navrongo: RES05).

Despite the general appreciation of the benefits of engaging in research collaborations such as opportunities for capacity development, the various stakeholders I interviewed in Kilifi, Nairobi and Navrongo highlighted tensions that may arise around the control of research samples, particularly with exported samples and long-term overseas storage.

6.3. Out of Africa! Destination of exported samples, does it matter?

As discussed in Chapter 4, p88, the destination of exported samples, largely depends on the nature of the collaboration and the types of analysis required. Although HICs are the main recipients, some collaboration may involve a main contractor (with high research capacity that attracts the collaboration) and a sub-contractor (mostly a less endowed institution with the capacity to deliver the samples). This will require sample transfer between laboratories in the same country. Such multi-layered collaborations were particularly common in Navrongo where samples are sent to the relevant institution in Accra. KWTRP and NHRC researchers suggested that in considering the destination of exported samples, their decisions are often driven by science-based needs. The priority for most researchers is where high scientific and ethical standards for the analysis of the samples would be met.

They argued that what is important is an assurance that the receiving institution and country have the requisite protection mechanisms to ensure that samples are used for the intended purposes:

> "… if we can maintain the same standards then it does not really matter where it goes. If an African centre could really maintain the same standards that you are going to meet out there to the international level, why not send it over but if you would have hesitancy that that will not happen then there is cause for worry" (Navrongo: RES17).

> "It's difficult to think for the community, but as an individual I would say it matters where the sample goes but it matters for a different reason, the sample should go to the place where the best results should be obtained, that would be my rationale. I would also want it to be sent where there are enough ethics regulations, where in case the sample was misused then I have recourse, as in I can easily petition and say the sample wasn't used the way it should be. So yes it would matter. So in countries which don't have strong ethics bodies and have a strong history of following international standards I would be reluctant to send it" (Kilifi: RES09).

Thus, from a scientific point of view, the destination of exported samples will largely depend on researchers' impressions of the capability of the receiving country (or other national centres). For example, if there is a technological advantage to be exploited and a suitable environment for doing good science in that country. There were varied responses on what may influence people's preference of the destination of sample export. When prompted about findings from Egypt (an Egyptian paper study showed that most patients preferred samples to be exported to Arab countries than western countries)(Abou-Zeid, Silverman et al. 2010), most of my interviewees expressed the view that historical relations between countries and societies could influence people's perceptions and reactions to various issues, including sample export:

> "I think we can speculate forever but I think in the case of Arab-West relations I think there is an issue there. I can imagine an average Muslim would probably not want a part of them or their sample handled by the infidels, it's my opinion, I might be wrong, so I would understand so if we look at it from the scientific simplistic view, it doesn't matter where the samples go but to the people it matters" (Kilifi: RES01).

> "It's a question of perception, perception has nothing to do with science and of course those perceptions will be stronger if they are coloured by other things, for us it's what will they do? Will they actually destroy them, will they keep them and so on. Now if we are taking it to people who are our enemies politically, then the suspicion will be increased, what do they want, do they want to study Arabs or understand our genetics" (Kilifi: RES03).

In the case of other African settings such as Kilifi and Navrongo, study responses suggested that participants' preference for the destination of samples will depend on how they perceive the receiving country and whether there is any trust-relationship between the countries involved. A Kenyan researcher suggested that local participants may prefer other African countries handling their samples because of their familiarity with the local culture and the feeling of being the same:

> "…if presented with that scenario, you would be more comfortable with another African country because of those issues of you feel somebody already understands you and how important your issues of blood are before you can even explain to them and you feel that you can access them and you feel you can reach them. You might have a language barrier but it is a different sort of language barrier. You feel that you can relate to them and you feel that they can relate to you more than the white man who you are being told is going to handle your samples. You don't feel they are accessible. You don't feel that they are relating to you so you feel like another African is your own" (Kilifi: CSKI02).

The assumption being made above is that Africans are more inclined to trust another African handling their research samples, but very few interviewees actually supported this idea. Interestingly, however, other interviewees expressed the view that in some cases it might be more acceptable to send samples to a western country because of perceived suspicions and mistrust in some African countries, as illustrated by this quote from a community representative in Navrongo:

> "What has Burkina got that we don't have and the worse is to say that my sample is going to Nigeria. Nigerians are known to be 419 [scammers]. My sample is being sent to Nigeria, for what? And then they watch movies about Nigeria and in the movies, you see that they are using blood for occultism purposes and so somebody would sit down and say no, this blood that they are sending there, we are not safe" (Navrongo: CKI01).

A REC member in Nairobi also remarked:

> "One of them is politics of suspicion. What would they do with it? Can we trust them? It's a question of perception" (Nairobi: REC03).

Other study responses suggested that distance and familiarity are factors that could also influence people's choice of destination for exported samples. As highlighted in the quotes below, people tend to get more anxious the farther samples are from the community and the less familiar the recipients are:

> "Obviously, I have been with you and if you come to tell me something it is easier for me to agree with you than have a stranger come and tell me that same thing for me to agree with that person in the traditional setting. And so if we are going to keep the samples here, the research centre is not far [from the community]. If it is going to Accra, they will say why are they taking it to Accra? and then if it is going outside the country, people start to get worried. They begin to associate the distance with the understanding of what is happening so people really have problems probably with the distance. And that is because they feel that when it is that far they don't have a way of monitoring it, to know whether they are actually using it for what they are saying or not" (Navrongo: RA01).

Some researchers in Kilifi agreed:

> "…some things are just perceptions, not based on facts, but you may be a little bit reluctant to send it to places you are not very familiar with, okay I'm more familiar with South Africa, Ghana, but I'm not familiar with for example other big countries, Middle East or China or India" (Kilifi: RES09).

Although there were varied responses on what might be an acceptable practice for sample export, there were some indications from most interviewees that it will be desirable to keep the samples as close to the community as possible and for host institutions to hold these samples *in trust* because of their long-term relationship and closeness to the sample donors and the communities. However, in situations where there is mistrust, based on previous experiences, the closeness of the samples does not necessarily address the ethical challenges arising in practice. These responses underscore the importance of taking into account these background relationships when considering what practices may be locally acceptable.

In addition to the question of which countries or institutions are involved in the collaboration and where samples are exported to, interviewees raised a number of other practical ethical issues. These include the fear of losing control and the lack of recognition for local contributions, and lack of local capacity and fairness in the distribution of research benefits. These issues are the focus of the next section of this chapter.

6.4. Losing control of exported research samples

As discussed in Chapter 4, there are compelling scientific reasons for exporting samples in the context of international scientific collaborations. They include lack of local capacity and requirements for uniformed analysis (see p88). Also, with novel scientific projects incorporating techniques such as genomic research which require access to more sophisticated laboratories that are currently only available in HICs and some emerging economies such as China, sample export is seen as an inevitable phenomenon (Parker and Bull 2009; de Vries, Bull et al. 2011). Despite the general appreciation of these compelling reasons, one of the macro-level issues that most researchers raised is the fear of *losing control* of exported samples. As I alluded to earlier, the concern is not only or even primarily in all cases about samples getting out of Africa but mainly about leaving the immediate environment of the sample donors and contributing researchers.

6.4.1. Researchers' fears

According to most of the KWTRP and NHRC researchers interviewed, although scientific collaborations are often based on a mutual agreement—which are sometimes spelt out in a material transfer agreement (MTA) — there are often concerns about who will ultimately control the management of the samples.

As illustrated by the quotes below, most researchers raised fears that local researchers and host institutions would be unable to control how the samples are eventually used once the samples and data leave the local institution:

> "Once the samples get out there, the local collaborators do not really have any control as to who uses it and if it is used and there has to be publications, who should be part of that publication so that is the limitation and that is the ethical side of it because there should be fairness in the; I mean attribution of the contributors to generate knowledge out of that" (Navrongo: RES13).

> "The fears of collaboration would be that you'd be sending people materials and you'd be just a supplier of material commodity I guess and then all the added value is done by the researchers from elsewhere and they write the papers and you have no intellectual contribution" (Kilifi: RES03, Expatriate).

The fears expressed above are about the tendency for the host institution to become a 'supplier of samples' without recognition for their intellectual contribution, for example in authorship of scientific publications. Against this background, researchers expressed a general desire to determine the fate of exported samples. Although most researchers indicated that they were aware of what the samples are expected to be used for and how they are to be destroyed and/or used up, some reported that they are unable to account for these samples:

> "But it is difficult for me to say I know exactly where these samples are. I know there's one institution, three institutions, maybe four institutions in the US that actually work these up but I can't tell you exactly what is happening. But I know some of the collaborations and of course I should, I do know every collaboration but I can't tell you exactly what is the outcome of the on-going assays" (Kilifi: RES05, Expatriate).

This response suggests a lack of feedback on exported samples. This is surprising, because the expectation is that this would be considered in drafting MTAs between the collaborating institutions. As suggested by an NHRC researcher, this uncertainty over the fate of exported samples creates anxieties that they may be used for other purposes or analysis without the knowledge of the contributing researcher.

Furthermore, in the absence of feedback, local researchers might assume that they have samples stored in external labs when in reality they have been used up and destroyed after the analysis:

> "Scientists from the developing part of the world are usually apprehensive of the fact that downstream, some of the samples that they send to the collaborators would be used for various investigations and research that they are not aware of and do not benefit from. It all boils down to having the right agreements and understanding. Before you could use or intend to use what has been stored you need to know what is there. If you ship samples to be used for a primary study and after the study you are not told that so and so is left, you might be assuming that you have samples sitting somewhere, meanwhile it is not there" (Navrongo: RES01).

As a result of these uncertainties and anxieties, most researchers were of the view that it would be desirable to focus attention on strengthening local capacity to enable most of the analysis to be done locally and for samples to be stored locally as well. As suggested in the responses below, KWTRP and NHRC researchers feel some sense of responsibility towards the participants (and community) who donated the samples and consequently the need to control how and what they are used for:

> "We can't definitely be sure how the samples are really handled when we ship them so we have to keep them here under our own supervision so that we definitely know that we've collected these things, we are attached to the people, we know what is going on and our samples are here. If we want to do analysis we specify exactly what we want to do, we define how many samples are required we carry them and go and do the reports and then we still have it here" (Navrongo: RES07).

> "….the whole hassle of sending things when you can do it locally, I mean, it's the control bit I think because legal jurisdictions are bound by boundaries even I as investigator, I have responsibilities, when they are in my fridges here I can take responsibility, well that goes back to the talk around trust, I have to trust my collaborators who are receiving that they are going to do what we agreed, I think that if they are not going to do what we agreed it becomes very difficult to address that, so if I could avoid that possibility of a problem then, that's why I think samples don't have to be sent unless there is a very critical need" (Kilifi: RES02).

These views and the need for local control of samples have implications for emerging fields such as genetic and genomic research which require the export of samples to well-established laboratories in HICs for genotyping and the sharing of samples across research sites and countries. It highlights the need to find effective ways of addressing these local fears and anxieties while still advancing scientific research. It also highlights once again the important role of trust in research collaborations, which is discussed later in the chapter.

6.4.2. Research Ethics Committees' anxieties

Local researchers are not the only stakeholders worried about the fate of exported samples. As illustrated below, REC members in Nairobi and Navrongo expressed concerns about their inability to control what happens after granting approval for sample export:

> "…once the samples have left our jurisdiction we really have no control over it. And this is something that really we need to look into, how best can we control the samples that have left here, how best can we ensure that they're used for the purpose that they were taken and they're not used for another study" (Nairobi: REC04).

> "You can't have a policing mechanism over there; ..in the current situation one only has to rely on the integrity of the collaborators in the receiving lab. Other than that, I mean I am not sure what else one can do. You can go there and stand and see to it that the samples are analysed and then you collect your samples back. And so what really will you do apart from.. you can establish all the policy and legal requirements within you country, yes I think that is useful but that doesn't still give the opportunity to go to sleep once the samples leave the country" (Navrongo: REC01).

Currently, there are no mechanisms in place to determine the fate of exported samples. What I observed in Navrongo is that MTAs are not common and until recently were not required by the REC. As discussed in Chapter 4, (p94), a new requirement in Kenya is for a local scientist to accompany the samples to the external laboratories as a way of building local personnel capacity. Although it was not clear if this happens in practice, a REC member in Nairobi explained that this mechanism will also allow for research sustainability at the local level:

> "We feel that for sustainability of research … there should be somebody who would be able to continue spearheading and training others to continue with that intervention and to improve on any intervention that comes as a result of research" (Nairobi: REC00).

Other interviewees questioned the feasibility of this requirement and suggested that projects should be considered on a case-by-case basis. REC members expressed an expectation that although they are unable to monitor the fate of samples overseas, the host institutions could take responsibility for the action of their local researchers and keep the REC updated on the outcome of overseas analysis. This places an additional responsibility on the host institution and local researchers to ensure that their external collaborators are also accountable:

> "But when it leaves our jurisdiction, that is where we have no control over it, extra additional ethical issues arise. .. we always demand to know where it is going to be stored and who is going to be responsible for it out there. This is all in an effort to protect the participant to ensure that even though the sample has left our custody or our control, we transfer this responsibility to another person and another institution. It's always our belief that they will comply and use it for that purpose only but again as I said it is something that is based on trust" (Nairobi: REC11).

Data from this project indicates that RECs rely on the integrity of researchers to act ethically in the conduct of their research and to use samples in ways that minimize harm and maximize benefits to research participants and the community. The question remains to what extent research institutions are reliable and what measures are needed to make them more accountable? According to REC members interviewed, sample export, storage and future uses are emerging issues they are still grappling with, suggesting the need to identify effective ways of addressing these issues while also protecting the interests of all stakeholders, especially research participants.

> "….issues of sample storage and the future use of these samples are issues that are emerging and many [RECs] in Africa are learning how to deal with these things because many are still new within our context" (Navrongo: REC01).

Group discussions with the KWTRP community facilitators also highlighted the limitations of RECs to monitor the fate of exported samples:

> "If you talk about exporting samples, so long as it's being used for the right thing, for the right reason, that is okay but we don't know, currently we have no structures because I think I started by saying even when we talk about ERC, the ERC is there as an academic structure but there are no structures in place to say we are going to monitor to see what happens, you see" (Kilifi: group discussions with facilitators).

These responses highlight the local concerns and uncertainties surrounding sample export and the need to identify ways of ensuring that samples that leave the immediate environment of its donors and contributors are used only for agreed and approved research purposes.

6.5. Lack of recognition for local research contributions

A major concern for most researchers is the lack of recognition for their contributions in scientific research collaborations. Interestingly, while the literature highlights issues related to ownership of samples as a major concern (Andanda 2008), data from my interviews suggests that key stakeholders are much more concerned about being appreciated or recognised for their contributions. It was not very clear from these interviews exactly what *recognition* local researchers expected, but most alluded to authorship in scientific publications and the fear that someone else might end up taking the credit for the research results. For example, NHRC researchers cited instances where some collaborators have used samples and the data obtained through the analysis without acknowledging the local researchers and the community:

> "Internally I have had occasion to see how the samples are handled in other labs within country where we have collaborated where the people just pick aliquots of the sample, run their studies, you meet them in international circles, they are making presentations, you see the map of Navrongo and you know that the presenter does not even know Navrongo but you know that this work has come from samples that were taken from a study you were part of, we are not acknowledged, the community, the participants are not acknowledged" (Navrongo: RES05).

> "In that one, it was a collaborative research between [X] and [NHRC] but apparently all the documentation was in the name of [X] and even though this was the trial site, almost all the documentation was in the name of [X] and even when publications came out of that trial, some of us who had worked on that project tirelessly were never included in the publications" (Navrongo: RES15).

It is worth noting here that the collaboration referred to in the above quotes involved two research institutions within the country (Ghana), one with more capacity and bargaining power than the other. Strikingly, while much of the discourse in the literature about research collaborations involving HICs and SSA have highlighted the potential for exploitation because of the economic disparity between the two settings, responses from this research suggest that this is possible in south-south collaborations and collaborations within country as well, depending on the relationship between the collaborating institutions. This finding has implications for initiatives such as the Human Heredity and Health in Africa (H3 Africa) (Tan 2010) which seek to promote scientific research collaborations within Africa. My research suggests that while initiatives like these are likely to focus attention on capacity strengthening in Africa, issues such as local control of samples remain pertinent. As illustrated in the following quotes, this issue persists as long as the samples are leaving the immediate environment of the donors and collectors of the samples:

> ".. it doesn't really seem to mean that the concerns or the issues will be resolved if samples do not go beyond the boundaries of Africa. As long as the sample leaves your immediate lab, I mean the issue of control and access that we are talking about is the same. I don't think it is easier to go to South Africa than it is to go to New York. I think in many cases it is even easier to go to New York. But that really is not even the issue. I believe the issue is that you have sent samples to somebody in your mind this is what the samples are going to be used for but there is no way you can ensure that the samples are used only for that particular purpose .. whether you are sending the samples….from here [Navrongo] to Accra the concerns are the same" (Navrongo: REC01).

> "I am an African, a very proud one but I think it's naïve of us Africans and sometimes I think we must not make the issues African or non-African, we should be a bit more objective than that. If I must handle the samples and test them, I must do so not because I am an African but because I would deliver the expected good result, you know it must not be about Africa or non-African to my mind" (Kilifi: CSK01).

The point being made above is that the issue about local control of research samples and proper recognition does not disappear because the collaboration is just between African institutions. As I highlight throughout this chapter, the data suggest that a lot depends on how these research collaborations are formed and managed and the relationship between the collaborating institutions. Some researchers suggested that because of past tensions, controversies and growing debates surrounding research collaborations, external collaborators in HICs are less likely to engage in exploitative research collaborations since '*they also have their careers and reputation at stake'* (Navrongo: RES 17).

6.6. Fairness and benefit-sharing: whose benefit? What benefit?

As discussed in the literature review chapter, (p32), a recurring theme in the debates around scientific research collaborations is benefit-sharing. Given the huge economic disparities between HICs and LMIC collaborators as well as the long history of exploitation in the context of international collaborative research it has been argued that benefits that are derived from the use of samples should be shared fairly between the parties involved in designing and carrying out the research and that researchers have an obligation to provide benefits to the community (Gbadegesin and Wendler). The principle of benefit-sharing is often discussed as a guide to avoid exploitation in international research and requires that each party is given an equal share in any potential economic benefit (as well as scientific reputation) to be derived from discoveries made from human samples (Upshur, Lavery et al. 2007).

As the research enterprise is increasingly being seen as a public good, there are concerns that sample export will further widen the existing inequalities between African and HICs. This is where we see a direct link between the issues arising at the macro-level and the micro-level issues, discussed in the previous chapter. While interviews with the researchers, especially principal investigators in Kilifi, highlighted the progress made to strengthen the capacity of local scientists and to improve laboratory infrastructure, interviews with the RECs, the community facilitators and fieldworkers painted a more complex picture. There were indications that there was a kind of gradation in how benefits are shared in research collaborations. External researchers and collaborators get the largest share, followed by local researchers and host institutions including other research staff – who may only benefit from having good salaries – leaving research participants and local communities at the bottom of the ladder:

> "The benefits of collaborative research stops at the local institution, ...by the time it gets down to the community they virtually will not have benefited except for the period of the study. Because like I said the trickle down effects, who are the PIs, who are the co-PIs and then it comes down to maybe people at a little bit senior level, the field worker sometimes, they are mostly the beneficiaries from the studies and even they, maybe those at the top, because you have publications, your name will become big, some people will use it for studies like you are sitting down and interviewing me, to get degrees, the community I don't think would [laughs] because maybe if the community will benefit is that you are family so when you come with your big car you can take them to town" (Navrongo: RES05).

However, the question about benefit-sharing is how it is defined by the various parties involved in the collaboration, what counts as benefit (either direct or indirect) and what counts as fairness. For example, what is often highlighted in the literature as benefits to research participants and to a limited extent the local community are benefits provided during the research – ancillary care – and post-trial benefits, such as the drug or vaccines that may be available to the population after the research (Merritt 2007).

Although previous studies in these settings have reported a general appreciation from the community of the local institutions' research activities (Molyneux, Peshu et al. 2005; Gikonyo, Bejon et al. 2008; Kamuya, Marsh et al. 2011; Tindana, Rozmovits et al. 2011), fieldworkers and some researchers I interviewed are concerned that research participants and the community, who are sample donors and who bear the risks of research participation, are not receiving their due share. For example, some REC members in Nairobi suggested that despite the increasing number of research projects carried out over the years, not much has changed in the lives of the people, especially for studies such as genetic and genomic research that have no direct immediate benefits to the local community:

> "These genetic studies just exploded on the KEMRI ERC soon after the human genome [project] and people realised that you can find out this, you can find out that, you can find out the other. But for goodness sake Paulina all those things they are finding out in this collaborative research have got nothing to do with improving lives in the sense that it doesn't change our lives a dot. You don't get more flour to make Ugali, you don't get less sick, your children don't get better, and really life remains the same. The people who are giving the sample may not benefit, the benefit of the study is for thirty years from now, they'll be dead maybe, so maybe their children will benefit. But how can the institutions benefit, how can the scientists benefit"? (Nairobi: REC02).

Thus, there seem to be some emphasis here on ensuring that collaborative research projects lead to some improvement in the lives of people in the local community. This is in line with suggestions made by some scholars on the need to focus on justice issues in international research. My interviewees' recommendations on how this should be achieved in practice are discussed in Chapter 7.

6.7. The role of trust in institutional relationships

As became apparent in the previous Chapter (5) in relation to micro level ethical issues, trust is an important motivating factor in research participation in Kilifi and Navrongo, which is based on the long-term relationship between the host institution and the community.

This also applies to institutional relationships at the macro-level. For, in the absence of mechanisms to determine how exported samples are used by external collaborators and the uncertainties surrounding the export and future uses of samples collected in the context of research consortia, researchers and institutions in my interviews reported that they have to resort to trusting their collaborators to use the samples in ways that do not undermine the contribution of host institutions and their communities:

> "You can't be too sure. And you can't also send policemen to be watching them while they are working on the samples so there's a need for trust, yeah a need for trust and a need to have legally binding documents such that they would know that if they did something else with the sample and it is discovered they could be taken on" (Navrongo: RES03).

> "I believe the concern of many scientists is that once the samples leaves your boundaries you virtually have no control over it but if we can be confident that our colleague elsewhere is not going to use these samples for any other thing other than what we have agreed on I don't think that anybody would be worried that I have to send samples to South Africa, or I have to send samples to the USA or London or wherever" (Navrongo: REC01).

Thus, a chain of trust is a key feature of the collaborative projects taking place in Kilifi and Navrongo. In relation to samples, research participants entrust their samples to local researchers who in turn transfer these samples to collaborators, trusting that they would be used only for agreed purposes. As suggested above, RECs also tend to trust researchers to use samples only for approved research purposes. These trust relationships seem to be based on the relationship between the various stakeholders, the uncertainties surrounding current scientific practices with samples such as export and future uses of samples and the limitations of existing governance mechanisms.

Trust also comes with risk. According to some interviewees, if society could rely on all research actors being honest in the way research is conducted and how participants and communities are treated, there would be fewer concerns about research collaborations and specifically on sample export and storage. However, because we do not live in an ideal world, my interviewees argued that it is important to put in place the necessary checks to guide responsible conduct of research and the handling and uses of samples.

> "Well, I wish that the world was honest, then we would not have any checks, people we are going to write this and say, okay get run and that's all they, but unfortunately the world is not like that , you know, the world is not like that, humans can be unscrupulous" (Kilifi: CSK01).

> "You have got to know that science is not the be all and end all. You have to have rigorous accountability and systems in place to make sure that yes, okay, trust is there but also you have to have all the formalities in place as well just to ensure that the pros and core communities, all the documentation qualifies and has passed through and has been approved by the various different communities" (Kilifi: CSK07).

As a result, both researchers and REC members across the two research settings argue that appropriate custodianship of samples will be best served through effective oversight and accountability. They also suggest that the closer samples are to donors (the community) the better, because of familiarity and trust in such processes. Responses from this research also appeal to openness, transparency and trustworthiness in research collaborations to ensure that the interests of all parties are protected. This further supports the need to identify innovative models of engaging all stakeholders in the research process taking into account these background relationships.

6.8. Kilifi and Navrongo: what sets them apart at the macro-level?

In my methodology chapter (Chapter 3), I justified my decision to present the data for this research around themes rather than presenting the data from Kilifi and Navrongo separately (page 73). This was due to similarities in the responses from both research sites. Besides, the aim of this project was not to compare the KWTRP and NHRC but rather to solicit a broad range of views from various stakeholders on the ethical issues arising from sample export, storage and their future uses. This worked well in Chapter 5, which discusses the micro-level and local issues. In this chapter, while the macro-level issues were in fact largely similar across the two sites, there were some significant differences in the stakeholders' perspectives and responses to these issues. The data suggest that two main factors could account for these differences; one is the level of local capacity in each of the two centres and the other is the (related) degree of the institutions' power to negotiate with their collaborators. Having explored the similarities above, in what follows, I now discuss these key differentiating factors.

6.8.1. Building local capacity

As discussed in Chapter 4, one compelling reason for sample export and overseas long-term storage is the lack of capacity at the host institution. While none of the interviewees advocated for a ban on sample export and storage, many of them highlighted the urgent need to strengthen local personnel and infrastructural capacity. Researchers in Navrongo believe that issues about local control of samples could be resolved by strengthening host institutions' ability to carry out required analysis locally.

In Kilifi, most researchers suggested that the KWTRP has avoided major ethical issues around collaborations and sample export because of the efforts made over the years to build local capacity and to maintain trust relationships between the institution and its collaborators and between the institution and the community. They expressed the view that some of the issues that arise in sample export are related to histories of bad collaborations and ideas of exploitation, both of scientists and of populations. Researchers believe that if efforts are made to strengthen the personnel and laboratory infrastructure of host institutions, it will give them the bargaining power to be able to control the use of research samples locally:

> "I think that once you develop expertise and you are able to do things well you will be attractive to collaborators and you will have choices and what am saying is that, research centres in Africa are having choices" (Kilifi: CSK01).

Also, interviewees from Navrongo agreed that having the right kind of capacity places the host institution in a better position to attract funding and partnerships, which seem to be the case in Kilifi. A recent published report suggests that Kenya is one of the few African countries where capacity for conducting genomic research exists (Thorsteinsdottir, Melon et al. 2010). As discussed in Chapter 4, the KWTRP has senior–level scientists (currently six UK professors and a Kenyan professor) who are leaders in their field and have contributed to building the capacity of a growing number of Kenyan scientists who have attracted their own competitive grants. Also, the institution has the capacity to store and analyse large collections of biological samples locally. In contrast, NHRC researchers highlighted the lack of some basic laboratory infrastructure which has led the institution to play assistants to some collaborators in-country. For example, at the time of collecting data for this research, the NHRC lacked PCR capacity and only one member of staff (a recent PhD) had some expertise in genetics and genomic research. NHRC researchers indicated that they could have directly attracted mutually beneficial partnerships with external collaborators, if they had the right level of capacity to contribute to major scientific projects.

As I will discuss in the next chapter, building local capacity requires commitment from funders, strong institutional leadership to negotiate and a commitment from all partners.

6.8.2. Host institutions' negotiating power

Another differentiating factor between the KWTRP and NHRC is the institutions' negotiating power. Most NHRC interviewees were of the view that some of the practical ethical issues arising from research collaborations and specifically from sample export and long-term storage are the result of the limitations of the host institution's ability to negotiate for fairness in collaborations.

On the other hand, KWTRP researchers expressed the view that what sets the institution apart is the negotiating power that it has built for itself over the years and some of the strengths in capacity highlighted above. They therefore have a choice when making decisions about their scientific collaborations and decline those that do not favour them. These include research projects that have already been developed elsewhere without local inputs and those that only seek to collect samples to be exported elsewhere:

> "I think that we refuse to especially participate in programs which come already made and I am not speaking from reserve I am speaking about even very recent experience where we have a protocol going on and collaborators come with a different idea and we review it, and we see that it's not in our best interest we say this will not fly and this will change. When they insisted we said fine, thank you very much, it will not happen here" (Kilifi: RES09).

> "So I don't know what the secret to collaboration is but certainly you need to be quite careful who you collaborate with and you need to set down the ground rules in advance. And I think certainly with the programme grant and the work we've done with [X institution] we've always sat down together and made decisions about where we were going before that formation of particular projects that we wanted to undertake and there's never been any concern about the division of you know names on papers or authorship, things of that sort, there's never been a significant issue. I think when you're dealing with sensible people" (Kilifi: RES07, Expatriate).

However, not all research institutions in Africa have the same kind of bargaining power. As indicated earlier in the chapter, in the case of Navrongo, researchers I interviewed highlighted the Centre's limitations in negotiating for fair collaborations. As a researcher in Navrongo explains:

> "…the local institution does not have the muscle to insist on what should rightly be their share because as you know, we are competing with other institutions for the same funding and if you are so rigid, you may not even get the funding to start with. I think that, that has been the issue and also because we have to largely rely on donor funding, the local government does not provide enough support so the leadership of the research institutions do not really have the will to insist so hard on what they think is a fair collaboration so sometimes, we go into collaborations then later on, we realize that it is underfunded but then at the time that we were going in for it, we didn't have any option anyway. The funding available is very few and we have so many competing organizations looking for the same funding so that does not allow people to be very fair and very thorough in what they insist on" (Navrongo, RES13).

The above response highlights several issues that may limit the host institutions' ability to negotiate for fairness in research collaborations. These include the competitive nature of current funding mechanisms, lack of core funding, the heavy reliance on external funding and the limited support from local government, all of which have contributed in the limitations in the bargaining-power of the institution.

Role of Institutional leadership

My data suggest that the ability of the host institution to negotiate for fair research collaboration also depends on the leadership of the host institution. There was a general perception that strong and visionary institutional leadership has allowed KWTRP to take a strong stance in negotiating its scientific collaborations. A REC member in Nairobi suggested that individuals in leadership positions, with the right level of networks and connections, can potentially influence funders to invest in locally initiated projects:

> "Let's start with Professor X, I think individuals do make a difference, even if they're not Africans, they can also influence guidelines, they can even go back to the people giving the money and tell them, if we want to stay here for long then we need to make a difference where people see we are making that difference" (Nairobi: REC02).

There was a general appreciation of the KWTRP leadership and the efforts made to secure strategic grants to strengthen local personnel and infrastructure capacity. Most researchers in Kilifi and Navrongo were of the view that strengthening host institutions' negotiating power through building of capacity will ensure that 'African scientists are not left with only the crumbs of the samples' (Navrongo: RES13).

6.8.3. Sustainable financial support for host institutions

Although both KWTRP and NHRC have grown over the past decade, there are significant differences. The historical evolution of the two research sites, Kilifi and Navrongo are different. As discussed earlier, in Kilifi, there are very senior expatriate researchers who have lived in Kilifi for several decades and who are leading research teams and building capacity in the field. With a growing local scientific staff, this has also made them eligible to apply for a wide range of grants, in addition to long term support from the Wellcome Trust. As part of the institutions' strategic award, fifty (50) PhD students are currently being trained in Kilifi compared to twelve (12) PhD students in Navrongo who had to compete internationally for studentships. The NHRC has no expatriate staff and at the time of conducting this study, only three members of staff had PhDs.

The NHRC and KWTRP's research activities are mainly funded by external sources – also in the case of KWTRP, such as the NIH, Wellcome Trust and the Gates Foundation. Heavy reliance on external funding affects the sustainability of research activities. In most cases, NHRC competes with other research institutions for funding or collaborates with bigger institutions in-country as sub-contractors to apply for international research grants. These kinds of arrangements sometimes pose difficult challenges to the institution in terms of how much of the research process it can control.

KWTRP is apparently better placed to negotiate for fairness in collaborations in part because of its relative financial security – which arises out of its close institutional link with the Wellcome Trust. This suggests that strong financial backing can play a vital role in empowering research institutions in Africa. However, study responses suggest that even in the case of Kilifi, there are concerns about inadequate funding mechanisms for project grants, especially with the short term nature of many grants.

It is however worth noting that despite the challenges that NHRC researchers raised about its financial limitations, the institution's profile suggests that it has been able to attract very important international research collaborations and is considered one of the leading research centres in Africa. As discussed in Chapter 4, this could be attributed to its strengths in carrying out community-based and field epidemiological studies.

6.9. Equal partnerships between unequal partners: a myth or reality?

One of the most influential documents for research in developing countries is Emanuel et al's elucidation of 'benchmarks' for ethical research, which highlights the centrality of collaborative partnerships (Emanuel, Wendler et al. 2004). The principle of partnership requires, among other things, the 'sharing of responsibility for assessing the importance of the health problem and the value of the research to the community' (*ibid, 931*). Study interviews suggest that most researchers enter into research collaborations with an expectation of this notion of partnership, with the host institutions – where the burden of disease is greater – having a strong voice in how the research priorities are set:

> "…..we see that as an equal partnership, yes, so that study is driven by all three of us and so we also contribute different ideas and have different sort of strengths and different experiences. So you couldn't do it with one of us lacking or you know it would be a very different study to that extent" (Kilifi: Kenyan, RES02).

However, given the concerns raised above and existing inequities between institutions in Africa and HICs, the question that remains is whether it is possible to have fair collaborations between unequal partners – and whether the principles guiding these partnerships can be implemented in practice. Some researchers interviewed expressed the view that contrary to some of the concerns raised about possible exploitation in international research collaborations, equal and mutually-beneficial partnerships can be achieved between African scientists and their partners in HICs:

> "But through some sensible collaborations which are mutually respectful and have appropriate checks and balances and data flow and sharing built in then I think we've been able to move, as I say instead of moving nowhere I think we've gone 100 years in the last 10" (Kilifi: RES13).

Other responses suggest that equal partnerships are only achievable in collaborative projects that are locally initiated and led and those that are adequately funded. Some NHRC researchers suggest a trend of 'he who pays the piper calls the tune' which limits the extent to which local researchers are able to control the research process. While there is a general recognition that these scientific relationships have gone beyond what has sometimes be described in the literature as 'Cinderella and her ugly sisters' (Jentsch and Pilley 2003), researchers feel that much more needs to be done to bridge the yawning gap between African institutions and collaborating institutions in HICs. As illustrated in this response from an NHRC researcher:

> "Sometimes it's difficult because he who pays the piper usually calls the tune….but I think usually we are so dependent on the goodwill of our better endowed collaborators and when they are fair in their contracts then we benefit and when they are unfair and we feel that we need for example as a research centre we need trials to be able to continue to run, to do research, so sometimes we rarely say no to protocols which may even disadvantage us because sometimes half a loaf is better than none. So we end up not getting the better deal but we don't have a choice because most of the time these things are competitive in nature and sometimes you can't really pick and choose what you actually want. So there are so many of the studies in which we may have wanted more or a better deal but our hands are tied by the fact that it's competition and at times we just accept anything so that we can also continue with our research activities (Navrongo: RES08).

Researchers perceive successful partnerships to be based on trust, mutual respect, understanding and mutual interest. Thus, some stakeholders expressed their dissatisfaction with relationships where these features are absent and where external collaborators were seen to be exerting power over local institutions:

> "Now our colonial masters from the other side they have a totally different idea, they feel they're coming to help us. They say it quite openly "Without the millions of dollars we bring to this country there'd be nothing happening here." And some of them are more polite than others" (Nairobi: REC02).

Interviewees in this research have proposed a number of possible solutions for addressing the macro-level issues arising from sample export and long-term storage and for making scientific collaborations more just and mutually beneficial. These will be the focus of Chapter 7.

6.10. Conclusions

The aim of this chapter was to examine the macro-level issues arising from sample use, export and long-term storage. The data suggest that many of the issues arising from these scientific research practices relate to how research collaborations are set up, what and how agreements are reached and how research projects are eventually managed. Although there was a general appreciation of the benefits of engaging in international scientific collaborations, such as the opportunity it offers for local research institutions to conduct locally relevant research and to build capacity, researchers and REC members highlighted concerns that may arise in practice.

With regard to sample export, researchers expressed the potential fear of losing control of the samples and their inability to determine the fate of the samples. Some explained that although there are usually MTAs on how samples are to be used in external laboratories, there are no mechanisms for determining if collaborators actually use the samples according to these agreements.

As a result, there are fears that samples and the data obtained from their analysis may be used for other research purposes without the knowledge of contributing researchers and sample donors.

Other issues raised in the data include the lack of recognition for the contributions of local researchers and host institutions especially in the publication of results, as well as the limited attention given to local capacity building. Despite the growing recognition and efforts made by some research institutions to address this gap, my research suggests that many institutions in Africa lack basic laboratory infrastructure to carry out the analysis required in some projects.

It is encouraging that new initiatives such as H3 Africa aim to address the increasing demand for scientific capacity in Africa. It is however worth noting that this does not resolve some of the issues arising from research collaborations such as local control and recognition for contributions. The concern highlighted by the researchers is not only or even primarily in all cases about samples getting out of Africa but mainly about leaving the immediate environment of the sample donors and contributing researchers.

Strikingly, while much of the discourse in the literature about research collaborations involving HICs and SSA have highlighted the potential for exploitation because of the economic disparity between the two settings, responses from this research suggest that exploitation can also be perceived in south-south collaborations and collaborations within countries as well, depending on the relationship between the collaborating institutions. Some researchers suggested that because of past tensions, controversies and growing debates surrounding research collaborations, external collaborators in HICs are less likely to engage in exploitative research collaborations.

The macro-level issues discussed in this chapter highlight the difficulties in achieving fair research collaborations between unequal partners. It supports much of the literature raising concerns about the tendency for host research institutions in LMICs to be short-changed in these collaborations and their limitations in negotiating for fair deals. However, the data also suggests that the situation may be improving and shows that some research institutions such as the KWTRP are increasingly becoming self-sustainable and assertive in their research relationships and may potentially act as a model for how this might be achieved elsewhere. This has been made possible through scientific leadership and strong financial security in the host institution.

The stakeholders interviewed for this research argue strongly that local research institutions cannot and are not interested in working in isolation. Especially in the field of genomics and studies which require large numbers of samples, which are best obtained through large research consortia involving several partners in different countries, scientific research collaborations will increasingly become the norm. What they have suggested is that the fairness of these collaborations needs to be strengthened. This would require putting in place mechanisms to address the concerns of local researchers and host institutions, and ensuring that research is carried out in an acceptable and ethical manner and that the potential benefits of research are shared equitably between all the parties involved, including research participants and their communities.

Stakeholders interviewed in this study have proposed a number of solutions for addressing both the micro-level issues discussed in Chapter 5 as well as the macro-level issues discussed in this chapter. In the next chapter, I will be discussing these proposed solutions and the challenges.

Chapter 7: Stakeholders' proposed solutions and recommendations for best practice

7.1. Introduction

The aim of this thesis is to examine key stakeholders' perspectives on and responses to the ethical issues arising from sample export, storage and the future uses. In Chapter 4, I presented data describing the current and changing practices around these phenomena at the Kenya Wellcome Trust Research Programme (KWTRP) in Kilifi and the Navrongo Health Research Centre (NHRC) in Navrongo. Then, in chapters 5 and 6 I discussed stakeholders' views on the practical ethical issues arising at the micro and macro levels. These include challenges with obtaining valid consent, concerns about sample export, cultural sensitivities around the uses of blood samples in research and the limitations of host research institutions' negotiating power in international scientific research collaborations.

So far, the data suggest that while stakeholders are not necessarily against the use of human biological samples in scientific research, they are concerned about how this enterprise can be conducted in an ethical manner. Taking this as my starting point, in this chapter, I will focus on their proposed solutions and recommendations for addressing the micro and macro level concerns discussed in the previous two chapters and investigate their views about what might count as best practice for international collaborative research more generally and sample export, storage and their future uses in particular.

Based on my analysis of the data and emerging themes, I have structured this chapter around five broad headings. These are; capacity building, better consent processes, more effective research ethics committees (RECs), fair scientific collaborations and sustainable local and institutional relationships.

Under these headings, I discuss the solutions proposed by my interviewees at both the micro and macro level and also examine whether stakeholders' arguments for these solutions are practical and realistic.

7.2. Sustainable capacity for scientific research in Africa

To address the ethical issues arising from sample export, storage and their future uses, sustainable capacity strengthening featured as a key solution in my interviews. This supports consistent calls in the literature for more focus on research capacity development in sub-Saharan Africa (SSA) in the context of international research collaborations (Nchinda 2002; Schulz-Baldes, Vayena et al. 2007; Burgess and Sulzer 2010; Gezmu, DeGruttola et al. 2011). Interviewees argued that building scientific capacity would enable African scientists to 'take the front seat' and generate good scientific data to address local health problems. Although there has been significant progress over the past two decades (Greenwood 2006; Kilama, Chilengi et al. 2007; Kitua, Corrah et al. 2009) and interviewees' accounts highlight existing and growing scientific capacity in Kilifi and Navrongo, they also suggested that much more needs to be done to sustain capacity development.

It is worth noting that no interviewee advocated for a *complete* ban on sample export, storage and their future uses. This could be attributed to the fact that most had direct links to research, either as researchers themselves or as facilitators or gate-keepers of research and thus appreciated the increasingly global nature of science and the importance of these research practices. Nevertheless, almost every interviewee expressed the view that it would be desirable for host research institutions to build the necessary capacity to conduct the required sample analysis locally and to minimise sample export; to store samples locally and control what and how they are used and to optimize the future uses of samples locally.

7.2.1: Personnel and infrastructure capacity to analyse samples locally

Most interviewees suggested that international research collaborations should provide more opportunities for strengthening the scientific capacity of host African institutions. They suggested not just the technology and infrastructure needed for the analysis but also training and retaining local personnel with specialized skills to contribute to the conduct, analysis and publication of research locally. Researchers expressed the view that it is more efficient to conduct good research if the required capacity is available locally:

> "….it's much easier for us to do good science if we have the capacity to do it here. I think we move forward faster if we have up to date technologies here and staff that are suitably qualified to do it. … we're also keen to make sure that we're developing local scientists so it's not the science of the project that's governing it, it's the need for developing a group of scientists for the future of this region" (Kilifi: RES07).

There were sceptical responses from most community facilitators, community representatives and fieldworkers as well as some RECs about the lack of local capacity being used as a justification for sample export, discussed in Chapter 4 (p88). As suggested in the quotes below, some could not comprehend why the required equipment could not be planned for and purchased for local analysis, considering the continuing infrastructural growth of these institutions:

> "…it's a matter of planning for the research, if …you want to do a test that requires you to have a machine that cost you 10billion, just budget for that machine first (laughs). .. then start budgeting for the research because I can't believe the 20 years we have been here there is a machine we have not been able to buy that costs like billions of money, because those 2 buildings the one that was built there and the other one that is coming up, I can't believe there is a machine that costs more than that" (Kilifi: Cfs).

> "..there should be a period of time if these kinds of analysis are going on over a period of time then that capacity should be gradually built locally, especially because people know the kind of studies that they do, they know the kind of analysis that would be required" (Kilifi: REC00).

Some researchers also suggested that strengthening local capacity that allows more local analysis and minimizing sample export could address many of the issues arising from this practice:

> "I think that there is a need to rather build capacity here. There is too much of these things becoming a problem lately, you know there's too much talk about what happens to samples. I believe all those things will cease to be a problem if the samples were to be analysed here" (Navrongo, RES03).

Capacity strengthening was also generally seen as a key way of enabling good scientific research to be conducted locally and allowing local researchers to have some control over research samples. Fieldworkers in both Kilifi and Navrongo called for the institutions' capacity building strategy to include participants' recruitment and sample collection stages as well. There were particular concerns that while senior-level scientists within the institutions are getting opportunities to advance their careers through training workshops and courses abroad, fieldworkers' capacity is not receiving the much needed attention. They claimed that this gap may be due to the lack of recognition of the important role of fieldworkers in research:

> "[the institution] should show that they really appreciate what we are really doing. The only thing that we need from them is appreciation, however it would come. Whether they are calling us, they are sponsoring us to go to take a course somewhere to really show that they really appreciate the work that you are doing. I think that one; it is kind of encouraging as well. ….. step there, the bosses would go" (Navrongo: FW01).

As suggested above, recognizing the important role of these front-line workers and maximizing opportunities for more training at that level would encourage them to perform their duties effectively. Whilst it is apparent that some forms of training for fieldworkers do take place at the institutional level and that before they are deployed into the field, they are taken through a series of workshops on the research procedures as well as communication skills for recruiting research participants, what was being suggested in these interviews is a call for genuine career development of frontline workers as well as this more practical task-based training, as reiterated in the following quote:

> "I think that all of us want to go ahead. We wouldn't like to be where we are, marking time all the time. We would like to go ahead so if there is any help somewhere just to push us ahead, I think to go forward a bit; I think that it would be good" (Navrongo: FW01).

This means that host institutions' capacity building strategy should be all-inclusive and enable frontline workers to grow in the field over and above simply being able to perform their current task well.

7.2.2. Capacity for local storage of samples

In addition to the forms of capacity-building described above, another proposed solution for addressing researchers' fears of losing control of samples is to store samples locally. Most researchers felt that this would also ensure that local researchers have the opportunity to easily access these samples and determine how they are eventually utilized.

> "..you can't go and take somebody's blood and leave it in a laboratory they don't even care about ... And that is why I think that we should store the [samples] locally. As we define what we want to do, the sample size of that analysis we just pick them as such" (Navrongo: RES07).

As I discuss later in this chapter, according to most interviewees, storing samples locally would also allow host research institutions to serve as custodians of these samples. They suggested that the interests of participants and communities will be best served if samples are stored as closely to the community as possible, thus, for exported samples, some researchers suggested that those that are not used up at the end of the analysis should be returned to the host institution for local storage:

> "I think that if an institution builds capacity to store samples, they should rather be stored there. In that case, the community has a sense of ownership as well because they know that their samples are not going outside, they are not going to be used for purposes other than the intended ones and they would feel more protected if they know that their samples are here" (Navrongo: RES19).

However, while arguing that local storage and custodianship of samples could potentially address stakeholders' concerns, it also requires proper facilities such as freezers, space and storage facilities to keep the samples in the best conditions for meaningful utilization. A laboratory manager in Kilifi explains that storing samples locally is a huge investment:

> ".. it is a very expensive business to maintain the samples but we feel that they are invaluable resource and why do we need to keep them for such a long time? Well, things change over time and for example, malaria, the whole pattern of malaria…, drug resistance, transmission, is changing over time and different pathogens are being identified. HIV for example, 20 years ago was not really well known in Africa really and there was very little in Kenya especially on the coast. Now it is a serious problem and there are emerging diseases as well and if that would be valuable results, we have to go back and say when did it actually emerge here so you can go back historically to samples and see exactly, when that virus or pathogen, when was it actually started to be seen" (Kilifi: CSKI07).

There were also calls for clear institutional policies and guidelines on what and for how long samples should be stored for and how these resources can be best optimized for the public good. Some researchers cautioned that the nature of some research projects will require the sharing of samples, including overseas sample storage and thus it is important for all research actors to keep an open mind and not assume that sample export will always lead to exploitation of contributing scientists in Africa. As illustrated in this quote from a KWTRP researcher:

> "..what is important is the whole research process and researchers' intentions not to do anything that will be detrimental to individuals and communities" (Kilifi: RES01).

I return to this point about the importance of fair research collaborations later in the chapter.

7.2.3. Optimizing the future uses of samples locally

Thirdly, and relatedly, interviewees recommended that local capacity should be strengthened to enable host institutions and scientists to optimize the future uses of stored samples. Given the compelling scientific rationales for the exchange of research samples across sites, discussed in Chapter 4 (p88), most researchers in my study were generally supportive of the idea of sharing samples and data with other researchers and institutions.

This is however on condition that they are adequately acknowledged for their contributions and there are opportunities for optimizing the uses of these samples locally. However, the spirit of sharing these scientific resources seems to be more acceptable in the context of research collaborations where the partners are known to, and trusted by the contributing investigator and can be made to account for the samples and data. The responses tend to support 'controlled access' to samples and data – which enables them to determine what samples are used for and who has access – rather than open access which might allow any researcher in the world to utilise them. There was a general view that acceptable practices would require all partners to be open and transparent in the research process. Some researchers cited the MalariaGEN consortium as an example of best practice:

> "Well in this context the only way that you can actually do anything with the data is if you've got people who have the capacity to analyse and interpret the data. I think we're trying to address that little by little although it won't happen immediately to increase the capacity of sites, local sites or African sites, Asian sites, wherever to analyse the data that emanates from their own studies. And have a fair chance of doing that before other people are able to access the data on their behalf and take any sort of credit for it" (Kilifi: RES13).

They suggested that MalariaGEN could serve as a model for other scientific collaborations such as the H3 Africa and could potentially resolve local researchers' fears about losing control of samples. However, such practices could only offer the potential to resolve the fears discussed in Chapter 6 p139, about losing control of samples if there is adequate scientific capacity locally for researchers to optimize the use of these samples.

Given researchers' views that no level of capacity at the host institution will be enough to exclude the export of samples, another recommendation is that local scientists should be given the opportunity to participate in analysis that are done in external laboratories as a way of building on local personnel capacity:

> "Maybe what I would add is the analysis should involve capacity building in developing countries where with each transfer if there is an identified young scientist who can develop capacity by developing the analysis and being part of it then slowly the developing world could begin to narrow the current yawning gap in terms of research between developed and developing countries" (Navrongo: RES01).

> "I think that the balance is very clear if we can always train people. So if you're going to ship samples to a lab in Oxford for example, I think the person to work on that sample should be someone from here because the technology transfer will only come from having local capacity to do the kind of work. I think the balance right there is insisting that that there should be an element of capacity building" (Kilifi: RES08).

As discussed in previous chapters, it is an institutional requirement in KEMRI for a Kenyan scientist to accompany samples to be exported to external laboratories (see p94). However, some researchers and RECs felt that while this requirement has the potential to provide more opportunities for strengthening local capacity, it may not be feasible in all research projects involving sample export.

Researchers and RECs also acknowledged that even if local capacity were strengthened, sample export will continue to be a key feature of international scientific collaborations because of other reasons, such as the need to compare results. It is therefore important for host research institutions and RECs to recognise these compelling scientific reasons and not make rules that may unnecessarily hinder the research process.

> "Ethics committees should not just flex their muscles because they have muscles, I think they should flex them judiciously and what we are saying is yes, they need to protect these things, they need to give approvals but those approvals must be based on the reasons why these samples should be allowed out, if that is a good enough reason, then the ethics committee in fact rather than banning they should be a facilitator because it's in the interest of the ethics committee also that science moves forward" (Kilifi: CSKI01).

While appreciating the progress made to strengthen the capacity of many African research institutions, most researchers recommended a more sustainable capacity strengthening strategy that will allow these institutions to keep pace with advances in science and technology and also place them in a better position to negotiate with their collaborators:

> "But the bottom line is to build ourselves up, I mean the labs they have there, our dreams should be to be able to have parallel labs here or similar labs and with that I think we will be calling the shots, because we already have the samples and they don't have the samples they have the labs once we get the labs here we will have a good step in all the negotiations with them and in all projects that we bring into the institution, we should see how can this project give us much better off in achieving our goal of self-sufficiency than we were before starting that project. I think that is the way we have to go" (Navrongo, RES17).

A REC member suggested that it will also require national policies and proper implementation processes that make local capacity building obligatory in all international research collaborations:

> "Our position as an ethics committee is that researchers have an obligation to do capacity building here. So the first thing we look at of course is whether we have the capacity ourselves because sometimes a researcher might say there is no capacity. There may be no capacity in KEMRI but the capacity is there in the country, we would then say no you are not going to take it out because it can be done at this place (Nairobi: REC11).

A recent initiative, H3 Africa – described in Chapter 2 (p29) – is timely and could potentially boost scientific research capacity in Africa. However, based on the issues discussed in the Chapter 6 about concerns even within south-south collaborations, some of the challenges with sample export are not likely to go away simply with building local capacity. There are other issues at the micro-level – discussed in Chapter 5 – that cannot be addressed this way. Thus, while capacity building was generally seen as a key way of addressing these ethical challenges, interviewees also highlighted and emphasised the importance of other complementary requirements such as better consent processes, ethics oversight and fair research collaborations, which I focus on next.

7.3. Better consent processes and community engagement

As I discussed in Chapter 5 (p103), one practical ethical challenge arising from sample export, storage and their future uses relates to the difficulties in obtaining valid consent for research participation. According to most interviewees, the achievement of valid consent (or refusal) is often hindered by the general lack of research understanding, local worries about what samples are used for, the uncertainties surrounding future uses of samples and the perceived trust-relationship between the local community and the host institution, which may affect the validity of consent to research participation.

According to most interviewees, against this backdrop, a key solution to addressing these micro-level issues is to develop better consent and community engagement processes. These include; demystifying the scientific research process to improve research understanding, redefining current consent regimes for the storage and future uses of human biological samples, identifying effective community engagement strategies to address local concerns and finally; ensuring effective feedback of research results to participants and their communities.

7.3.1. Demystifying the uses of samples in research as a way of addressing fears and anxieties

> "What seems to work very well is the use of public meetings, communications group to demystify science" (Kilifi: RES01).

A common response from most interviewees across both Kilifi and Navrongo is the need to find innovative ways of improving research participants' understanding of scientific research more generally but particularly projects that involve human biological samples. Interestingly, most of these proposed recommendations focus on engaging the wider community and not just individual participants. They recommended that one way of doing this might be to expose host communities to the analysis done in the laboratory and what actually happens to the samples from each stage of the research process – from the *village* to the laboratory.

For example, a REC in Navrongo recommends using videos of the analysis process as part of the consent process. This is a strategy that is already being experimented with in Kilifi. Most interviewees felt that this approach to seeking consent could help potential research participants to understand what it means to collect a quantity of blood from a participant and to visualize how these samples are actually analysed:

> "...I think we need some kind of audio visual kind of demonstration of the process of taking the sample from the research participant to processing that sample and establishing what really it is we have found in that sample and then how the rest of the sample that we have taken is handled for people to physically and mentally imagine what the samples we take from them go through" (Navrongo: REC 01).

A researcher in Kilifi explained that in the context of research on parasites, using audio-visual tools may be helpful in breaking down the science to enhance participants' understanding:

> "We could provide a view of it visually that shows what it actually consists of. But I guess that would be slow magnification of seeing all the cells in it and then seeing parasites in the cells. It's no good just showing pictures of parasites because that's too abstract but it needs to be seen in context so you'd need to see, a slow magnification of that red liquid resolving into individual cells and then, maybe even a microscope enabling you to see it as well" (Kilifi: RES03).

NHRC researchers also suggested *open days* for local residents to visit the institutions' laboratories. They expressed the view that such an approach could also dispel local rumours about blood selling:

> "We need to go beyond just talking to them but maybe even invite people from some of the communities to come and visit our laboratories. … there may be an open day where we bring people from the communities, they should come and see what really happens, at least for those ones that we are doing analysis here, come and see how their blood ends up so that it can help to dispel some of the worries and fears that they have. Otherwise those things remain entrenched and it has some implications for the work that we do" (Navrongo: RES03).

Noteworthy, laboratory tours are already being utilized in Kilifi as part of training programs for the KEMRI community representatives (KCRs), described in Chapter 3 and for chiefs and opinion leaders and school kids (Kamuya et al 2013; Davies et al 2012). Most interviewees in Kilifi viewed this process as quite successful as it has assured the community that the KWTRP is not involved in any kind of devil-worshiping, a major concern discussed earlier in Chapter 5:

> "The KCRs normally assist us in explaining where we keep our samples because they come for training here, they're taken round for a tour, so they get to see the labs and the freezers and they get to see that the samples are being frozen. So they really assist us in explaining that [to the community]" (Kilifi: RES06).

While fieldworkers and community facilitators in Kilifi also viewed these tours as an effective engagement tool, they were concerned about the limitations of targeting just the KCRs since they may not be in a position to disseminate their observations in the laboratories widely to the community, which raises a question of the representativeness of KCRs:

> "I think the number compared to the community is like a drop in the ocean so that the changes that we are expecting from the knowledge that we are trying to impact on the community, I think is coming very gradually but slowly so I think that it would take some time for everybody else to be aware" (Kilifi, FW01).

There was also a general recognition that it might not be feasible to get every local resident to visit these research laboratories. Also, this approach might serve more as a tool for engaging the wider community about the institutions' research activities more generally than for individual research projects. According to some interviewees in both settings, one way of addressing the challenge of bringing the community to the laboratories might be to take the laboratory closer to the village through the use of video documentaries that trace the journey of the samples from the collection stage, through the analysis in the laboratories to how they are exported, stored locally or destroyed at the end of the research. This is similar to a video project started recently in Kilifi to improve participants' understanding of research involving blood samples. [15]

As was seen in Chapter 5, some interviewees suggested that some of the concerns around the uses of samples in research are culturally deep-rooted and stakeholders felt that these concerns were not likely to be resolved with more education and exposure to the analysis of samples.

[15] At the time of conducting the interviews for this research, Mr. Alun Davies of KWTRP was involved in a video documentary project which traces the journey of the samples from the village to the laboratories. This could be extended to include sample export.

However they still felt that researchers have a responsibility to explore these innovative approaches to enhancing research literacy in these research settings:

> "For our particular setting, the illiteracy level is very high and therefore these misconceptions would be there. The culture is very rich. People believe in certain core values and there is some kind of thinking that people have been brought up to go through and so they would naturally move those thoughts into research and our duty is to try to diffuse that. Try to ensure that community members appreciate what we are doing. If it simply means that going to community members, having a durbar and showing videos and having an interaction with them for them to understand what goes on, then we have to move to that extent rather than denying them information that is rightfully theirs" (Navrongo: REC03).

> "..it's going to be very difficult for, particularly illiterate or semi illiterate participants to appreciate all these complex issues about genetics, data protection, issues of confidentiality, so it always remains doubtful to me in my mind whether you can truly get an informed consent for future storage and use of this, particularly given the African context" (Nairobi: REC11).

To address participants' fears about the quantity of blood samples obtained for research, this key informant in Kilifi had this to say:

> "I think there's got to be a balance here, on the one hand we know that to enjoy health and have good medical care…..research has to go ahead to develop tools and this knowledge that is required and for research to go ahead it needs samples. On the other hand I think as researchers we must not therefore use this as a blackmailing tool to the community and demand blood as if we're vampires (laughs) I think we've got to be very sensitive and very judicious as to how much blood we get" (Kilifi: CSKI01).

He further indicated that in Kilifi the current practice is for researchers to justify 'every drop of blood' by explaining and describing in research protocols the exact tests and analysis relevant for a particular study. This is also increasingly being required by the ethics committee in Nairobi. Thus the recommendation being suggested here is for researchers to recognise the fears and anxieties that research participants and their communities have about the uses of blood and only collect what is necessary to address a research question. Anticipating these fears will also enable researchers to plan to address them adequately through the consent and community engagement processes.

Participants' right to better information about sample export

According to most interviewees, quite apart from its role in addressing fears, better consent processes also mean providing adequate information to potential research participants on all relevant aspects of the research including where samples will be analysed. Interviewees argued that the whole premise of informed consent is to declare all relevant information about the research so that participants can make informed decisions about research participation:

> "Ethically, in research, everything should be explained to the participants so it is their right to know that their samples are being transported but also again, we should make sure that the information we give them is good information. We should explain all the processes on the consent and if they understand, then they agree that we do that" (Navrongo: FW01).

> "I think they should be told and that's what should determine whether consent is truly voluntary" (Nairobi: REC05).

Informing participants, about sample export is generally recognised as important, the right thing to do and a demonstration of the ethical principle of respect for persons. It was not clear if interviewees endorsed a general rule requiring explicit consent for sample export, such as ticking a box – an increasingly common feature in consent forms. However, most of them suggested that what was important is for potential research participants to have a good understanding of the scientific rationale for sample export. An NHRC researcher suggested that participants are generally receptive to sample export if they are informed and understand the rationale:

> "Things might change but for now, I don't think that the average person here really bothers where that sample is going in so far as s/he knows what is going to be done to that sample. So the issue is not where is the sample going? They are more interested in what you are going to do with the samples" (Navrongo: RES 19).

Other interviewees were more concerned about the consequences of not informing participants about sample export and how that may create more suspicion within the community. They generally felt that lack of information feeds into fears and suspicions, as discussed earlier, whereas more information, despite its limitations could reduce these suspicions.

Thus, they called for more transparency and openness in the research process to sustain participants' interest and trust in the process.

7.3.2. Redefining broad consent for future uses of samples

Another set of recommendations put forward by my interviewees relates to addressing the uncertainties surrounding future uses of stored samples and the validity of broad consent. There are two separate, although somewhat related, issues. The first is whether participants should give one-time prospective consent for future uses of samples and the second is whether broad consent – defined as consent to cover a broad range of future research activities – can be considered as valid consent.

Generally, most stakeholders, especially RECs, fieldworkers and community representatives, recommended a re-examination of these two approaches to consent for future uses of samples. While one-time consent was generally deemed acceptable, interviewees were concerned about the *broadness* of the consent and the potential for tensions to emerge between broad consent and valid consent. The majority view was that it is important to move away from granting *blanket* consent for future uses of stored samples. One suggestion was the need to have a separate consent form for storage and future uses of samples:

> "I believe there should be a separate consent form just for sample storage and for future use so that the person knows …it is clear from the outset that not only am I, providing the samples for this particular research but the samples would be stored in this place, therefore in the future you can still go back to this institution and say I no longer want my sample to be stored or I no longer want my sample to be used for future research. And also to give the person the opportunity to say yes I want my samples to be stored and used for research so there should be clear check boxes" (Kilifi: REC00).

According to RECs in both Nairobi and Navrongo, there are limits to the acceptability of broad consent. They expect researchers to state in clear terms what stored samples will be used for in future and not to be vague or too general, to avoid possible misuse.

One of the implications of this is that it would also require limiting the future use of these samples, for example, to the disease studied during the initial consent:

> "..what we have tended to do is to say future – "related"- research, so if you are collecting the samples for malaria research, that future research should be malaria related, it cannot be HIV or something that has nothing to do with the initial purpose for which the samples were collected" (Navrongo: REC01).

> "If they're going to say genetic studies it's too broad, we still try to pin them down because at the end of the day anyway for secondary analysis we will look at the merit of a proposal and say is there scientific value, is there benefit and we will stand in for the research participants and say we would, we have agreed upon their behalf. But that's for secondary analysis. So we are being very particular now about what you mean by future studies" (Kilifi, REC02).

As discussed in Chapter 5, there is a potential tension between this position and that of researchers who highlighted the unknown and open nature of future research, in the context of which these RECs' expectations and requirements for specifics appear problematic. There was therefore a general appeal from researchers for caution in the implementation of guidelines and policies governing these research practices:

> "If you're doing research you can't ever completely know what the next step is because if you did then you wouldn't be doing research, you'd just be exploring the known. But if you're exploring the unknown you can't anticipate, you can't anticipate everything you're going to do" (Kilifi: RES03).

In the same spirit and intent of respecting research participants' rights, some RECs, fieldworkers and community representatives recommended that efforts should be made to ask participants to re-consent to future uses of their samples and data. This was more acceptable than the notion of broad consent which does not require re-consent. However, there are some practical challenges with this requirement, especially long term prospective studies and samples that have been de-linked or anonymised. Recognizing these limitations one research assistant in Navrongo suggested:

> "My strong recommendation would be that we need to store samples for future studies and so if we are storing such samples let's not anonymise the samples to a point where we cannot trace back to the donors, those whose samples were taken, so that if there is the need to use those samples we should get back to those people and have their consent to use those samples for those studies" (Navrongo: RA01).

According to some researchers it might be impossible to trace research participants several years later for their consent, an argument rejected by other interviewees:

> "...you cannot say that it is very difficult. You see I think that it is just something that we researchers take to fool people, … I've worked here for ten years and I know that it's very easy, if you get up now, without even the NDSS you just know that I come from Navrongo and you know the type of work I do and you go to at least one or two or three people you will get somebody who will be able to direct you to [me]" (Navrongo: RES05).

There was a heated argument during the group discussions with fieldworkers in Kilifi about re-contacting participants and/or the wider community about future uses of stored samples. While some strongly argued for re contacting participants and relatives, others were of the view that given the complexities involved in tracing back to participants, broad consent should be accepted as valid consent:

> "Maybe during that time, my mother consented for the sample to be taken but now I am grown up and I have the right to decide what is to be done with my sample so it is good that we even if we trace the people even if you don't get the person, you would get a family member or anybody linked to that family to explain to the person" (Kilifi: FW01, Female).

> "I would go for the idea that after signing now and consenting for whatever is being done here plus the storage, the storage means that in the future, the stored blood can be used for any research. If I am to specify, I would say maybe malaria, maybe in 20 years down the line, maybe malaria would have been eradicated completely so the blood would be there idle but I would say that for any research that would come up, it should be used" (Kilifi: FW01, Male).

Other fieldworkers recommended opt-in and opt-out provisions on current consent forms – which has recently gained some attention in the literature on biobanks (Johnsson, Hansson et al. 2008; O'Doherty, Burgess et al. 2011; Giesbertz, Bredenoord et al. 2012) – as one option for addressing the uncertainties surrounding consent for future uses of samples:

> "Maybe on the consent form, there should be a part that gives opportunity to the respondent to indicate whether she does not care or whether she cares. For example, if the future comes and this research is about to begin, there should be contact so that she can tick if she wants to consent to that future research. So some provision for her opinion that when the future comes, they shouldn't come back to her or come back to her for her second opinion so both should be provided for in the consent form" (Kilifi: FW01).

Generally, while most interviewees felt that efforts should be made to re-contact research participants for future uses of stored samples, to enable participants to exercise their rights, they also recognised the practical limitations of this approach.

> "The question about informed consent as a governance mechanism is who is the custodian of the consent especially for samples that will be stored for several years, researchers could build some kind of contract with communities initially however, with whom will this contract be severally decades down the line?" (Kilifi: RES01).

Furthermore, most researchers and RECs recommended that the decision to return to participants and their community to re-consent to future uses of samples should be deferred to the local REC. This quote from a REC in Navrongo attempts a balanced view of what might be a reasonable solution to addressing the issue of broad consent for future uses of samples:

> "The issue of coming back to the initial or the original participant in the event that you are doing the future research on those samples I think it is a practical issue. Many or some of these participants may not be easily available on that future date and it might be even much better to just collect and recruit a new set of participants all together rather than tracing these original participants. But that doesn't mean that the researcher should have a blank cheque once the participants agreed to long term storage of the samples for possible future use. I think that the least that can possibly happen is for the ethics committee to require at least a review of the protocol and approve for that future protocol to be implemented. In that case, it would be the committees responsibility to determine how feasible it would be to go back to the initial subjects for consent to use the samples that they have previously provided, for a different study. If the committee decides that much as everyone would wish that we went back to the initial participants and get their consent now, this is not going to work and the look at the study that is proposed and are conceived that there is nothing in there that is going to hurt the initial participant in any way and they approve of it for me. I think that is appropriate but I don't think that once a researcher has obtained approval from research participants to store their samples for say 5 years for future research then after 3 years if the researcher decides that this question is important and I have these samples let me just use those samples without some ethics approval, I don't think that is acceptable" (Navrongo, REC01).

As we shall see later in this chapter, there is significant emphasis and reliance on the gate-keeping role of RECs in regulating the export, storage and future uses of samples. The question remains; do RECs have the required capacity to take on these responsibilities and are RECs actually in touch with the local context to determine what would be culturally acceptable in a given context? These issues will be taken forward in the next chapter.

A few researchers also cautioned against making general rules for all types of research based on some bad experiences with the uses of stored samples, such as the case of the Havasupai tribe of Arizona which has generated much debates in recent times (Mello and Wolf 2010).

> "I don't think the fact that there have been two or three famous cases should dictate practice for literally hundreds of thousands of other studies. I think we should accept that sometimes things go awry and we should learn from them, we should try and anticipate the circumstances in which it might, but I think to react to one or two famous examples by assuming that every time a sample is stored it's going to end up in some group you know having their cultural identity denied, I think it's just an overreaction to it" (Kilifi: RES011).

There was a general sense from this researcher and a few others that it is important to bear in mind that people may have different opinions about how much protection they want over their samples and who should have access to them. Participants' preferences may also vary significantly and could change overtime. This has implications for determining best practices for future uses of samples.

7.3.3. More effective community engagement (CE) strategies

With the open nature of research collaborations, the uncertainties surrounding future uses of samples and questions around the validity of broad consent, interviewees suggested that other mechanisms for communicating scientific procedures to communities, beyond the individual consent process, may be warranted. For example, some supported the utilization of CE strategies prior to individual consent processes:

> "I understand consenting to be a process, it's not a onetime event and that requires that we should do more and more education prior to studies so that if the people appreciate what we are doing, the people appreciate some of the issues that will come up, they can clarify them before we go to the individual level so that when you are talking people appreciate what you are talking about" (Navrongo: RES07).

> "I would feel that for a centre like us and for the respect that they have and the understanding of the community, we would hope that we would be able to get a blanket type of approval or at least if we want to do a study to go back to; there are some specific villages, not part of each individual but maybe going to the leaders is one way of doing it possibly" (Kilifi: CKI07).

As discussed in Chapter 3, both KWTRP and NHRC have established mechanisms for communicating with local residents about the institutions' research activities. The processes involved in these CE strategies have been reported elsewhere (Marsh, Kamuya et al. 2008; Tindana, Rozmovits et al. 2011). They include using the role of the Health Systems and Social Science research (HSSR) group in facilitating the engagement process, KCRs and barazas (community gathering) in Kilifi and community entry and durbars in Navrongo. Interviewees in both sites were confident that these engagement activities are effective ways of improving research literacy and strengthening the trust relationship between the host institutions and the community and could potentially provide an important opportunity to engage the wider community around issues about sample export, storage and their future uses.

> "So I think, there are some [research teams] that really appreciate that through the C.A.S.T group, they have been able to get valuable information and most of them find it useful because the community engagement plan looks at sensitive issues regarding a particular study and how to address them. So when we develop the key messages we take into consideration what sensitive things, issues and area that are there in the community that we need to address and I think this has benefited them as forethought of what to find in the community" (Kilifi: CSKI03).

Other stakeholders such as fieldworkers and community representatives generally shared this view but added that much more needs to be done:

> "..apart from what is already been done, massive activities should be put in place like meetings in the community should be increased because although we go to the community but the meetings are maybe a whole occasion, only one meeting and the people that attend that meeting are very few so if the number of meetings are increased and resources are also increased, then there would be information flow and feedback with the community and it would assist" (Kilifi, CSK105).

Community engagement was also viewed as a solution to the issue of going back to individual participants for consent for future uses of samples. For studies which can sometimes have potential implications for the wider community such as genetic and genomic research, interviewees argued that, although it is practically difficult to trace individuals for re-consent – as discussed earlier; CE strategies could be utilised to solicit community views about what is culturally appropriate for future uses of research samples, especially blood. As demonstrated in the quotes below, there were strong arguments that although individuals cannot be traced, communities are easily identified and should be consulted for future research purposes:

> "There are some studies that you probably would not be able to get the original donors of those samples. One, they are dead, two, some of those people have migrated, they are no longer within the system but it is a community thing so certainly, those that are alive, there are different channels of community engagement or contacting community members so if it is something that you cannot trace back to the individuals, ..You can use radio; you can use durbars as we always do. You can use durbars in the communities that these samples were collected and in actual fact, that would be a very effective. Effective in the sense that the community members know that at the end of it all, the reference is going to be made to them. If they think that they are going to be stigmatized in one way or the other, they would take a decision as to whether those samples should be used or not" (Navrongo: REC03).

> "There is nothing like we cannot get back. We can because as long as we are calling them community and not individuals, we know that these samples came from Matsangoni. …I think that we can start from the community's whole point of view because we want to anonymise. We would not identify your sample but we would come back and tell the whole community again that " remember those samples that we took 20 years for this study about this and that?" so that they can remember, so now we are using them to try and answer these questions" (Kilifi: CSKI03).

Currently, consent forms only state that future research projects will be conducted only with approval from the local REC. However, another suggestion from the above quote is for consent forms to also indicate that the community may be informed or involved in decisions about future uses of these samples. CE is also seen as an effective mechanism for incorporating the views of potential research participants in future research processes:

> "Re-consenting participants is very difficult but we must find a way of involving the community in the decision making process" (Nairobi: REC09).

> "So I believe for example if we plan without their involvement in the sense that without getting their views on some specifics aspects, we might fail in executing the plan we have for the research. So in my view, there are some things which are not accepted in the community and you might want to do this or that but the approach might not be acceptable in the community so understanding that is important and thus not only save time and resources for the researcher but create that relationship where the research is going to take place" (Kilifi, CSK05).

These suggestions for CE are in line with the growing recognition in the wider literature about the value of engaging local communities in scientific research (Emanuel, Wendler et al. 2004; Newman 2006; Tindana, Singh et al. 2007). The question is, what counts as effective CE? Is it effective if it sustains research activities in the community? Is it effective if it builds trust? Is it effective if the community feels empowered to say no to research participation? These are on-going issues that will require further examination and will be discussed in the next chapter.

Again, other interviewees were more worried about the consequences of not engaging community members about future uses of samples and how results from future studies may affect the communities' relationship with the research institutions:

> "…if you use those particular samples for any future research without the knowledge of the community or the donors, if any publication comes out that is adverse, that has adverse consequence for .. research in those particular communities. They could give consent for future use of samples, the community members might not know the implications of that but then when you publish the document and then information is trickling down that oh, you say that in this particular community, women are more likely to deliver kids who end up being prostitutes in future, that community would be stigmatized and then they get to realize that no, you didn't treat them fairly" (Navrongo: REC03).

Generally, most interviewees expressed their confidence in the effectiveness of the KWTRP and the NHRC's community engagement strategies. They suggested that the institutions have been able to build the necessary respect and trust of the community which has facilitated the successful conduct of research in these settings.

However, not everyone shared these emphases on the role of CE and the idea of engaging communities around future uses of samples.

As one researcher in Kilifi points out:

> "The community is always described as a sort of amorphous group but there are presumably some people that have strong opinions in one way and others that have a view very much like the people doing the research, which is perfectly fine. But it's the reporting, the qualitative analysis is such that you take examples rather than take numbers of people who share particular views and so there's always going to be a mixture of people with divergent views within the community…..we need to understand the differences between individuals and communities because I can't believe that there is only one view out there" (Kilifi: RES 03).

Another Kilifi researcher questioned:

> "…can a generation that come up several decades down the line act in the interest of past generations"? (Kilifi: RES 01).

Thus while there was a general support for CE as a tool for getting communities' views about acceptable uses of samples for future research and as a means of protecting the interests of individual participants and local communities, some interviewees are sceptical about how this can be achieved in practice and who has the best interest of individual participants. This will be discussed further in the next chapter.

7.3.4. Feedback to research participants and communities

As discussed in Chapter 5, most interviewees reported that the lack of feedback of the research process and the implications to research participants has contributed to some of the micro-level issues arising from sample export, and future uses. This was a major concern for most fieldworkers interviewed and almost all the other stakeholders felt that feedback to the community should be taken seriously. According to them, feedback keeps the community informed about the institutions' research activities and prevents rumours and suspicions about what blood samples are used for:

> "We need to also ensure that when samples are stored for long term usage and analysis, then whatever results come out of it, we should inform the local community about the further advances that have been made" (Navrongo: RES13).

> "It doesn't matter. It is not because you are sending it abroad, you should bring results. If we are doing it here, we should put results" (Navrongo, FW01).

As the above quote suggests, feedback is not only important for exported samples but also for those stored locally. Feedback to the community could be done through the media (radio), which is increasingly becoming accessible to community members, as well as through the existing CE strategies in Kilifi and Navrongo highlighted as a possible solution above (see 7.3.3).

> ".. by feeding back to them some of the results that we are finding they will know really this is what their blood is being used for. I don't know if some of the collaborators even talk to them that may convince them, maybe not because they will believe we are just engaged with them so they will tend to believe us more if we talk to them, but I believe there should be openness and dialoguing for them to know that there is nothing really at stake here" (Navrongo: RES17).

> "We need to always communicate back to the community exactly the outcome of the study. Some projects do and others don't" (Navrongo: CRs).

A research assistant in Kilifi also raised the issue of having a community exit strategy which relates to some of the CE issues discussed earlier. A good exit strategy facilitates future research projects, sustains the relationship between the community and the institution and ensures that researchers fulfil the promises made to the community:

> "…[when] you have completed your study, if you just walk out like that the next group that is going to come into [the community] to do a study will have problems. So the way we say goodbye to a community really matters a lot you know. Now a lot of engagement is involved, we still call for meetings and tell them we have finished and then if there's anything, for example the benefits that it promised, once you ….are exiting a community and afterwards you make sure that the benefits you promised" (Kilifi, RA06).

Given my earlier discussion in Chapter 5 about the fears and anxieties surrounding the fate of exported samples, the data suggest that feedback between collaborating institutions will also be desirable.

7.4. Effective governance by ethics committees (REC)

Another set of recommendations – in addition to those around capacity-building, consent and community engagement, relate to the gate-keeping role of RECs and the need to have clear institutional and national policies and guidelines governing sample export and future uses. According to most interviewees, RECs are the most appropriate system for governing research involving human participants including serving as gate keepers of research samples. They suggested that RECs could advise researchers on when participants should/should not be re-contacted for their consent for future research projects:

> "I think that role of export should clearly be defined and supervised by the IRB to make sure that the community's interest is also preserved" (Navrongo, RES07).

> "Now the IRBs are there actually to protect the subjects, so I think in certain circumstances they should be able to speak on behalf of the subjects especially if the subject has in the past given them that blanket storage.. the IRBs we presume would have been keeping abreast with how things have gone so they should have the power to say that well we think you should be able to go ahead, we are standing in trust for them but at the same time too they should also be able to use their judgment to say that for this particular one we think you still need to go back to the subjects to go and see them, so they should serve as a sieve" (Navrongo, RES17).

A further point suggested above is for RECs to serve as trustees of research samples. It is worth noting that fieldworkers and community representatives in both Kilifi and Navrongo did not specifically mention RECs as a solution spontaneously but only supported the idea of such a system only when they were prompted in the interviews. Generally, responses from both researchers and RECs place a huge responsibility and reliance on RECs, not only to make these decisions on behalf of research participants, but also to determine the implications of future research on these participants. This will however require that RECs are adequately trained and equipped to assess scientific projects using stored samples and to also stay in touch with the local context.

7.4.1 Strengthening capacity of local RECs

Given researchers' expectations that local RECs could serve as gatekeepers of research samples and advise researchers on what may be acceptable for future uses of samples, there was a call for strengthening the capacity of these RECs. For example, interviewees in Nairobi highlighted the need for RECs to keep pace with advances in science and to utilize modern technology for monitoring the progress of approved research:

> "As science is advancing, so must the review process, IT provides an opportunity to streamline the review process and keep track of progress of research projects" (Nairobi: REC05).

> "For ethics committees, we need to be trained totally. I think when you finish this PhD you can start training us or giving us materials…..to train ethics committees" (Nairobi: REC02).

In relation to the issues raised around sample export, storage and their future uses, the training proposed for RECs involved having a clear understanding of the scientific approaches to medicine and the ability to determine the ethical implications of these processes. For example, a KWTRP researcher suggested that RECs should have the capacity to differentiate between the implications of using cell lines and parasite lines for research purposes since they raise very different issues:

> "Some more detailed consideration for cell lines and parasite lines and be more specific instead of anything from humans being problematic, for example. synthetic is not taken from a person but derived from a person and so we need to understand the differences" (Kilifi: RES03).

This researcher adds that it is also important for RECs to recognise that parasite lines would be used by others 'whether we like it or not'. This may require that REC compositions include members with expertise on genetics and genomics or at the least the provision of some form of training in this field for RECs reviewing these scientific projects.

In Navrongo some RECs I interviewed discussed a number of strategies to keep them in touch with the community. One, having a community representative on the committee; two, informing the wider community about the work of the REC through radio discussions and three, monitoring approved research through field visits:

> "As an ethics board, we have organised radio discussions to inform the community about our existence and what we do and we do this in English and in the local dialects so that the information can be disseminated and the people know that there is this body which is overseeing this aspect of the research implementation process and then we also carry out oversights. When we give approval, it is not the end of it. We go to the field …we introduce ourselves as an independent body coming from the centre to oversee what is actually happening so that at least the few community members who are there at the point that we are doing our monitoring, know that there is someone out there who is also cross checking on the centre in its activities. So that is how we come into contact with the community" (Navrongo REC 02).

Navrongo interviewees believe that these practices have proved a useful way of not only monitoring approved research projects but also to some extent assuring the local REC of the fate of samples, a practice they felt needed to be sustained.

In Nairobi, some interviewees suggested that although the KEMRI REC is far removed from the context in Kilifi, the community representative on the committee is able to bring in a lay perspective that would reasonably represent the voice of the community:

> "A well trained community representative should be able to decipher issues, ethical issues from a study and represent the people by being their voice, even if he does not meet them. And I think to me that is the best way, someone who is able to understand these issues and raise the flag and say no this not going to happen" (Nairobi: REC11).

The question is whether there is the need for another committee in Kilifi to allow lay community members to participate in the review and approval of scientific research. This will be discussed further in my concluding Chapter 8.

7.4.2. Improving communication between RECs and researchers

Another recommendation for addressing anxieties about the fate of exported samples and future uses is to improve communication between RECs and researchers. Most interviewees suggested that RECs should establish clear, transparent and appropriate guidelines for sample export, storage and their future uses:

> "SOPs should be able to govern, to guide us, so that people know once you've identified the national interest, spell them out, spell them out as a form of guideline that you can guide everybody" (Nairobi: REC 11).

As discussed in Chapter 4, many interviewees believe that researchers are generally willing to follow the rules to conduct their research in an ethical manner but are either unaware of what the requirements are or there is lack of clarity in existing requirements. Thus, some interviewees recommended that opportunities should be created for more dialogue between researchers and RECs. As illustrated below, this dialogue will allow research actors to understand that scientific research is important and needs to be conducted ethically:

> "Dialogue and openness.. I think that's very important....the people who were doing the Nazi camps who were doing all kinds of tests on human beings, they thought they were pursuing science.. but it was unethical science. So I think it's dialogue, you can't do without ethics, you can't just do things in pursuit of science and the best thing is to have dialogue" (Nairobi: REC07).

> "But as you know the trouble has always been to try to balance the protection of the human subjects against the interest or the development of scientific advancement. That has always been the tug of war. The scientists on the one hand wants possibly to override ethics and get going, but the ethicist must come in to say wait a minute let us control the wheel of science and look at it from also an ethical point of view" (Nairobi: REC11).

Another way of improving communication is for researchers to provide periodic reports on what analyses have been done and whether samples have been used up or destroyed:

> "So I think that the ethics committee has the responsibility also to ensure that researchers are doing the right thing in which case, if they say that they would submit half yearly reports and they are not doing it, they should call them to book. If at the end of the trial, they are supposed to write a report, they are not doing it, they should call them to book. The ethics committee has the power to stop a trial and has the power to say go ahead. But somehow, I think probably, we have somehow reneged on this and we are not fully exercising the powers that we do have so some investigators are taking advantage of that" (Navrongo: RES15).

The quote above raises two important issues: One; is the need to have clear guidelines and policies such as requirements for progress reports from researchers on the fate of samples for. those exported and those stored. The second is the need for effective mechanisms for implementation such as REC's power to query researchers if they fail to adhere to these requirements. The question is whether RECs have that power over scientific research. A REC member in Navrongo does not think so:

> "I don't think that they are powerful and well equipped enough. .. if we ask some studies to stop, do we have the power without the director? Would you have the power to ask certain studies to stop around here? We don't have that power. We can only make recommendations, suggestions and all that and are they followed 100%? Those are the issues. So talk of monitoring, that you are talking about crossing borders, that is more tasking and that one, it is not only the committee that can do that. You need political will so I think that the ethics committee needs to become better equipped and they need to really work with the government and not as distinct bodies because they cannot succeed" (Navrongo REC04).

As suggested by other interviewees and discussed later in the chapter, empowering RECs to take up these responsibilities would require a national framework which gives them the legal backing to exercise this power.

> "..I would like as an ethics committee for every sample that is shipped, at least a primary shipment, that we get back some kind of feedback from that analysis. Now secondary and tertiary analysis right now there are no structures to govern that but I would like to see the government taking a precedent in helping us to come up with legislation or a framework to ensure that there's kind of some level of tracking this kind of samples and the kind of work that's done on samples from the country" (Kilifi: REC00).

7.4.3. Improving communication between local and external RECs

Some researchers and RECs also suggested that because of the logistical challenges involved in determining the fate of exported samples, one possibility for reassuring local RECs is effective communication with external RECs, where approval is required by these committees, as recommended in various guidelines. There was a suggestion that some of the oversight responsibilities could be transferred to external RECs:

> "I believe that agreements should not only be between the local partners or the foreign partner, it should also be institutional. It should be between maybe the IRBs, because the foreign IRB can ensure that the study principles and agreements, transfer agreements and all that are adhered, so I think maybe they should go beyond the investigator signing something, it would be beyond the investigator signing the transfer agreement some oversight body in the advanced country should ensure that this agreement is adhered to" (Ghana: REC00).

> "I think these days you cannot work in isolation so we need to work with other IRBs outside. They would be able to let them know whatever is happening to the samples that is out of the country so they can help formulate some common binding decisions that's of use" (Navrongo: RES15).

These suggestions support calls in the literature for more and better communication between RECs involved in the review of international and multicentre trials (Silverman, Hull et al. 2001). However, given variations in REC decisions which have sometimes raised concerns in the literature it might be important to anticipate potential disagreements that may arise in these dual review processes and put in place strategies for addressing them.

7.4.4. A national framework for sample export

In addition to strengthening RECs, some interviewees advocated for a national framework to govern the export of samples out of Africa. For example, there was a general sense from these interviews that some of the issues arising from international research collaborations are beyond the scope of RECs and that African countries need to also have clear national policies to guide researchers:

> "addressing this problem has to go beyond ethics committees particularly in the African setting... it has to start with some kind of national legislation or national policy, that has some legal backing and some enforcement mechanism that would ensure that anything leaving the boundaries of the country at least in the name of scientific research has a certain or meet certain conditions" (Navrongo: REC01).
>
> "the national legal framework to guide the exportation of samples could be a good starting point" (Kilifi, REC01).

A proposed national framework will have something in line with this suggestion from a REC member in Nairobi:

> " …there is a need for very comprehensive and appropriate governance structures, both at the institutional level and national level. Issues surrounding commercialisation, finance, benefits sharing, ownership, even ownership of samples I think are areas which require resolution and resolution can be reached by having all stakeholders participating in this debate and reaching a consensus. One type of consensus is how are samples going to be collected, data analysed, who is going to access at what time, at what point, what do we need in place, who can access when, when you get information that was derived from a particular jurisdiction are you going to return that information to that particular population or the particular institution or country, what are you going to do with it, what is the purpose of this analysis, what's the purpose of secondary and tertiary use. So I would like to see very comprehensive governance structures in place, both at regional, national, regional and international level" (Nairobi: REC00).

Although the above suggestions seem to appeal more to legal or regulatory frameworks they could also potentially be applicable in the formulation of ethical guidelines and policies at the national, regional and institutional level. These suggestions seem to relate to on-going discussions around genomic sovereignty – highlighted earlier. As was seen in Chapter 4, Kenya seems to be making progress in streamlining their national requirements for sample export and Ghana may need to learn from these practices. However, in the case of storage and future uses, there are still no clear guidelines on what may be an acceptable practice and the suggestions from interviewees from this study may provide some ideas for moving this forward. According to most interviewees a more effective national framework will also require political will and more commitment from local governments to invest in scientific research.

Although interviewees called on external funders such as the US NIH, UK Wellcome Trust, and the European and Developing Countries Clinical Trial Partnerships (EDCTP) to provide more support for research capacity, some emphasised the need for local governments to play a more proactive role in supporting local research institutions:

> "African governments must make a deliberate effort for technological advancement so that this will close the door to the perennial requests of export of samples" (Nairobi: REC11).

> "..first of all if our African government or our authorities would redirect funds into research and motivate research involvement they would even be the first to scrutinise any collaborations that come and really weigh the benefits and make sure that the benefits may outweigh the risks" (Navrongo: RES05).

Interviewees' accounts bore some similarities to the notion of *genomic sovereignty* (Seguin, Hardy et al. 2008) – which has sometimes been used to emphasise notions of ownership over nation's human genetic resources. However, these responses were not concerned with ownership of samples per se, they were rather of the view that local researchers and institutions should be stewards of these samples and ensure that they are used for the intended purposes and not present harms to participants and/or communities:

> "[Principal investigators] don't own the samples, it is in their custody, you can own the tubes but no one can claim ownership of samples. But somebody has to look after them so that they are not wasted. You have a duty to look after them but it shouldn't be their property" (Kilifi: RES03).

7.5. Fairness in research collaborations

In addition to their suggestions about ways of addressing micro-level problems, researchers and RECs proposed a number of possible solutions for addressing the macro-level issues arising from sample export and long-term storage. A common response to questions about this was to call for scientific collaborations to be fair, equal and beneficial to all parties involved.

There was an emerging view that this might be achieved through workable research agreements (about the use of samples), ensuring proper recognition of local researchers' contributions and giving back to local communities.

7.5.1: Workable research agreements agreed in advance at the start of the research

According to interviewees, one way of concretising the notion of fairness, would be to have transparent and equitable research agreements. Thus, the need for material transfer agreements (MTAs) featured prominently in all the interviews conducted with researchers as well as some RECs. They recommended that these agreements should clearly spell out the responsibilities of each collaborating partner and there should be openness and transparency in the negotiation process:

> "one of my recommendations [which] is being gradually implemented now is to state upfront in your protocol, to be clear what you want to do. In our MTA in this institution, it is stated that unused samples would be returned. In the event that you don't want to run any more test on them then evidence as to their destruction should be fed back to the institution" (Navrongo: RES21).

> "From the outset I think you want to see that there is transparency, there should be no hidden agendas, if it's a funding agreement, arrangement, you want to negotiate the budget and agree clearly and know that you stick to it, if it is research which is done and publications are done its good for there to be mutual recognition of who did what, you know, if its storage of data and access to samples, there is going to be that transparency and clear understanding of what belongs where and nobody would then do things under the table" (Kilifi: RES03).

Thus, projects that had agreements in place prior to the initiation of the research activities were generally perceived positively than those that did not. The data suggested that while these MTAs are important, it would also require that host institutions are in a position to negotiate for what should be incorporated into the agreements, such as insisting on local capacity building and equitable benefit-sharing.

> "[samples] should be exported for specific reasons and those reasons have to be stated upfront, what kind of sample you need to transfer for that purpose, you state it upfront and if there's a need for any other thing to be done, potential use of the samples have to be focused and put on paper and that understanding is made right from the beginning that these samples are being transferred for this purpose and potentially for science or papers" (Navrongo, RES01).

Other researchers highlighted the importance of accountability in the exchange of samples across collaborating sites suggesting that there should be effective feedback from external collaborators on the fate of exported samples to allay researchers' fears:

> "I think as a site or as a country we are entitled to better information from the collaborators on what they do, but it often becomes very nebulous when you send your sample away. Only when something is found people get really excited about it and you hear back" (Kilifi: RES05).

7.5.2. Recognising the contribution of host institutions in scientific collaborations

Another proposed macro-level solution to addressing local researchers' fears about sample export and the possibility of being short-changed in collaborative projects was for contributing researchers to be duly acknowledged. Researchers specifically emphasised the need for fairness in the authorship of scientific papers and for presenters of data that are collected from these African sites to acknowledge the local institutions and community:

> "Partners should not read papers in press when they are supposed to be collaborators in fact they should be involved in the process so it's those kind of things that are key" (Kilifi: RES09).

If the host institutions and researchers are demanding this recognition, they should also be given the opportunity to contribute significantly to the research process, not just collecting samples but initiating the research ideas and contributing to the analysis process. Thus some RECs specifically advocated for more local inputs in international scientific collaborative research proposals:

> "So you see that the material that is presented has no local input and no local relevance at all in this collaborative work and I would want to see more involvement of the local participants in how little input they can provide. There should be an attempt to involve the local participants in the design and writing of the proposal. Firstly to give them experience in the writing of the proposals, secondly it would give the proposal the chance to address cultural, local cultural problems and issues that may be overlooked by overseas partners alright? I want to see local content in proposals, I want to see that local participants are not just playing the courier role and just sample shipping, but will be involved in analysing data" (Ghana: REC00).

Other interviewees suggested that the scientific publication process could also potentially serve as a check for the appropriate uses of exported and stored samples and for ensuring proper acknowledgement of contributing researchers, host institutions and local communities. This may call for journal editors to require proof of ethics approval for future uses of research samples as part of the peer-review process and this links directly to the work by the committee on publication ethics (COPE) (Wager 2012).

7.5.3. Benefit-sharing: Giving back to the host community

There were also calls for research institutions to recognise the contribution of local communities and maximise the benefits of research for these communities. Interviewees' arguments were mainly based on the *principles of reciprocity* and the *principle of justice.* As discussed in Chapter 5, interviewees claimed that while research participants and communities contribute immensely to the research endeavour – for instance. without their samples, these scientific projects cannot be conducted – they do not receive enough benefits apart from the ancillary health care provision during their participation, which is not felt to be sufficient for benefit sharing alone. Researchers on the other hand may benefit by advancing their careers and also earning a living. There was therefore a general appeal for institutions to make efforts to ensure some equity in the distribution of research benefits.

As discussed in Chapter 5, benefit-sharing is a recurring theme and yet one of the most contentious issues in the bioethics literature. While there is a general recognition of the importance of ensuring a fair distribution of research benefits, there is no broad agreement yet – both from the literature and my data – on what constitutes fairness and which benefits of research can and ought to be shared.

> "..benefits to the community is a very tricky issue and …the community you're dealing with for them the most important thing would be to get some extra food and that's an area that is seen to be one which we ought not to proceed with. Because we're a research team, we're not an aid agency. But it's, I think it's a massive dilemma" (Kilifi: RES07).

Thus, while most interviewees called for fair benefit-sharing agreements, it was still unclear what exactly this might mean. There was however a common response that scientific research should be beneficial either in building local capacity – as discussed earlier, addressing an important health need and/or providing health benefits to research participants and their communities. Although there was a general recognition of how research has improved health indicators in Kilifi and Navrongo, most interviewees felt that host institutions could do more for the communities. For example, interviews with fieldworkers and community facilitators suggest that there is a growing expectation that research institutions with a long-term (over twenty-years for both KWTRP and NHRC) research relationships with the local community should *give back* to the community:

> "..it's true that in this community when you go out, people will say, this organization has been here for 20 years but they have got nothing here to show that they have been here, why don't you put up something maybe a classroom or a building or something which we can easily say, KEMRI was here ten years, but you find you people you come in, take samples, you vanish, you will never come give us feedback, after 10 years you are back asking for more" (Kilifi: CFs).

> " ….we should be prepared to assist them if there is the need. Like schools in the communities, we can offer them something. We can just pick some exercise books and go to the community and say that "okay, because we have been doing research with you for these number of years, the kids are ours too. Let's give them these exercise books or the poor but brilliant students should be given some support" (Navrongo: CKI01).

These narratives highlight both the expectation of feedback of results, as discussed earlier and the need for host research institutions to contribute to improvements in the lives of people in the community through other non-research related developmental projects, such as schools. Some researchers expressed the view that while giving back to the community is laudable, not all research involving human biological samples results in a commercial profit for individual researchers and/or institutions. Thus, it is important for research institutions not to raise too many expectations within the local community.

> "So you have to do things in a way that is least disruptive to that community, least likely to result in tensions. And offer things that, yeah try and think of things that won't cause that tension" (Kilifi: RES07).

Interestingly, most interviewees were not supportive of paying research participants because of concerns that such a move may unduly induce participants into risky research. However, others were concerned that as a result of this fear of inducing participants, they are not receiving their due share of the benefits of research. One NHRC researcher recommended that instead of paying individual participants, that money could be used to develop the wider the community:

> "We should get to a stage where we don't cheat our study population because of that, … instead ….if it's $1,000 that they would give to the participant outside and they decide to give $10 [to the African participant] at least the balance of $990 should be used to build something in the community so that the community as a whole will benefit and I don't think that's coercion because informed consent is taken at the individual level" (Navrongo: RES08).

Whether this recommendation can be implemented in practice may require some more empirical research exploring local communities' views about payment for research participation and/or what would count as a reasonable research benefit to the local community in the context of different kinds of research.

7.6. Sustainable micro and macro-level relationships

In Chapters 5 and 6, my analysis suggested that the issues arising from research collaborations and sample export and from the future research uses of samples depend significantly on the nature of the host research institutions' relationships at the micro and macro levels. And in proposing solutions for addressing these issues, many interviewees often referred to the importance of building better relationships at these levels. Stakeholders' responses suggested that although having the necessary checks and oversights over research is important, as discussed above, much depends inevitably on the host institutions ability to manage and sustain such relationships both with their external collaborators as well as with local participants and communities.

7.6.1. Building better research institutions to serve as custodians of samples

At the micro-level, most interviewees felt that in addition to RECs, the host institutions – in this case KWTRP and NHRC – should serve as custodians of research samples and ensure that these scientific resources are adequately protected. They are better placed to play this role because of the responsibilities that they have towards research participants and the local community. For example, the responses below highlight the important responsibility of the host institution to ensure that samples are used only for the intended purposes:

> "I think that KEMRI as a Unit has a responsibility because the respondent has that direct contact with KEMRI" (Kilifi: FW01).

> "…the onus lies on the institution to take proper care of the samples [and] ensure that the right things are done to protect these samples" (Navrongo: REC02).

The general feeling from most interviewees is that while the recommendations suggested by the various stakeholders could potentially address these practical ethical issues, what is important is for researchers to be accountable to research participants and their communities.

> "..much of the burden is on scientists to have high integrity in terms of the collaborative work that they do. I personally don't think that any amount or level of policing will solve the problem if scientist on their own do not decide that look, this is what I have committed myself to do with these samples and I am not going step outside that banking but as long as scientists are willing to use all kinds of means to what should say to discover things whatever this issue would continue to be there" (Navrongo, REC 01).

Some researchers and RECs called for scientists in general to look beyond what they personally gain from conducting research such as the money, honour, degrees or publications and focus more on ensuring that research addresses local health needs and provides health benefits to the community. According to most interviewees, sustaining trust relationships requires host institutions to prioritize research that are relevant in addressing the health needs of local communities. Study responses seem to appeal for virtuous researchers and for institutions to be honest, open and transparent in their research dealings and also ensure that the export and future uses of samples do not expose the community to harm. According to many interviewees, these are likely to sustain participants' and communities' confidence in scientific research.

> "As you know Paulina there isn't an answer to the question, all you do in the end is to try and to be as honest and open with research participants as possible. And, I think it's perfectly reasonable that people are informed the basics about what is likely to happen to their sample after they've consented. If they were to consent what will happen to the sample where it will go and what sort of, but in, in generally the, by consenting to involvement in research is to some extent a leap of faith on the part of the participants that they have to develop a sense of trust in those people that are asking for that consent" (Kilifi: RES13).

The above quote raises an important point about the possibility of researchers negotiating with local communities about future uses of samples. The challenge is how these contracts can be negotiated and with whom. This is an issue that will be explored further in my next chapter.

Almost all the different stakeholders interviewed (researchers, fieldworkers, community facilitators, RECs) mentioned the importance of trust in the relationships between institutions in research collaborations, between local institutions and the community and between

researchers and research participants. As demonstrated in the two previous chapters, both the KWTRP and NHRC have been able to build and maintain a trust relationship with the community over the past twenty years. They suggested that to sustain research activities in these research settings, research institutions should develop structures that will strengthen sustainable working relationships with collaborating institutions and scientists as well as with participants and communities.

7.6.2. Scientific leadership in and by African research institutions

At the macro-level there was emphasis on the importance of strong scientific leadership in African institutions to negotiate with external collaborators and scientists, which is a key part of capacity building and building better institutions. Stakeholders were of the view that having a visionary leader who understands the nature of science and the ability to negotiate for fair research contracts will go a long way to address some of the macro-level issues raised in the Chapter 6:

> "I think that we need leadership with the power to negotiate. In which case they need to understand the issues … systematic planning and you need people who have that ability and knowledge so that in the negotiation process, they put their knowledge to work. But when the wrong people are put in positions, they don't have the knowhow and so what is A does not appear like A to them" (Navrongo, RES015).

In Kilifi, there was a general appreciation of the KWTRP leadership and the efforts made to secure strategic grants to strengthen local capacity and to attract good research collaborations. Other responses suggest that although individuals do make a difference and having a strong scientific leadership is important, what is important is to work with a strong research team.

A strong leader will also be able to support the research team to prioritize its research activities and also create an enabling environment to attract funders:

> "..in terms of capacity building I think our institutions need to, once we have our key objectives then I think we can easily say we need to build capacity and insist on capacity building with our collaborating institutions. But again it can only be if we have a general plan on how we want to run the programme" (Kilifi: RES13).

> "I think that for health research, I think that scientists have to be trustworthy. Trustworthiness in that,, we should move away from our personal benefits to thinking about institutional benefits. What benefits the people? What benefits the system? And so our scientific leadership should seek to do things that would promote the institutions and most of these agreements of collaboration, be it north-north or south -south or north south collaboration, it should be a win-win situation for everybody" (Navrongo: RES15).

7.7. Conclusions

The aim of this chapter has been to investigate stakeholders' proposed solutions and recommendations for addressing the practical ethical issues they identified as arising in sample export, storage and their future research uses. These proposed solutions include capacity building, better consent processes, effective ethics committees, equitable research contracts and agreements, benefit-sharing and sustainable research relationships.

Sustainable scientific capacity development in African research institutions featured as a key solution to addressing the concerns arising from international collaborative research more generally and sample export, storage and their future uses in particular. Study responses suggest that focusing more on local capacity building would allow samples to be analysed locally, thereby limiting sample export. Also, local storage of samples would allow host institutions to have more control over samples and capacity to optimise the future uses of samples locally.

As discussed in Chapter 2, the literature suggests that there are efforts being made to address some of the concerns relating to sample and data-sharing issues in large-scale research collaborations. There are also some cases of research collaborations which are aiming to address at least some of these issues. For example, the MalariaGEN consortium has developed guidelines to allow local researchers to retain control of their samples as well as 'access genotyping data as soon as it is generated via a web-based system' (Chokshi, Parker et al. 2006; Parker, Bull et al. 2009; de Vries, Bull et al. 2011; de Vries, Jallow et al. 2012). This model could be adopted by other scientific collaborations such as H3 Africa and could potentially address local researchers' fears about losing control of samples.

For addressing the micro-level issues presented in Chapter 5, interviewees recommended that innovative ways of explaining scientific research such as the use of audio-visual and video documentaries as well as exposing participants and local residents to the analysis of samples in the laboratories could be useful. Given that RECs also face challenges with understanding some of the scientific aspects of research projects, they could also benefit from being exposed to these laboratory processes. They have also suggested a re-think about the concept of broad consent and to make the consent process more meaningful. Community engagement and feedback were highlighted as possible solutions for addressing the uncertainties surrounding the fate of exported and future uses of samples. While these recommendations could potentially improve research literacy in these research communities, some of the issues surrounding possible uses of samples – as discussed in Chapter 5 – are not likely to be resolved this way. It may require other forms such as providing benefits and maintaining the on-going trust of participants and the wider community.

As other authors have also suggested (MacQueen and Alleman 2008), it may also require a model of consent that takes into account the local relationships and interactions between research institutions and the community and how that influences and sustains research participation.

Another set of recommendations relate to having effective RECs to serve as overseers of research samples. Interviewees believe that RECs have an important gate-keeping role to advise researchers on when participants should/should not be re-contacted for their consent for future research projects. This huge responsibility placed on RECs would require significant resources to train members to appreciate the complexities surrounding emerging scientific methodologies such as those applied in genetic and genomic research and to determine the implications of these types of research on individual participants and their communities. Without this, RECs may be making unrealistic demands on researchers which could serve as a hindrance to the research enterprise or failing to notice important ethical considerations.

There is a growing global effort to strengthen ethics review systems in Africa. Since 2000, there have been a number of initiatives by big international funders such as the US National Institutes of Health, the UK Wellcome Trust, the Bill and Melinda Gates Foundation and the European and Developing country clinical trials partnerships (EDCTP) to provide financial support to RECs in Africa (Nyika, Kilama et al. 2009; Nyika, Kilama et al. 2009). With the increasing number of trials in Africa and the complexities involved in the review of these scientific projects, sustaining these training programs and capacity building initiatives may be warranted.

To address the issues arising at the macro-level, researchers and RECs have appealed for equitable and fair international scientific collaborations.

They have suggested that host institutions should be custodians of research samples and should ensure that the agreements they enter into with their collaborators are fair and equitable. In reality most international scientific collaborations are initiated in and funded by HICs (Maina-Ahlberg, Nordberg et al. 1997; Jentsch and Pilley 2003). There is therefore the tendency for some collaborators to control the research process. While recent initiatives such as the H3 Africa will potentially address this disparity, it will also require that African scientists are able to identify and initiate locally relevant projects which could be integrated into the local health-care system to promote the social value of research (Emanuel, Wendler et al. 2004; Lairumbi, Molyneux et al. 2008).

Most of my interviewees argued that while the recommendations suggested by the various stakeholders could potentially address these practical ethical issues, it is particularly important for researchers to be accountable to research participants and their communities. Study responses seem to appeal for virtuous researchers who will ensure that the export and future uses of samples do not expose the community to harm. They emphasised on the importance of values such as honesty, integrity, transparency, openness and consistency of behaviour to sustain the trust-relationships between the various research actors. Table 13 summaries the key recommendations and the challenges with implementation discussed in this chapter.

Stakeholders' solutions: Moving forward the science and ethics of research involving samples		
Solutions	*Principles*	*Challenges with implementation*
Building scientific capacity	• Capacity strengthening as an ethical obligation • Local sample storage and custodianship of samples more desirable to resolve concerns around loss of control • Improvements in local funding of scientific research	• What capacity? • Capacity building doesn't necessarily resolve issues about sample export. • Progress made in recent times • Will require more local funding and commitment from external funders
Better consent processes and community engagement	• Demystifying the uses of blood samples in research • Redefining broad consent for future uses of samples • Identifying effective community engagement (CE) strategies • Improving effective feedback to research participants and communities • Respect for persons	• Some of the issues raised at the micro-level are culturally entrenched and more education is not likely to resolve them. • What counts as effective CE? • While feedback is important, it is not clear what ought to be fed back and how this can be done effectively • How does better consent processes take the issue of trust into consideration?
Effective oversight by ethics committees	• Strengthening capacity of local RECs through training • Improving communication between researchers and REC • RECs as gatekeepers of research samples	• RECs are currently not adequately supported • Growing efforts to address these challenges still externally funded • Are RECs in touch with the local context?
Fair scientific collaborations	• Equitable benefit-sharing agreements • Recognising local contributions in scientific publications • Maximising research benefits to sample donors and communities	• Challenges with determining appropriate benefit-sharing agreements. • What counts as benefit, how these should be shared, who should be the focus, participants? Communities?
Sustainable micro and macro-level relationships	• The role of trust and trustworthiness in scientific research • Respect, transparency, openness, consistency of behaviour, integrity, honesty, trustworthiness	• Requires researchers and research institutions to be trustworthy and accountable • But trust has limits • Can an entrustment model be appropriate in these contexts?

Table 13: Stakeholders' proposed solutions

Chapter 8: Discussion, Recommendations and Conclusions

"I'm not against scientific research. I just want it to be done right. They used our blood for all these studies, people got degrees and grants, and they never asked our permission."
(Carreta Toulisi, Havasupai Tribe Member)

8.1. Introduction

My primary aim in this thesis has been to contribute to an empirically-informed understanding of the ethical issues arising in the export, storage and future uses of human biological samples from Sub-Saharan Africa. As discussed in Chapter 1, the empirical research for this thesis was motivated by growing tensions in scientific collaborations around these research practices, challenges faced by research ethics committees, the limited body of scholarship on biobanks in SSA and the lack of clarity and limited guidance to inform review and best practice.

In this chapter, I critically reflect on the findings of my empirical research, and their relationship with current research ethics literature and international ethics guidelines, and explore their implications for the ethics of the export, storage and future uses of human biological samples. I begin with a summary of key findings of the empirical study and reflect on ways in which my research contributes to the field of bioethics. I then propose a framework for addressing the ethical issues arising in this increasingly important aspect of research with a set of points to consider. In this thesis, I used human biological samples as a lens to offer insights into the need to refocus attention on the key ethical values and governance mechanisms that can move both the science and ethics of international biomedical research forward.

8.2. Summary of key findings of the empirical research

The findings of the empirical research were discussed in depth in chapters 4 to 7. In Chapter 4, I highlighted the evolving nature of scientific research, the increasing role of collaborative partnerships and the compelling scientific rationales for the collection, export, storage and future uses of samples. These include the lack of facilities and expertise to process samples locally, the need for uniformity of analysis, quality control and the opportunity to utilise samples in future research at a lower cost without further bleeding of participants. However, despite some existing institutional requirements and mechanisms governing these research practices, several practical ethical issues arise both at the micro-level (host community-host institution relationships) and the macro-level (institutional relationships).

At the micro-level – discussed in Chapter 5 – consent emerged as a major ethical challenge. The data revealed that while there is a general agreement that researchers have a duty to ensure that the basic elements of consent such as information, understanding and voluntariness are met, in practice, there are challenges. These range from a misunderstanding of scientific research more generally to issues related to use of blood samples in specific research projects and the export of samples. Nonetheless, despite these difficulties in research understanding and local rumours about uses of blood, it was apparent from the data that the host community – in Kilifi and Navrongo – generally has a positive appreciation of the work of research institutions and are in many cases willing participants of research. This was attributed to perceived and expected health benefits of research participation and the good relationship that exists between the research institution and the community.

In Chapter 6, I found that many of the issues arising from these scientific research practices relate to how research collaborations are set up, what and how agreements are reached and how research projects are managed. Although there was a general consensus about the benefits of engaging in international scientific collaborations, such as the opportunity they offer for local research institutions to strengthen research capacity, and remain visible in the wider scientific community, researchers and REC members highlighted concerns that arise in practice. These macro-level issues include fears and anxieties around sample export, loss of control of samples, the lack of recognition for the host institution's contribution, inadequate capacity building and the inequities in the distribution of research benefits.

To address these micro and macro-level issues, stakeholders have proposed a number of solutions and recommendations, which were discussed in Chapter 7. These included; local capacity strengthening, better consent processes and community engagement, effective research ethics committees, equitable research contracts and agreements, benefit-sharing and sustainable research partnerships and relationships. These findings also highlighted the limitations of current governance mechanisms and the importance of trust-building in sustaining research in these resource-constrained settings.

Reflecting on these findings, I have drawn three main conclusions;

1. The nature of scientific research is changing and collaborations across borders and access to samples (including export and future uses) will continue to be important for much of the research taking place in SSA. In relation to this development, many of the ethical issues arising in practice relate to the nature of the interactions between host research institutions and host communities (micro-level) and those between collaborating institutions (macro-level).

2. There are limitations with current governance mechanisms such as the role of research ethics committees, which require improvement.
3. Appropriate forms of trust-building at the micro and macro-level are important in moving both the science and ethics of international biomedical research forward.

In what follows, I will discuss each of these conclusions and explore their implications for research involving human biological samples. Although the focus of my research was on the practical ethical issues arising in the context of international scientific collaborations in two research settings in SSA, many of the issues discussed in this thesis are likely to be relevant to research in many contexts.

8.2.1. The evolving nature of science and role of collaborative partnerships

In my analysis of the data – discussed in Chapter 4 – it became apparent that biomedical research is evolving rapidly and its growth and future will increasingly depend on access to human biological samples and collaborative partnerships. This is consistent with much of the current literature on biobank research highlighting the important societal value of biobanks in advancing biomedical research (Kaye 2006; Cambon-Thomsen, Rial-Sebbag et al. 2007; Gibbons and Kaye 2007; Kaye, Curren et al. 2012). Biomedical research is also a complex and expensive enterprise requiring the pulling together of expertise and resources to achieve important research goals which include alleviating suffering, advancing knowledge, preserving life and promoting human well-being (CIOMS 2002; WMA 2008).

Like health systems, international scientific collaborations are also intrinsically relational and involve what Lucy Gilson calls ‘a complex web of relationships’ (Gilson 2003) at the macro-level (between collaborating research institutions) and the micro level (between host institutions and local communities).

Many research projects particularly those focussing on genetics, genomics and epidemiological studies on common diseases with rare components, require large numbers of samples which can be best achieved through research consortia involving several research sites. In many cases, this also involves collaborations across national borders and between researchers and institutions in SSA and HICs (Chokshi, Parker et al. 2006; Parker and Bull 2009; de Vries, Bull et al. 2011). My research supports other views in the literature that with advances in science and technology, biomedical research will continue to be cross-national and cross-cultural (Zumla and Costello 2002). Thus, what is needed is developing mutually advantageous interactions between collaborating parties (Wertheimer 2008; Wertheimer 2011).

Given the above development, my research suggests that most of the ethical issues arising in sample export, storage and future uses relate to the nature of the interactions between the host research institution and its collaborators (macro-level) and between the institution and the host community (micro-level), as discussed in Chapter 5 and 6 respectively. These complex relationships present a number of challenges which could potentially cause tensions between research partners and potentially impede important research. The concept of collaborative partnership is seen as one key way of addressing these concerns (Emanuel, Wendler et al. 2004).

Collaborative partnerships at the macro-level

As noted in my literature review, in the bioethics and international research ethics literature, the research relationships between SSA and HICs have sometimes been described as exploitative, semi-colonial in nature and as some have put it akin to 'Cinderella and the Ugly sisters' (Costello and Zumla 2000; Jentsch and Pilley 2003; Binka 2005; Molyneux and Geissler 2008).

Scandals and controversies arising from collaborations with research institutions in HICs, particularly those involving big pharmaceutical companies as well as publicly-funded research institutions have sometimes overshadowed the important contributions of many international collaborative projects. Examples include the infamous tenofovir trials in Cameroon (Mills, Rachlis et al. 2005; Mack, Robinson et al. 2010), and the Pfizer Trovan trials in Nigeria (Stephens 2006; Ezeome and Simon 2010). Most of these controversies arose from failures to obtain appropriate consent, failures to engage with local research actors and failures to provide tangible benefits to host communities.

These criticisms have given rise to a growing recognition of the importance of collaborative partnerships (Emanuel, Wendler et al. 2004) and community engagement in global health research (Rotimi, Leppert et al. 2007; Tindana, Singh et al. 2007; Parker and Bull 2009). As discussed in Chapter 4, it was apparent in my research that while some progress has been made to develop mutually beneficial research relationships between SSA and HICs, achieving this in practice is often complex. This is because currently, these research relationships often involve unequal partners, and thus the collaborations are asymmetrical from the outset, with external partners driving the research agenda, either as initiators of the research idea or as sole funders of research. As scientific research becomes more technologically sophisticated, research participants, host communities and indeed local researchers will become more dependent on the expertise of those with the scientific knowledge to use the samples entrusted in their care responsibly (Pellegrino 1992). For example, as discussed in Chapter 4 and also later in Chapter 6, the sophisticated equipment needed for certain types of analysis – such as genome sequencing – and the expertise needed to process the massive amounts of data produced, require host institutions to depend on more advanced collaborators – as well as more advanced institutions within country.

What works: A focus on local capacity strengthening

My research suggests that one practical solution to these macro-level issues is to strengthen the capacity of host research institutions to enable much of the research process to be conducted locally and to enhance local control of samples. However, because no level of local capacity can completely eliminate sample export – such as requirements for uniformity of analysis and quality control – there is the need for some assurance that the interests of the less dominant partners in the collaboration (host institutions, participants and communities) will be adequately protected, against the background of inevitable sample export. This may require effective governance mechanisms including strengthening institutional trustworthiness.

I have also shown that while much of the discourse in the literature about research collaborations involving HICs and SSA highlights the potential for exploitation, similar issues arise in south-south collaborations and even between institutions within the same country (Chapter 6, p144). This suggests that the macro level issues such as local control of samples are not just about samples leaving national boundaries. Rather, they are related to the management of power relations within collaborations in which samples will leave the host institution. This has implications for other south-south scientific collaborations, such as H3 Africa projects, as well as those involving HIC and LIC settings. It is important to recognise that irrespective of where research is conducted and which partners are involved in the collaboration, what counts as a good scientific collaboration depends on key values such as trustworthiness, mutual respect, partnership, mutual understanding and mutual interest. I return to this later in the chapter.

Collaborative partnerships at the micro-level - Local communities as research partners

At the micro-level, my research suggests that, not all research actors, such as sample donors, communities and fieldworkers, are at the same level of knowledge and understanding of the justifications for research collaborations and the rationales for sample use and export in research. The perceived lack of understanding has been attributed to low levels of literacy in these settings and the unfamiliarity, uncertainties and complexities associated with novel research projects such as genetic and genomic research. Although some authors (Nyika 2009) have cautioned against exaggerating the effect of illiteracy on research understanding, to a large extent these perceptions of the complexities of scientific research hindering research understanding hold true and need to be taken seriously (Tekola, Bull et al. 2009; Tindana, Bull et al. 2012).

Consequently, in my research, suggestions for resolving these ethical challenges have focused on improving research understanding and 'demystifying the science' of research (see Chapter 7 170). Even in settings with high literacy, recommendations have been made for more carefully considered or locally relevant information as well as providing appropriate training and support structures for field and frontline staff who give out this information (Mandava, Pace et al. 2012; Kamuya, Theobald et al. 2013). With growing evidence globally of the challenges with obtaining valid consent and that research participation is not necessarily based on informed consent (Kass, Sugarman et al. 1996; Molyneux, Peshu et al. 2004; Mfutso-Bengo, Ndebele et al. 2008), I believe that examining the nature of researcher–participant relationships (and by extension local communities–host research institutions) could provide insights into the underlying issues arising from research practices involving human biological samples.

The relationship between research participants and researchers (and by extension between the local community and host research institutions) in many SSA settings can also be described as asymmetrical in nature. Yet they also need each other to address important research questions. Research participants and their communities are important partners in research – but how much power and control do they have over the research process?

Findings from this research suggest that research participants' difficulty in understanding the complex nature of scientific research, the lack of access to good health care as well as problems with the unknown nature of future research have resulted in a dependence on research institutions and upon their agents using samples appropriately. There is an unspoken understanding that when participants consent to blood sampling in research, they invariably entrust researchers and their institution with the responsibility of using these valuable resources to address health problems relevant to them. However, the existing power imbalances and dependency also presents concerns about the potential for abuse and exploitation if not appropriately managed. Interestingly, despite these concerns, host communities continue to have some confidence in the host institutions. As discussed in Chapter 5, this community confidence in research has been attributed to the steps that these research institutions have taken to actively engage with the host community and the provision of tangible health benefits.

Thus, it is important for research institutions to recognise research participants and host communities as important partners in biomedical research and to identify innovative ways of actively engaging them in research, particularly around the use of human biological samples.

At both macro and micro levels, my research also suggests that trust plays an important role in the successful implementation of research. What is needed is an assurance that the community's trust will not be taken for granted. As proposed in many international guidelines and influential reports such as the Nuffield Council on Bioethics report and follow-up

discussions (Nuffield Council on Bioethics. 2002; Nuffield Council on Bioethics. and Hepple 2005), researchers have a duty to avoid exploiting vulnerable populations. Building collaborative partnerships through genuine community involvement is a key way of avoiding exploitation and preserving public trust and confidence in research. I discuss the practical ways of achieving this later in the chapter.

8.2.2. The limitations of current protection mechanisms

The second conclusion that can be drawn from this project is that current ethical standards such as requirements for consent and research ethics committees have limitations in responding to the complex, sometimes messy, unpredictable and uncertain ethical issues arising from sample storage, export and future research uses. As discussed in Chapter 2, p11, much progress has been made to regulate research with human participants since the infamous Nazi trials in the mid-20th century. There are currently a great many codes of ethics, declarations, guidelines, policies and documents guiding the conduct of biomedical research in general across the globe (OHRP 2013). Several research institutions in SSA such as the KWTRP and NHRC have also established institutional policies and research ethics committees to ensure that research is conducted according to strict ethical standards, although some are still rudimentary (Kass, Hyder et al. 2007; Nyika, Kilama et al. 2009). The plethora of rules and regulations governing research would suggest that perhaps we do not need more guidelines, if we take the principles underpinning them seriously. What may be important is ensuring that these guidelines actually work and improve practice in the 'field'. However, while rules and guidelines may have contributed to promoting good research practice and to some extent ensuring ethical and lawful research, responses in my research suggest that several practical ethical concerns associated with uses of human biological samples remain unresolved.

Some of these concerns, especially around consent for future uses of samples, reflect current debates in the literature – particularly on biobanks (Hansson, Dillner et al. 2006; Karlsen, Solbakk et al. 2011).

In what follows I discuss the limitations of the two key protection mechanisms governing the collection, export, storage and futures uses of biological samples in research; consent and review by RECs.

Issues with consent, future research and the fear of unknown

Most international research ethics guidelines and regulations place emphasis on informed consent as an ethical requirement for protecting the rights and interests of participants (CIOMS 2002; WMA 2008). Yet, consent remains one of the most contentious issues in the bioethics literature. Not surprisingly, this also emerged in my research as a key ethical challenge in sample export, storage and future uses. As discussed in Chapter 5 p103 – seeking valid consent especially for sample export and future uses remains a challenge in Kilifi and Navrongo. There is still lack of guidance and uniformity on how sample export should be regulated and whether explicit consent for sample export should be obtained from potential research participants. There are inconsistent findings from the limited empirical studies in SSA addressing the issue of sample export and data sharing (Langat 2005; Wendler and Pace 2005). Responses from my research suggest that views about the country of destination for exported samples largely depend on whether participants trust the systems in place in that country to protect their interests and as Igbe and Adebamowo found in Nigeria, whether the people running the biobanks are trustworthy (Igbe and Adebamowo 2012). This suggests that addressing the concerns around this research practice would require effective governance structures and an assurance from host institutions that the interests of participants and their communities will be protected.

Recent controversies surrounding the use of samples in scientific research such as the Havasupai case in Arizona in the USA have raised concerns about the limitations of current consent regimes and growing fears about maintaining public confidence and trust in scientific research amidst the uncertainties (Mello and Wolf 2010). It is widely acknowledged that the fact that consent has been obtained for future uses of samples does not in itself make all such research ethical. As we saw in the Havasupai case – and as supported by my empirical research findings – research communities are often not against scientific research, they only want it to be done right (Mello and Wolf 2010). Doing it right requires not just relying on consent but also ensuring that donors are not used even inadvertently solely as a means to an end by others. As the stakeholders I interviewed have suggested, it would take more than putting in place guidelines. It would also require that research institutions develop an institutional culture of trustworthiness and take the necessary steps to bolster public trust and confidence in the research enterprise.

Contributing to the debates around broad consent for future uses of samples

My research findings are consistent with current debates in the bioethics literature on the challenges with maintaining the traditional standard of informed consent for sample storage and future uses (Cambon-Thomsen, Rial-Sebbag et al. 2007). There was a general perception that obtaining fully informed consent in this context is impossible because the specific research questions that will be addressed and who might have access to the samples and associated data, cannot be predetermined. These uncertainties are likely to increase with advances in genomics and bioinformatics (O'Doherty, Burgess et al. 2011). Yet, most of my respondents felt that nonetheless important research should be conducted without necessarily breaching ethical standards. The dilemma here is how to balance the interests of sample donors with the broader societal value of research with human biological samples (Secko, Preto et al. 2009).

In the biobank literature in HICs, several approaches have been proposed ranging from broad consent, consent authorization, public deliberation and effective governance (Caulfield, Upshur et al. 2003; Secko, Preto et al. 2009; O'Doherty, Hawkins et al. 2012).

Much of the current debate focuses on the validity of broad consent, such as asking participants to consent prospectively to future research without specific information. Proponents like Hansson and Sheehan (Hansson, Dillner et al. 2006; Sheehan 2011; Sheehan 2011) have argued that broad consent is legitimate because it is consistent with current practices, it respects the autonomy of participants and the risks involved are minimal. Some international guidelines such as the 2006 supplement to the CIOMS guidelines also support the concept of broad consent for future uses of samples and tissues (CIOMS 2006). The argument put forward is that insisting on informed consent in its strict sense would mean returning to research participants for re-consent, which is practically not feasible and could undermine important research. The conditions for legitimising broad consent are that personal details are handled safely, 'future' research is reviewed and approved by a REC, and participants are given the opportunity to withdraw at any time.

Critics of broad consent like Arnason have argued that 'it is misleading to use the notion of informed consent … in research that is unforeseen and has not been specified in a research protocol' (Arnason 2004, p41). This latter argument was the general view in my research albeit there was recognition that for genomics and many epidemiological studies, obtaining specific consent would be practically impossible and may hinder important research projects. As I argue later, a form of governance grounded in the concept of entrustment may be a helpful way of addressing this ambiguity.

Gift Models

Another approach is the gift model. For example, the UK Medical Research Council's guidelines for research with human tissues recommend that samples should be considered as 'gifts' (MRC 2011). In a gift model, the receivers has no obligation to give back to the donor and the donors have no control or claim over how the gift is used (Wendler 2012). In other words, the receivers can do whatever they like with the gift.

The argument for this approach is that considering donated samples as gifts reflects the altruistic nature of research participation (Glantz, Roche et al. 2010; MRC 2011). While the gift model may be appropriate in the context of tissue donation in some clinical settings, in the context of research collaborations in LMICs, asking participants to donate their samples and tissues as gifts to a research institution without placing responsibilities on the institution to give back to the community may raise concerns about exploitation. In the light of my findings, what is needed is a framework that allows research participants and communities to donate their samples for research purposes out of their own free-will but also makes the recipients, in this case research institutions accountable to the community. Accountability requires regular feedback to the community about the status of the samples, ensuring that samples are only used for ethically approved and acceptable purposes and under the principles of non-maleficence, preventing harm to research participants and their communities (CIOMS 2002; Beauchamp and Childress 2009).

The limits of Research Ethics committees

This research has also highlighted the important role of research ethics committees in addressing the issues arising in sample export, storage and future uses, as discussed in Chapter 7. Especially with future uses of samples, interviewees believe that RECs have an important gate-keeping role to advise researchers on when participants should/should not be re-contacted

for their consent for future research projects and what would be an acceptable future use of samples. The assumption being made is that RECs are independent and better informed to make these decisions. However, as my data also suggest, there are concerns that some REC members may also not fully understand some scientific aspects of research and their implications on the rights and well-being of research participants and communities. This has implications for determining the role, composition and training of RECs in SSA and suggests that the ethics review mechanism need to evolve with advances in biomedical research.

Research ethics committees also have limits. As discussed in Chapter 4 and later in Chapter 5, currently, RECs have no way of determining the status of stored and exported samples and have had to trust the integrity of the institution overseeing the samples to ensure their appropriate use. Determining what counts as acceptable future uses of samples should not depend on RECs alone, particularly in SSA where many RECs are still rudimentary and facing numerous challenges (Benatar 2007; Kass, Hyder et al. 2007; Nyika, Kilama et al. 2009). The huge responsibility placed on RECs would require significant resources, training of members to appreciate the complexities surrounding emerging scientific methodologies such as those applied in genetic and genomic research and to determine the implications of these types of research on individual participants and their communities. Without this support, RECs may be either making unrealistic demands on researchers which could impede important research or failing to notice important ethical considerations. This also suggests that there is the need to 'rethink' the current role and function of RECs to meet the evolving nature of scientific research.

8.2.3. The importance of Trust-building in moving the science and ethics of research forward

"Public confidence in the ethics and integrity of the research process translates into popular support for research in general" (US NBAC report 1999)

A third conclusion from this research is the important role of trust-building in advancing the science and ethics of research involving human biological samples. Trust emerged from my research as an important value in sustaining collaborative partnerships at both the micro and macro-level and in mediating some of the ethical challenges arising in practice. As discussed earlier, there was some evidence that this often 'unspoken' and 'unwritten' principle is what contributes to successful conduct of international collaborative biomedical research. The concept of trust has however not received the needed attention in international research ethics.

What is trust and why does it matter in scientific research?

There are various conceptions and theories of trust in the literature (Pellegrino 1992; O'Neil 2002). There are also disagreements among scholars about the definition and the nature of trust (Levi 1998). In the context of health care systems, Gilson defines trust as a relational notion concerning voluntary actions that involve "an element of risk derived from one individual's uncertainty regarding the motives, intentions and future actions of another on whom they depend" (Gilson 2003, p1454). Trust also defines a relationship between actors or groups, "in which one party adopts the position, expressed either verbally or behaviourally that the other will pursue a course of action that is considered preferable to alternative courses of action" (Braithwaite 1998, p47). Key elements in these definitions of trust are – uncertainty, motives, intentions, future actions and dependency – which are directly relevant to the current nature of scientific research and research interactions at the macro and micro-levels discussed earlier in the thesis (see Chapter 5 and 6).

Much has been written on interpersonal trust between physicians and patients and between researchers and research participants, highlighting virtues that researchers are required to possess to sustain this trust (Baier 1986; Pellegrino 1992; de Melo-Martin and Ho 2008). The central theme of trust in biomedical research has also been reported in previous empirical studies conducted in Kilifi and Navrongo and other research contexts (Molyneux, Peshu et al. 2005; Tindana, Rozmovits et al. 2011). Perhaps surprisingly, however, impersonal trust such as those with and between research institutions has hardly been explored. As institutions become the key players in advances in biomedical research and with recent calls on the need to restore public trust in scientific research (Yarborough and Sharp 2002; Yarborough and Sharp 2009), it is important that this subject is given the much needed attention in international research ethics.

What does it mean to trust an institution? What 'virtues' should research institutions possess? To what extent should research participants place their trust in research institutions and their agents? These are very difficult questions but very important nonetheless. In the social science literature, there is a debate on whether institutions can be trusted (Levi 1998). As discussed throughout this thesis, the nature of scientific research suggests that appropriate forms of trust-building are important to advance both the science and ethics of biomedical research. First of all this thesis has shown that participants' decision to participate in research or to donate samples for research also depends on whether they find the research institution trustworthy.

Secondly, scientific research is increasingly becoming complex. This makes understanding research challenging for all but the most sophisticated scientists. These complexities and uncertainties require some form of trust-building and a reliance on research institutions to use samples in a responsible way to provide some health benefits to the community and alleviate suffering. As we saw in Chapter 5, even REC members have had to resort to trust because of the challenges with monitoring exported samples.

Thus, there is a strong reason for investigating and considering ways of promoting appropriate and well-placed trust in the biomedical research field. Responses from my research on the value of trust and trustworthiness are to some extent in line with virtue-based theories of normative ethics, which place emphasis on the role of character in determining ethical behaviour (Beauchamp and Childress 2001). In a trust-relationship, it is expected that 'the person trusted has explicitly or implicitly made a promise to act well with respect to the interests of the other person' and that this promise will be kept (Pellegrino 1992, p72). Extending this conception of trust to institutions would require an 'institutional character' that respects and protects the interest of research participants and their communities. I discuss the 'character' of a trustworthy institution later in the chapter. As Gilson has also advocated;

> *"[research] institutions build their legitimacy when they demonstrate through organizational and managerial practices values and norms that underlie or are associated with trust" (Gilson 2003,* p1458*).*

Thus, institutions need to establish appropriate structures to demonstrate that they are worthy of the trust placed in them. It is also important to recognise that trust is fragile and risky (Kass, Sugarman et al. 1996). According to Pellegrino, 'to trust and entrust is to become vulnerable and dependent on the good will and motivations of those we trust', which is sometimes problematic (Pellegrino 1992). The history of human subjects' research has taught us that when trust is breached, it can have dire consequences. However it is important not to generalise research scandals in biomedical research to all scientific collaborations. While it is important to recognise the role of trust in the relationships at the macro and micro-level, what is needed is to establish appropriate oversight mechanisms to promote institutional trustworthiness, responsibility and accountability in the research enterprise. This is the basis of my argument later in the chapter.

A research model that allows research participants and communities to voluntarily entrust their samples to trustworthy research institutions will not only enable important scientific research to take place but also ensure that the latter are accountable to the community. Taking forward the findings of my research and stakeholders' proposed solutions, in the next section of this chapter, I develop my arguments for what should count as good ethical practice in the export, storage and future uses of human biological samples.

8.3. Towards an account of *Entrustment*

Given the lack of clarity and limitations of existing guidelines and governance mechanisms for research involving human biological samples, I argue that *entrustment* would be a helpful way of addressing the practical ethical issues arising from sample export, storage and future uses. My proposed 'entrustment framework' is influenced by the central role of trust in scientific research arising from my data, the uncertainties surrounding future research uses of samples and the level of engagement between host institutions and host communities.

What is entrustment?

The Oxford English Dictionary defines entrustment as the act of "assigning the responsibility for doing something to someone". In the context of research involving human biological samples, entrustment will mean participants/communities *giving over* (entrusting) samples to research institutions to advance scientific research. But this act involves not just handing over samples but also assigning responsibilities. To some extent, there is evidence that this is what happens on the ground, what is needed is to concretise it in practice. For example, Sheehan's defence of broad consent highlights aspects of entrustment when he argues that 'the relevant information is about the person (or institution) who will make the decision for me' (Sheehan 2011).

But, to what extent is entrustment valid in the interaction between sample donors/communities and researchers and their institutions? I argue that valid entrustment is possible *under certain conditions*, which I discuss later in this chapter.

Entrustment requires that the one to whom responsibility is entrusted is trustworthy (O'Neill 2002). In other words, if A entrusts responsibility for samples to B, the expectation is that B is trustworthy. According to authors such as Valerie Braithwaite (Braithwaite 1998) and Margaret Levi, when citizens and clients say they trust an institution, "they are declaring a belief that on average, its agents will prove to be trustworthy and that they will live up to the trust placed in them" (Levi 1998, p80). Thus, the key requirement here for valid entrustment is trustworthiness.

To some extent we can relate this to researcher-participant relationships in scientific research, at least in Kilifi and Navrongo as my research suggests. As discussed earlier, there is an 'unspoken' understanding that when research participants consent to blood sampling in research, they also entrust researchers with the responsibility of using samples wisely. In return, research institutions have a moral obligation to ensure that they use these samples responsibly and reciprocate by providing tangible health benefits. This can be seen as a cyclical journey from the village to the lab and back to the village.

My interest is however in the relationship between host communities and host institutions and the increasing role of the latter as stewards of samples. The evolving nature of research and scientific understanding of diseases and the complex web of relationships involved suggest that this enterprise is no longer an individual matter. Whilst individuals do make a difference, institutions are the key players. Due to the increasing collaborative nature of scientific research, the stakeholders I interviewed have suggested that no individual researcher should own research samples; rather research institutions with oversight from research ethics committees

should remain the stewards of these samples. This suggests that the ultimate responsibilities should lie with research institutions to manage the uses of these samples appropriately bearing in mind both the scientific and cultural value of human samples. It is therefore important to focus on building trustworthy research institutions as a way of addressing the ethical issues that arise in practice.

Entrustment creates moral relationships between participants and researchers including the notion of responsibility. And in contrast to gift models, in an entrustment, researchers and institutions cannot do whatever they like with samples because they have responsibilities as well. Entrustment with some form of accountability also encourages altruistic motives for research participation, and protects research participants and their community from unacceptable uses of samples that may affect their wellbeing and values.

Drawing on entrustment models in other discourses, such as Richardson and Belsky's partial-entrustment model (Richardson and Belsky 2004), this model seeks to build in trustworthiness and accountability into the research enterprise. While the partial-entrustment model and subsequent discussions specifically touch on researchers' responsibilities to provide ancillary care (Richardson 2007; Merritt 2011), key elements of this model directly relate to how we ought to address institutions' responsibilities in managing human biological samples. For example, the nature and strength of the engagement between researchers and participants (including participants' vulnerability and dependency) is an important element in the entrustment model.

Another model influencing my proposal for 'entrustment' is a charitable trust model proposed by Winickoff and Winickoff (Winickoff and Winickoff 2003). Here, tissues are held in trust for the donors by a trustee who oversees uses in accordance with the wishes of the benefit of the trust. This model requires the establishment of an independent party to manage the trust.

The authors argue that this model would allow the donor community to maximise the altruistic value of its gift (ibid). Although this model could potentially protect the interest of sample donors, it may face challenges in its application to the research context in resource-constrained settings such as deciding who serves on the trust and ensuring that they are adequately funded. Strengthening existing bodies such as local ethics committees and community advisory committees in these contexts could be one key way forward (Strauss, Sengupta et al. 2001).

Recently, Emerson et al also proposed a tissue trust model to build scientific capacity in the developing world, to facilitate local research and reduce exploitation by eliminating the need for sample export (Emerson, Singer et al. 2011). While I agree with the key features of the tissue trust, such as host capacity building and local research, my data suggest no real support for the complete elimination of sample export. Given the compelling scientific reasons for sample export – such as facilitating uniformed analysis – what is important is building accountability into the research process to ensure that samples are sent for specific purposes and accounted for by external collaborators. An entrustment framework could help in this direction. It will involve a chain of trust between all the key research actors as illustrated in figure 7:

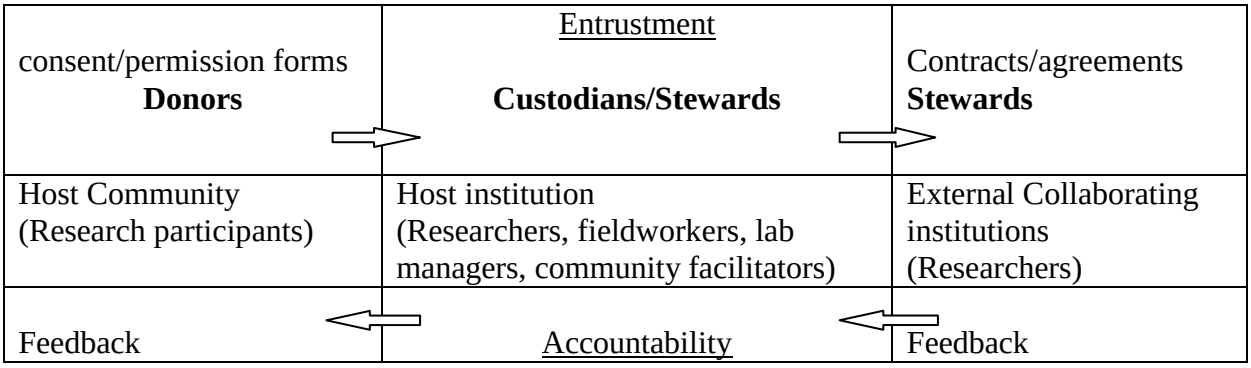

Figure 6: A chain of trust

Key elements of an Entrustment and points to consider

Key elements of an entrustment framework for addressing the ethical issues arising from sample export, storage and future uses are;

1. Developing trustworthy research institutions to serve as stewards of research samples
2. Establishing clear, transparent and workable national and institutional guidelines for human biological samples and tissues
3. Strengthening consent and community engagement practices
4. Strengthening research oversight by research ethics committees
5. Establishing a board of trustees with representatives of all stakeholders to support trust-building at the micro-level.

In what follows, I expand on each of these key elements of the proposed framework.

8.3.1. Host research institutions as stewards of samples

As highlighted in Chapter 6, stakeholders' accounts suggested a desire for host research institutions to serve as stewards of research samples. My reason for supporting this view is that I believe that they bear the ultimate responsibility for the ethical conduct of research. They also have a long-term relationship with the donors and communities of samples, understand the context better, they are close to donors and can be made to account for the samples. They also feel that they have a special obligation to the local community because of this long-term interaction. This is similar to Wertheimer's 'interaction principle' which maintains that 'people often acquire special obligations to those with whom they interact and particularly when they have benefited from that interaction' (Wertheimer 2011). However, to play this important role, certain conditions have to be met. It is important to provide an enabling environment that will allow research institutions to make optimum use of these scientific resources in ways that allows participants and communities to flourish.

Next, I discuss key conditions that could make host institutions' stewardship role possible. They include, setting the right research priorities, sustainable capacity strengthening, strong scientific leadership, clear and transparent institutional guidelines and policies on samples and trustworthiness.

Promoting institutional trustworthiness

As discussed in Chapter 5, many researchers – at least in Kilifi and Navrongo – believe that they have been able to earn the trust of the host community by being consistent in their behaviour, being open and not going contrary to promises made to the community. They have suggested that their closeness to the community and their knowledge that the community trusts them should motivate them to do the right thing. As some suggested, losing the trust of the community and access to samples – which biomedical research depends on – will be at a huge cost to the existence of the research institution. Host institutions should therefore promote a culture of research integrity and also have an interest in doing so. As some respondents in my research have suggested – in Chapter 7, p198 – having clear guidelines alone is not sufficient to address the ethical issues arising from these research practices unless researchers are willing to follow them and conduct their research activities responsibly. The key principles to promote institutional trustworthiness include: good motives/ intent, scientific integrity, honesty, transparency and openness, minimising harm/risks of uses of samples and data. Host research institutions should therefore establish effective mechanisms for promoting these values such as through regular meetings between research teams including field staff, and local training workshops. It is in the interest of research institutions and their agents (researchers, laboratory and field staff) to be trustworthy. They must recognise that the continuing existence of the institution depends on the continuous cooperation of the communities they work in.

1. Set clear goals for research institutions

The primary goals of a research institution should be to promote health and alleviate suffering. Therefore research institutions should carry out research that addresses locally relevant health problems. This position is clearly stipulated in existing international ethics guidelines and should be taken seriously (CIOMS 2002; Nuffield Council on Bioethics. 2002; WMA 2008). The development of collaborative research proposals should be a joint effort and as much as possible should be initiated at the host institution. These goals should be shared with the various research actors within the institution and also with the local community. The institution should periodically reflect on their research goals and priorities and ensure that they meet their obligations to the communities they work in. Host institutions also have a responsibility to ensure that the type of research collaborations they engage in do not leave the communities they work in disadvantaged.

2. Strengthen research competence

Following consistent calls in the literature and supported by findings from my data, it is clear that host research institutions need sustainable personnel and infrastructure capacity to enable them make optimum use of human biological samples locally (Benatar and Singer 2010; Burgess and Sulzer 2010; Ijsselmuiden, Kass et al. 2010). Research institutions can only achieve their research goals if they have these capacities, which would also strengthen their trustworthiness. An institutional strategic plan for strengthening local capacity is therefore important. This also suggests a set of responsibilities for funders and researchers from HICs, to try and incorporate capacity strengthening into big scientific grants. It also requires getting clear on priority areas such as the type of personnel, the equipment required for data analysis. Whenever feasible, sample export should incorporate an element of capacity building, providing opportunities for local researchers to participate in sample and data analysis abroad.

Capacity strengthening should include all levels of staff particularly fieldworkers (who are often community members). For example, host institutions must recognise the vital role of fieldworkers as the 'face' of the institution in the community. Thus, how they manage their interactions with participants and the quality of data they obtain from the field is crucial for the scientific and ethical conduct of research.

While it may not be practical to carve out a career path for fieldworkers, providing them with the necessary training and support to handle the ethical challenges they face in the field would keep them motivated to conduct good quality research.

3. Advocate for local core research funding

Good local research can only be possible if the host institution has adequate funding to strengthen its capacity and sustain research activities. While external funding has proved valuable in many resource-constrained settings, the current over reliance and dependence on external funding for training of local personnel and infrastructure development is not sustainable. As suggested by other commentators such as Gostin (Gostin 2010; Gostin 2012), I also believe that local governments should play a key role by providing adequate core funding to host research institutions. As I indicated in Chapter 2 (p27), Ghana and Kenya's research and development budget of 0.3% of GDP is not adequate. Host institutions should develop effective strategies for engaging policy makers to attract sustainable local research funding and to also work towards the translation of research findings into national policies and subsequently to improve practice. Such an approach could enable research institutions to realise the social value of biomedical research (Emanuel, Wendler et al. 2004; Lairumbi, Molyneux et al. 2008).

4. Strengthen institutional leadership

A key ingredient in sustaining scientific research in SSA is strong scientific leadership. As was seen in Chapter 6, the leadership of the KWTRP has played a key role in the institutions' ability to strengthen local capacity and negotiate for fair research collaborations. Leadership is not only required in the technical aspects of research but also managing human relationships within the institution and keeping members of the team motivated. In '*Managing scientists: leadership strategies in scientific research',* Alice Sapienza suggests a number of ways in which human interactions in a scientific research environment – such as those between investigators, post-doctoral fellows, and laboratory managers – can be improved (Sapienza 1995). These include the ideas of self-learning (such as understanding what motivates the leader/manager and what motivates others in the team), communicating effectively and resolving conflicts within the organization. Dewan and Myatt have also suggested that the qualities of effective leadership include; sense of direction and clarity in communication (Dewan and Myatt 2008). In an increasingly competitive scientific environment, a strong scientific leader should also have good connections with the international scientific community and a good track record to attract good funding opportunities and collaborators.

5. Reciprocity: Give-back to the community

Research institutions should recognise their reciprocal obligations to host communities and develop mechanisms for returning benefits to participants and the wider community. Recognising the important contribution of research participants and communities to scientific research and communicating research results back is a key way forward (Knoppers and Chadwick 2005).

A pragmatic way of doing this is working collaboratively with the district hospitals and health management teams to strengthen local health facilities to provide the needed healthcare services (Lairumbi, Molyneux et al. 2008; Benatar and Singer 2010; Molyneux, Mulupi et al. 2012). Public trust and confidence in scientific research can be bolstered if research institutions are seen to be achieving their goals and if there is evidence of improved health in those communities such as decline in overall morbidity and mortality. Unlike HIC settings where access to good healthcare is available, in LICs, especially those in SSA, it is widely acknowledged that research institutions may have specific obligations to contribute to improving existing healthcare infrastructure in these settings (Benatar 2001; Benatar and Singer 2010).

8.3.2. Establish clear and transparent institutional guidelines and policies

Because there is community trust in the host institutions, it is important to have rules and oversight institutions to protect participants from effects of misplaced trust (Pellegrino 1992). Thus, research institutions also need clear, effective and transparent guidelines and policies on the management of human biological samples (clearly stating the conditions for sample export, storage and future uses). This should include; how samples should be collected, stored and shared between various projects in the institution, who can have access to the samples and the conditions for sample export and future uses. These should be informed by key ethical principles of respecting the rights of research participants and their communities, avoiding harm and minimizing the risks of research and maximizing benefits of research to participants and their communities.

In the case of institutions such as the NHRC, an institutional guideline for human biological samples is urgently needed as none currently exists. Instituting these guidelines would require engaging all levels of staff such as research scientists, laboratory personnel and fieldworkers/ frontline staff and in consultation with RECs and experts in the field.

Engaging with fieldworkers in particular could be helpful in identifying some of the practical challenges in the field, especially at the sample collection stage and ensuring that these are adequately addressed in the guidelines. While some guidelines exist at KEMRI and the KWTRP, some research actors especially fieldworkers and community facilitators are not aware and do not understand the current guidelines to explain to research participants and community members appropriately. It is therefore important to make these documents transparent and available to all research actors.

Institutional guidelines informed by community perspectives could also feed into the development of national frameworks for research involving human biological samples. This bottom-up approach could be the key to ensuring that rules and guidelines work in practice.

8.3.3. Strengthen consent and engagement with participants and community

Host institutions need to develop appropriate consent and community engagement strategies for soliciting community's views on acceptable future uses of samples. As Marsh et al (Marsh, Kamuya et al. 2008) have also suggested, this could also be an important way of balancing the power relations between research institutions and communities. This is a core aspect of the entrustment framework, discussed later in the chapter. My proposal is that consistent with current research ethics guidelines and regulations, specific consent should be obtained for all current studies including appropriate forms of community engagement.

Even with the uncertainties surrounding future uses of samples, research participants should be given the opportunity to grant permission for their samples to be exported and/or stored for future uses out of their own free-will. But this would require some level of trust-building as well as future engagements with the community on acceptable uses. Next, I discuss the various steps to strengthen consent and engagement with participants and host research communities.

1. Obtain informed consent for sample collection and research participation

Consent is an important ethical requirement in research and thus the current practice should be to obtain informed and voluntary consent for sample collection and research participation for all defined research projects. If sample export is anticipated, this should be made clear during the consent process, including the rationales for sample export and what will happen to samples after the initial analysis process. Research teams should identify innovative ways of improving research participants' basic understanding of scientific research and the value of human biological samples in research, particularly for genetic and genomic studies.

As suggested by many stakeholders I interviewed, open research days, laboratory tours and the use of analogies and pictographs could prove very helpful in this direction.

2. Seek entrustment for sample storage and future research uses

Specific consent should also be obtained for sample storage and for future analysis that have been planned and anticipated. For unplanned and unanticipated future uses of samples, I believe that while blanket consent should be discouraged, the current proposals for broad consent –providing the minimum information for future research purposes – are acceptable and participants should be given the option of deciding on future uses of their samples. Unlike other commentators (Sheehan 2011) my position is that what is currently being described as broad consent is not informed consent but an *entrustment* and should be called as such.

This means that research institutions have an obligation to periodically account for these samples and ensure that their future uses are supported by appropriate levels of community consultation.

The concept of entrustment would be a better way of conceptualizing the transaction between research participants and researchers around the export, storage and future uses of samples. It goes without saying that all currently archived samples – collected without consent for future uses – should be regarded as a scientific resource *entrusted* to the host institution by the community. There are obligations on researchers and research institutions to ensure that these are utilized in appropriate and culturally acceptable ways to address locally relevant health research and for the common good.

Secondly, current consent forms should include a clause requesting the permission of individual participants for samples to be stored for future research purposes including the duration of sample storage and the possibility of sample storage failure. If sample and data sharing is anticipated, this information should be included in the consent forms. And as widely recommended in the literature, all future research should be approved by relevant RECs and appropriate levels of community engagement.

3. Seek entrustment for sample export and sample sharing with external collaborators

As much as possible the host institution should build the necessary capacity to store all samples locally. However, sample export should not be entirely ruled out – because of other scientific rationales such as the requirements for uniformity of analysis, inevitable lack of local expertise and contributions to research consortia. I support views by other authors that material transfer agreements should accompany sample export and such agreements should be mutually agreed on (Muula and JM 2007; Andanda 2008; Nyika 2009). External collaborators should however also regard samples in their care as an entrustment, which means they have an obligation to

provide appropriate updates to host institutions on the status of exported samples and ensure that they are only used for studies and analysis that have been mutually agreed upon.

The MalariaGEN data release policy, which encourages local capacity building of data-fellows in malaria-endemic countries to enable them to use samples and data locally, is a great example (Parker, Bull et al. 2009). Institutions should also encourage the transfer of knowledge by ensuring that local scientist get the opportunity to participate in the analysis done abroad. This should however be on a case by case basis. There should also be recognition of local contributions in scientific publications and presentations. As stakeholders have suggested authorship issues should be discussed upfront to avoid any future tensions.

4. Engage with communities for future uses of samples

As discussed in Chapter 7, effective community engagement practices would be important in ensuring genuine partnership with the community to determine acceptable future uses of samples. This process will be particularly important in the utilization of existing archived samples. Effective community engagement strategies should be an integral part of research institutions' scientific activities. Determining what counts as effective community engagement should be context specific and would require some form of deliberative processes (Abelson, Forest et al. 2003). An institutional approach to community engagement may be a useful way of addressing communities' concerns about the use of samples in research more generally. How future uses of samples should be conducted must be guided by a conscientious effort to engage with the relevant local community. There are examples of deliberative processes that have proved useful in soliciting public views that could be explored in specific contexts (Parker 2005; Secko, Preto et al. 2009). Also, conducting empirical studies could also help shed light on how these types of methods would work in practice and in specific settings.

8.3.4. Strengthen research oversight by research ethics committees

While I advocate for host institutions to bear the ultimate responsibility for the ethical conduct of their research, I also acknowledge that researchers and indeed research institutions have personal interests in the conduct of research, including scientific reputation. Taking forward stakeholders' recommendations –discussed in Chapter 7 –RECs should have an important role to play in providing proper oversight over these research practices. However, their roles and functions must also evolve with advancements in biomedical research. Below are a set of recommendations on how RECs can function effectively.

1. Provide adequate training to REC members

RECs would require significant resources to train members to appreciate the complexities surrounding emerging scientific methodologies such as those applied in genetic and genomic research and to determine the implications of these types of research on individual participants and their communities. Regional research ethics training workshops such as those hosted by the Afrian Malaria Network Trust (AMANET) and South African Research Ethics Training Initiative (SARETI) have proved very helpful and should be sustained. Also, recent online courses by the US NIH and the MRC Centre for Genomics and Global Health[16] which aim at improving lay understanding of genetic/genomic research could prove very useful for RECs in Africa. RECs should also develop appropriate ways of getting expert opinion on complex scientific methodologies to facilitate the review process.

[16]see http://globalhealthtrials.tghn.org/elearning/education/lectures/elearning-courses/introduction-to-reviewing-genomic-research

2. Provide adequate resources

Research institutions should provide adequate logistic support to enable RECs function effectively. It would have been desirable for local governments to recognise the important role of RECs and fund their activities directly so that they can be independent from the research institutions in the review process. However, given the relatively low recognition of RECs in SSA, research institutions would have to bear this responsibility. There are now a number of funding opportunities for establishing and strengthening the capacity of RECs in SSA, notably the NIH Fogarty Training Program and the European Developing Countries Clinical Trials Partnership (EDCTP). However, these opportunities are still inadequate to address the growing demands for building the capacity of RECs in SSA. More commitment from major research funders could go a long way to sustain capacity building activities in Sub-Saharan Africa.

3. Develop effective communication with researchers

RECs should also develop effective communication strategies to engage with researchers and understand the practical challenges encountered in the field. This could be done through periodic joint meetings and workshops within the institution. Such communication will not only enhance the protection of participants but would also facilitate effective conduct of research by avoiding unnecessary delays and ambiguities for researchers. RECs should develop appropriate mechanisms for engaging with local communities as well to ensure that local community perspectives are incorporated into the review process.

4. Develop effective communication between RECs

In international research collaborations, multiple REC review is inevitable. Effective communication between RECs would be very important in streamlining the review process and avoiding unnecessary delays. One approach may also be to explore joint reviews in multicentre studies to improve the efficiency of the review process.

5. Actively monitor approved research

RECs should develop effective mechanisms for actively monitoring approved research. This could involve requesting for periodic updates from the institution on the status of exported and stored samples. As we saw in the case of Navrongo in Chapter 5, observing actual informed consent processes in the field would enable RECs to understand the practical challenges in the 'field'. This will ensure that requirements for review take into account these practical challenges. As well, it is important for RECs to be given adequate regulatory backing and power so that they can hold institutions to account for meeting –or failing to meet their obligations to the host community (O'Neill 2004).

8.3.5. Active trust-building and genuine community involvement

Responding to the ethical issues arising from sample use in research would require genuine community involvement, especially, in deciding what is culturally acceptable for future use of samples. Currently, the practice is to relegate this decision to the local ethics committee. While RECs, as independent review bodies, are appropriate for making these decisions, there are also limitations, as discussed earlier. Therefore it is important for research institutions to consider setting up a board/committee of trustees to protect the interest of participants and communities. This independent advisory committee could also provide opportunities for genuine community involvement in deciding acceptable future uses of samples.

Membership of this committee should include scientists, field staff, laboratory personnel and well informed community representative (such as the KCR model in Kilifi). This committee would be responsible for advising the institution on what would count as an acceptable use of samples in research. Table 14 on the next page presents a summary of the key points to consider.

Recommendations	Points to consider
Trustworthy research institutions	Develop clear and transparent research goals Strengthen research competence Advocate for sustainable core research funds Strengthen institutional leadership Reciprocity- give appropriate benefits
Clear institutional guidelines	Develop institutional guidelines for sample collection Develop institutional guidelines for sample export and data sharing Develop guidelines for collaborations and access to samples and data
Effective consent and community engagement Processes	Obtain informed consent for sample collection and research participation Seek entrustment for sample storage and future uses Seek entrustment for sample export and data sharing Engage community in future uses of samples
Effective and efficient research ethics committees	Develop workable standard operating procedures (SOPs) Provide adequate training Provide adequate resources Develop effective communication between REC and researchers Develop effective communication between local RECs and external RECs Actively monitor approved research
Trust-building	Set up a board of trustees or community advisory boards with representation from all stakeholders

Table 14: Key points to consider in an Entrustment Framework

8.4. Summary of key contributions of this thesis and the way forward

In this thesis, I set out to contribute to an empirically-informed understanding of the ethical issues arising in the export, storage and future uses of human biological samples in sub-Saharan Africa (SSA). Given the current lack of clarity and limited governance mechanisms for these research practices in Africa, it was important to examine the current and changing status of these practices, the ethical issues and challenges arising in practice and possible solutions for addressing these issues.

To the best of my knowledge this is the first empirical ethics project to specifically elicit and analyse key stakeholders' views on the ethical issues arising from sample export and future uses in sub-Saharan Africa.

My research demonstrates that to get a better understanding of these issues, it is important to elicit the views of people who are informed, such as researchers (including fieldworkers), laboratory managers, and not just that to reflectively conduct research in ways that provide informed views and recommendations on what should count as good practice. It also illustrates the value of empirical research. For example without speaking to researchers and understanding the compelling reasons for sample export, it would have been possible to draw the conclusion that sample export will necessarily lead to exploitation. Without assessing the capacity and research priorities of host institutions, one is likely to make recommendations about storing samples locally which cannot be implemented. As well, without speaking to fieldworkers and getting an in depth understanding of the practical challenges in the field; it would have been possible to assume that rumours about blood use in research are just based on research misunderstanding.

Findings from my research suggest that the nature of biomedical research is changing and there are compelling scientific reasons for research collaborations and sample export, storage and future uses in particular. These research processes also involve a complex web of relationships between research institutions and between institutions and local communities. Examining the nature of these relationships is a helpful way of understanding the underlying ethical issues arising in practice.

The thesis also demonstrated that current governance mechanisms have limitations in responding to the complex, unpredictable and uncertain ethical issues arising from sample export and future research uses. In this chapter, I have highlighted the importance of establishing clear and transparent institutional guidelines and polices on sample collection, export, storage and future uses in international collaborative research.

These are important to bolster host communities' confidence in the research enterprise and protect participants and communities from the effects of misplaced trust.

However, while having clear guidelines is helpful in specifying the duties and responsibilities researchers owe to their participants as well as promoting trustworthiness, in practice what makes research work 'in the field' are often the 'unspoken' and 'unwritten' rules and agreements guiding the relationship between the host institution and the host community, and the host institution and external collaborators. As my research has demonstrated, what actually makes research work in many resource-constrained settings is the type of relationships that are developed and nurtured at the micro and macro-level.

My proposed 'entrustment' framework seeks to promote trustworthiness and accountability in the scientific research enterprise as a way of protecting the interests of research participants and their communities and also promoting appropriate research in resource-constrained settings.

Despite its limitations, this thesis makes important contributions in a number of ways. One, that the ethical issues arising research practices involving human biological samples need to be understood in the context of the nature of relationships at the micro and macro-level; two, these issues are not limited to collaborations involving HICs but also relevant to south-south collaborations as well; three, guidelines are important but are of limited value alone in promoting the ethical conduct of research and four, that appropriate forms of trust-building and governance mechanisms are necessary to advance both the science and ethics of biomedical research.

Next steps and suggestions for future research

The findings of this research would be shared with the KEMRI/Wellcome Trust Research Programme (KWTRP) and the Navrongo Health Research Centre (NHRC). Based on the feedback I received from the dissemination exercise in Navrongo, I am hopeful that the recommendations from this research would feed into the establishment of institutional policies on the collection, storage, export and sharing of human biological samples and eventually inform the development of national and international guidelines.

Throughout this chapter, I have hinted at a number of areas that would require further research. It would be worth exploring how my proposed entrustment model would work in practice, particularly to explore innovative ways of soliciting communities' views on what acceptable future uses of samples would be desirable. This could link directly to further work on how to assess the effectiveness of community engagement strategies specifically for research involving human biological samples.

Further research to examine the capacity of research ethics committees in resource-constrained settings to effectively monitor and keep track of future uses of samples is needed. This would involve examining the expertise required in the composition of RECs and to incorporate local communities' views in the review process. Who should serve as a community representative on RECs in these settings? And how should RECs ensure that communities' views are incorporated into the review process, particularly on decisions on future uses of samples. These are all questions that need further exploration.

Finally, further investigation on what and how research benefits ought to be shared at both the micro and macro level is needed.

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Appendix 1: Ethics approval letters

The approval letters originally presented here cannot be made freely available via ORA because of they contain my personal details as well as details and signatures of the Chairs of the research ethics committees that approved the research.

Appendix 2: Study Information Sheet and Consent forms

The study information sheet and consent forms originally presented here cannot be made freely available via ORA because they contain detail information of the ethics committees which approved the research.

Appendix 3: Guide for semi-structured interviews and Focus Group Discussions

3A. Guide for interview with researchers

Title of Project: Ethical Issues in the Collection, Export and Long-term Storage of Human Biological Samples from Africa

Introduction

- thank the respondent for participating and briefly describe objectives of project
- review Study Info Sheet & provide copy of Consent Form for signature
- outline the format of interview

Background of Interviewee

Could you please tell me a bit about yourself? i.e. your background and training?

Nature of Research Collaboration

- Can you tell me a bit about the project/projects you are currently involve in?
- Probe for clinical trials, genetic/genomic research? Probe for research collaboration
- Now let's talk a bit more about (focus on one specific project)
- Which countries are involved in this collaboration? Probe for other developing countries? Africa? Developed countries?
- What is the nature of this collaboration? Prompt: How is the grant for this collaboration managed? What are the roles and responsibilities of the various partners in this collaboration? How were these roles decided?
- In what way is collaboration important for this type of research? Pulling resources, expertise etc.
- Why is this research important? Probe for science, patients, community/country, global health
- What in your opinion is working well in this type of collaboration?
- What are the challenges you encounter in this kind of research collaboration?
- Importance of Human Biological Samples in Research
- What types of samples are involved in your research and why are they important for this type of research? Probe for blood, and its derivatives (DNA, serum etc.), what are the alternatives to the uses of samples in research?
- What capacity exists locally to handle and analyze these samples? Probe if biological sample transfer/export is involved, If not locally probe for reason(s), what types of samples are exported?

Export of samples

- What is the main reason(s) for the export of samples? Probe for capacity related issues, centralized analysis etc., where specifically are these samples exported to?
- What are the oversight systems in place for export of samples from Kilifi? National/institutional policies and processes

- MOU/Material Transfer Agreement for this research? Does the MTA cover long term sample storage?
- If yes, how were these agreements drafted? Who signs them? Are local ethics committees involved? How are they involved? If no, why? Who takes responsibility for the materials transferred?
- What approvals are required for the export of these samples and in what way have these processes facilitated the research process?
- What specific issues or challenges does the export of samples raise for your research? Does it matter where samples are exported to? I.e. Egyptian study 2010?
- Some people have advocated for a ban on export of samples, what are your views on this? What are the alternatives to sample export? Probe for local capacity building
- What processes would you recommend for the export of samples?
- What is needed to be put in place to govern sample exportation? Probe for type of consent needed, oversight by ethics committee? Inclusion of local personnel on advisory board, Return of samples to local institution?

Storage of Samples and future uses

- What are the main reasons for storing samples beyond the current research?
- How long are these samples often stored? Probe for rationale for the length of storage
- In what way should we deal with future unforeseen uses of stored human samples?
- Should such samples be used to address research questions in diseases other than the one that was originally investigated? Probe for ownership/benefit sharing issues if research leads to a new discovery?
- What do you think about the long term storage of samples in general?
- What is needed to be put in place to govern sample storage and future uses? Probe for type of consent needed, oversight by ethics committee? Inclusion of local personnel on Advisory board, Return of samples to local institution?
- What institutional policies are in place to guide the export of samples? How about long-term storage of samples? What are the requirements? Probe for forms that need to be filled? When it was introduced? Why? How useful this form is?

Consent process

- Now I'd like to ask you more specifically about your experiences with obtaining consent for your research focusing on sample collection and export.
- Can you briefly describe the consent process for your research?
- Is there a community engagement process in your research?
- Please describe this process and what issues are often addressed
- Does the information you provide to your participants include overseas samples export? Probe for separate consent for collection? Export? Storage?
- What are the challenges with seeking consent for this type of research?
- What are your views on obtaining one-time prospective consent for future use of samples
- Need to re-consent for future uses? Systems for checks? Use Havasupai example?
- Do you think that research participants attach any identity to samples? Probe specifically for blood samples?
- Do you think research participants will be concerned about the export of their samples?

- In your view, should participants be involved in discussions around sample export and long-term storage? Why? How? What are the consequences?

Ethics/Governance Issues

- How should the governance of samples be managed? Who should be involved?

Closing Remarks

- Do you have any suggestions about addressing the challenges related to sample export and long-term storage?
- Is there anything that we haven't covered that you would like to mention?

Thank you very much for your insightful inputs to this project

3B. Draft Guide for Interview with Member of Ethics Committee (Nairobi/Navrongo)

Title of Project: Ethical Issues in the Export and Long-term Storage of Human Biological Samples from Africa: Using Ghana and Kenya as Case Studies

Introduction

- thank the participant for participating and briefly describe objectives of project
- review Study Info Sheet & provide copy of Consent Form for signature
- outline the format of interview

Background of interviewee

- Could you please tell me a bit about yourself? i.e. your background and training?
- How long have you been a member of the ethics committee?
- What specific training have you received to serve in this capacity?
- PROMPT: what training have you had in research ethics?

Types of research reviewed

- What types of research are reviewed by your committee? (probe for clinical trials, genetic/genomic research)
- Is the review process different for projects that involve international collaboration? Probe for reasons
- What approvals are given for such studies? What informs the approval process?
- What common ethical issues does the committee often raise during the review of such projects?
- Review Process with focus on sample export and storage
- How often does the committee review research projects that require the export of samples?
- What samples are often involved? Blood samples? DNA? Other human biological samples
- What is the rationale often given by researchers for exporting these samples?
- From your perspective, are the reasons given justified?
- In your view, does it matter where the samples are exported to? Probe for USA, Europe and other African Countries. Probe for reasons
- What specific ethical issues does the export of samples raise?
- What institutional policies are in place to guide the export of samples? How about long-term storage of samples?
- What are the requirements? Probe for forms that need to be filled? When it was introduced? Why? How useful this form is?
- How does your ethics committee ensure appropriate use of exported samples?
- To what extent is the ethics committee in control of samples once they leave the shores of the country?
- Does the committee give approval for such samples to be used in future research? Probe for whose decision it is to allow for samples to be used.
- What kind of approval is usually given? Probe for reasons

Ethics/Governance Issues

- Is it acceptable for samples to be stored abroad? Probe for reasons
- Who should take responsibility/ownership of exported samples?
- How should the governance of samples be managed? Who should be involved?
- Should such samples be used in future research? Probe for whose decision it is to allow for samples to be used.
- Should such samples be used to address research questions in diseases other than the one that was originally investigated? Probe for ownership/benefit sharing issues if research leads to a new discovery?
- What framework should be adapted to data access and control?
- Some people have advocated for one-time prospective consent for future use of samples. What are your views on this?
- Do you think that research participants attach any cultural meaning to samples? Probe specifically for blood samples? Probe for reasons
- Do you think research participants will be concerned about the export of their samples?
- In what way can participants be involved in discussions around sample export
- Should research participants and the wider community be informed about sample export and possible future uses?
- Why is it important for them to know?
- How should they be involved? Probe for best practices
- What is needed to be put in place to govern sample exportation? Probe for type of consent needed, oversight by ethics committee? Communication between ethics committees in SAA and HICs? inclusion of local personnel on Advisory board, Return of samples to local institution?

Closing Remarks

- Based on our discussions, what recommendations would you give for addressing the challenges related to sample export and storage?
- Is there anything that we haven't covered that you'd like to mention?

Thank you very much for your insightful inputs to this project

3C. Guide for Focus Group with Fieldworkers

Title of Project: Ethical Issues in the Export and Long-term Storage of Human Biological Samples from Africa

Introduction

- thank the respondent for participating and briefly describe objectives of project
- review Study Info Sheet & provide copy of Consent Form for signature
- outline the format of interview

Background of Interviewee

- Could you please tell me a bit about yourself? i.e. Your educational background and training?
- Are you from the Kilifi community or from elsewhere?
- How long have you been working for this institution/community?
- What specifically do you do as a fieldworker of this institution (KEMRI/NHRC)?
- Could tell me a bit more about the type of research you are currently involved in? What does the research involve?
- Probe for clinical trials, genetic/genomic research?
- Probe for research collaboration
- What specific training have you received to conduct these studies?
- PROMPT: what training have you had in research ethics?

Sample Collection/Storage/Export

- What types of human biological samples are involved in your research? Probe for blood, and its derivatives (DNA, serum etc.)
- What do you think is the purpose of samples in research?
- What are the samples used for?
- What happens to these samples once they are collected?
- Where are these samples analyzed? If not locally probe for reason(s)
- Are you aware that some samples could be exported to other countries for analysis and possible storage? If yes, what types of samples are exported?
- What is the main reason(s) for the export of samples? Probe for capacity related issues
- As a fieldworker, what do you think about the export and long term storage of samples in general?
- What specific issues does the export and long-term storage of samples raise?

Informed Consent process

- Now I'd like to ask you more specifically about your experiences with obtaining consent for your research focusing on sample collection and export.
- Can you briefly describe the consent process for your research, how you approach the community and potential research participants?
- Is there a community engagement process in your research?
- Please describe this process and what issues are often addressed

- What specific information do you provide to research participants
- What specific information do you provide participants about the purpose of blood-taking?
- Does the information you provide include the possibility of sample export? Probe for separate consent for collection? Export?
- Does information cover overseas sample storage and potential use for investigations other than the current research?
- What are the challenges with seeking consent for this type of research?
- What specific issues do participants often raise during your interaction with them?
- Do you think that research participants attach any meaning to samples? Probe specifically for blood samples?
- Do research participants and/or community members discuss concerns about taking of blood?
- In what way can participants be involved in discussions around sample export?
- What are your suggestions as the best ways of improving the informed consent process?

Ethics/Governance Issues

- As a fieldworker and a member of this community, what are your views on sample export?
- How about storing samples for future research purposes?
- Who should take responsibility/ownership of stored samples?
- Is it acceptable for samples to be used to address research questions in diseases other than the one that was originally investigated? Probe for ownership/benefit sharing issues if research leads to a new discovery?
- Is it acceptable for samples to be stored abroad? Why?
- What do you think are the issues that will be raised by the community about sample collection and export?
- Does it matter where the samples are exported to? USA? Europe? Other African countries? Probe for reasons
- What do you think is the best way of informing research participants and the wider community about sample export and possible future uses?

Recommendations/Concluding questions:

- Do you have any suggestions about addressing the ethical challenges related to tissue export?
- Is there anything that we haven't covered that you'd like to mention?

Thank you very much for your insightful inputs to this project

Appendix 4: List of Interviewees and data collection schedule

4A: Nairobi and Kilifi, Kenya

Target	Key Respondents	Date of Interview	Time/Location
Researchers	1. RES002, Female, Expatriate, PI	20th October 2010	12-1pm, Kilifi
	2. RES001, Male, Expatriate, PI	21st October 2010	1.00-2.00pm, Kilifi
	3. RES003, Male, Expatriate, PI	22nd October 2010	9-10.50am, Kilifi
	4. RES005, Male, Expatriate, PI	22nd October 2010	2.20-3.15pm, Kilifi
	5. RES007, Male, Expatriate, PI	25th October 2010	2-3.35pm, Kilifi
	6. RES004, Female, Kenyan, PI	29th October 2010	10am, Kilifi
	7. RES009, Male, Kenyan, PI	29th October 2010	2pm, Kilifi
	8. RES011, Male, Expatriate, PI	29th October 2010	3.15pm, Kilifi
	9. RES013, Male, Expatriate, RA	1st November 2010	11am, Kilifi
	10. RES006, Female, Kenyan, RA	2nd November 2010	2pm, Kilifi
	11. RES015, Male, Kenyan, PDF	3rd November 2010	12 noon, Kilifi
	12. RES008, Female, Kenyan, PI	3rd November 2010	3pm, Kilifi
	13. RES010, Female, Kenyan, PDF	3rd November 2010	4pm, Kilifi
Cross-Study Key informants (5)	1. CSK001, Male, African Expat.	22nd October	1pm, Kilifi
	2. CSK005, Male, Kenyan	27th October 2010	11am, Kilifi
	3. CSK003, Male, Kenyan	1st November 2010	4pm, Kilifi
	4. CSK007, Male, Expatriate	2nd November 2010	2pm, Kilifi
	5. CSK004, Female, Kenyan, PDF	13t November, 2010	10am, Kilifi
Community facilitators	4 Males and 1 Female	27t October 2010	3pm, Kilifi
Fieldworkers	CLG fieldworkers, 3 Males/3 Females	15th November 2010	8am, Kilifi
	MalariaGEN fieldworkers,	16th November 2010	3pm,, Kilifi
Members of Ethics Committee (5)	1. REC02, Female, Kenyan	24th September 2010	4pm, (oxford time)
	2. REC01, Male, Kenyan	8th November 2010	3pm, Nairobi
	3. REC03, Male, Kenyan	9th November 2010	10am, Nairobi
	4. REC02, Female, Kenyan	9th November 2010	2.30pm, Nairobi
	5. REC0, Male, Kenyan	10th November 2010	9am, Nairobi
	6. REC07, Male, Kenyan	10th November 2010	4pm, Nairobi
	7. REC09, Male, Kenyan	11th November 2010	11am, Nairobi
	8. REC11, Male, Kenyan	11th November	3pm, Nairobi
Total number of Respondents	43 (32 Males and 11 Females)		

4B: Accra and Navrongo, Ghana

Target	Key Respondents	Date of Interview	Time//Location
Researchers	RES001, Male, Research Officer	April, 2010	12.30pm/Oxford
	RES003, Male, PI	May 2010	Navrongo
	RES00, Male, Research Officer	May 2010	Navrongo
	RES007, Research Officer	May 2010	Navrongo
	RES008, group Discussion Male/Female, PIs	May 2010	Navrongo
	RES009, Male, PI	14t Dec, 2010	2.30pm, Accra
	RES0011, Male, Research Officer	3rd January 2011	3.20pm, Navrongo
	RES013, Male, Research Officer	18th January, 2011	2.30pm, Navrongo
	RES015, Male, PI	26th January, 2011	12.05pm, Navrongo
	RES0017, Male, Co-PI	20th January, 2011	2.38pm, Navrongo
	RES019, Male, PI	20th January, 2011	5.00pm, Navrongo
	RES021, Male, PI	24th January, 2011	1.38pm, Navrongo
Research Assistants	MalariaGEN – RA003, Male	7th January, 2011	3.20pm, Navrongo
	MVP - RA002, Female	14th January, 2011	10am, Navrongo
	Rotavirus/RSV- RA001, Male	10th January, 2011	11am, Navrongo
Fieldworkers (2 FGDs)	BCS fieldworkers (5 Females, 4 Males)	27th January, 2011	9.28am, Navrongo
	MVP Fieldworkers (6 Females, 4 Males)	27th January, 2011	2.10pm. Navrongo
Members of Ethics Committee (5)	NREC00, Male		10.13am, Oxford
	NREC01, Male	14th January, 2011	12 noon, Navrongo
	NREC03, Male	13th January, 2011	10.25am, Navrongo
	NREC02, Female	20th January, 2011	9.25am, Navrongo
	NREC04, Female	20th January, 2011	3.54pm, Navrongo
	NREC05, Male	28th January, 2011	10am, Navrongo
Community Representatives (1 IDI and 1 FGD)	NCK101, Male	20th January, 2011	9.25am, Navrongo
	CR03, Male	22nd January, 2011	3.25pm, Kandiga, Navrongo
	CR00 _ Group Discussion - Upper Nangalikania assembly members (4 members)	2nd February 2011	11am, Navrongo
Total number of Respondents	46 (15 females and 31 males)		

APPENDIX 5: AUTHORISATION FOR SAMPLE EXPORT FORM (KEMRI)

The KEMRI authorisation for sample export form originally presented here cannot be made freely available via ORA because of copyright reasons. They were obtained directly from the Administrator of the KEMRI Ethical Review Committee in Nairobi.

APPENDIX 6: SLIDES FOR DISSEMINATION OF FINDINGS

The slides for dissemination of findings originally presented here cannot be made freely available via ORA because they contain pictures and maps which are copyright protected.