An evaluation of ethical concerns raised by a Ghanaian research ethics committee using the principles and benchmarks proposed by Emanuel et al., (2008)

Pamela Emefa Selormey

BSc

Submitted in partial fulfilment of the requirements of the Degree of Masters of Social Science, (Health Research Ethics), in the School of Applied Human Sciences, College of Humanities, University of KwaZulu-Natal, Pietermaritzburg, Republic of South Africa.

Supervisor: Professor Douglas Wassenaar

South African Research Ethics Training Initiative

(SARETI)

October, 2015

DECLARATION

I, Pamela Emefa Selormey declare that the thesis titled *An evaluation of ethical concerns raised by a Ghanaian research ethics committee using the principles and benchmarks proposed by Emanuel et al. (2008)*, which I hereby submit for the degree of Master of Social Sciences at the University of KwaZulu-Natal, Pietermaritzburg, is my original research except where otherwise indicated. I also declare that;

1. This thesis has not been submitted for any degree or examination at any other university.
2. This thesis does not contain another person's data, pictures, graphs or other information, unless specifically acknowledged as being sourced from another person.
3. This thesis does not contain another person's writing, unless specifically acknowledged as being sourced from other researchers. Where other written sources have been quoted, then:
    a. Their words have been re-written but the general information attributed to them has been referenced
    b. Where their exact words have been used, then their writing has been placed in italics and inside quotation marks, and referenced.
4. This thesis does not contain text, graphics or tables copied and pasted from the Internet, unless specifically acknowledged, and the source being detailed in the thesis and in the References section.

Pamela Emefa Selormey
Student Name

_____
Signature

Professor Douglas Wassenaar
Name of Supervisor

_____
Signature

ACKNOWLEDGEMENTS

I wish to acknowledge with sincere appreciations to:

- Professor Doug Wassenaar, my supervisor - for his mentorship, guidance, support and great working relationship.
- The South African Research Ethics Training Initiative (SARETI), for funding which supported my studentship from a United States National Institutes of Health (US NIH) Fogarty International Center training grant number: 4R25 TW001599-14. The opinions expressed in this study are those of the author and not of the US NIH/Fogarty.
- I also thank SARETI for arranging the services of an anonymous editor who assisted with editing an earlier draft of this thesis
- Dr Mike Yaw Osei-Atweneboana, my boss and co-ordinator for the European and Developing Countries Clinical Partnership Trial (EDCTP) his guidance, supervisions and care.
- The Council for Scientific and Industrial Research (CSIR) under the leadership of Dr Abdulai Baba Salifu (Director-General) for the great opportunity afforded to me, for implementation of skills acquired from SARETI training, and their flexibility which ensured completion of the programme.
- The REC and its responsible officers for making their minutes available and also their support.
- Miss Samira Issaka, Mr Francis Balungnaa Veriegh and Mr Salim Nelson for their immense support and contributions.
- Mr Emmanuel Tetteh Adjabeng for his love, encouragement and indefinite support.
- Finally, the SARETI 2013 masters students, for their time, opinions and cooperation. This study would have not been possible without them.

ABSTRACT

Research Ethics Committees (RECs) and Institutional Review Boards (IRBs) are critical in biomedical research to ensure protection of human participants. However, increased international collaboration with multi-country, multi-site research projects has increasingly given rise to complex ethical issues with which local RECs may not be readily familiar. Therefore, the important question to ask is what ethical issues do African RECs typically raise when reviewing biomedical or health related social science research proposals? To assist researchers and RECs with review processes, Emanuel, Wendler and Grady (2004, 2008) proposed a universal framework/tool which could be used in many countries or contexts. The framework comprises eight systematic principles and accompanying benchmarks that specify core and practical considerations necessary to justify ethical research in developed and developing country settings. In this study, the ethical framework designed by Emanuel and colleagues was used as a tool to analyse (assess, code and rank) the ethical issues considered by a Ghanaian REC during their ethical review process. This was done through a content analysis of the minutes recorded for the period 2012 to 2013. Out of the 22 protocols assessed and 232 queries that emerged, informed consent (34.05%) and scientific validity (24.57%) were the two ethical issues most frequently considered by the REC. The least frequently considered issue was social value which recorded only 0.86% of queries. Collaborative partnership was not considered at all throughout the two-year review period under study. These results show that the REC has fairly considered most of the eight Emanuel et al. (2004, 2008) principles, suggesting that the work of this REC can be accommodated by the Emanuel framework, and vice-versa, that the framework was compatible with the work of this REC. It can thus be concluded that the framework is useful and applicable, and can be adapted by RECs for training and review processes.

KEYWORDS

Institutional Review Board (IRB), Research Ethics Committees (RECs), Africa, Emanuel framework, principles and benchmarks, Ghana.

LIST OF FIGURES

LISTS OF TABLES

LIST OF ACRONYMS

AMANET	African Malaria Network Trust
CIOMS	Council for International Organization of Medical Sciences
COHRED	Council on Health Research for Development
DoH	Declaration of Helsinki
DHEW	Department of Health, Education and Welfare
EDCTP	European and Developing Countries Clinical Trial Partnership
GNBC	Ghana National Bioethics Committee
LMICs	Low and Middle Income Countries
IRB	Institutional Review Board (often also referred to as REC outside of the US)
REC	Research Ethics Committee (often also referred to as IRB in the US)
NIH	National Institutes of Health
NEC	National Ethics Committee
OHRP	Office of Human Research Protection
SARETI	South African Research Ethics Training Initiative
US	United States
UNESCO	United Nations Educational, Scientific and Cultural Organizations
WMA	World Medical Association
WHO	World Health Organization

TABLE OF CONTENTS

LIST OF APPENDICES

CHAPTER ONE

INTRODUCTION

1.1 Orientation and motivation for the study

The history of biomedical research involving human participants has seen instances of abuse of those participants (Abbot & Grady, 2011). As a result, most institutions have established Institutional Review Boards (IRBs) or Research Ethics Committees (RECs) to protect the rights, dignity and well-being of research participants to hopefully avoid or minimise future possible exploitation and harm. Regardless of location, these RECs are bound by national and international guidelines for the review of research protocols. Although several sets of international guidelines exist, their common goal is to ensure maximum protection of research participants from potential harm and exploitation.

There is no doubt that the existence and functions of RECs are very important in biomedical research. However, the increase in collaborative research in African and most other developing countries in recent years poses more complex ethical issues than those that the RECs are already familiar with (Nyika, Kilama, Chilengi, Tangwa, Tindana, Ndebele and Ikingura, 2009; Silaigwana & Wassenaar, 2015). There is therefore a need to examine the findings of RECs, especially since multinational studies are often conducted in accordance with regulatory framework of the wealthier sponsoring countries (Milford, Wassenaar & Slack, 2006). "It would be unethical to approve a poorly designed study involving human participants, since data generated from such research would not necessarily contribute to the improvement of health or management" (Nyika, Kilama, Chilengi, Tangwa, Tindana, Ndebele & Ikingura, 2009, p. 189) ; it would be equally unethical to reject a well-designed study. It is debatable though a study may be scientifically valid, well designed and relative to its hypotheses, it may be of no value because the hypothesis may be uninteresting or otherwise trivial. Therefore, if a study is poorly designed but can yield possible scientific facts which may contribute to improved health, then there is the need to correct or improve upon the design. Freedman (1987) also pointed out that if a study is scientifically invalid all other ethical considerations become irrelevant.

With the above possibilities in mind, it is worrying because since the introduction of RECs across the world, including Ghana in 2000, there have been few or no empirical studies to evaluate the functioning and the decision-making processes of RECs. Furthermore, there are no established criteria for evaluating the outcomes of research ethics review (Nicholls, Hayes, Brehaut, McDonald, Weijer, Saginar & Fergusson, 2015). It is not known whether RECs comply with the various international guidelines; rather, more concentration has been focused on capacity building through training and infrastructural strengthening in order to equip REC

members and the secretariat (see e.g., Ndebele, Wassenaar, Benatar, Fleischer, Kruger, Adebamowo…. Meslin, 2014).

Several studies conducted in the United States (US) and other regions have shown that "different RECs reach different conclusions when reviewing the same study" (Kass, Hyder, Ajuwon, Appiah-Poku, Barsdorf, Elsayed, Mokhachane, Mupenda, Ndebele, Ndossi, Sikateyo & Tindana, 2007, p.26), for example, studies by Dixon-Wood (2008), Gray and Crook (1980) and Lidz, Appelbaum, Arnold, Candilis, Gardner, Myers and Simon (2012) in the US. These studies evaluated the decision-making process and performance of RECs through general surveys and the use of audio recording of meeting proceedings.

Articles published about research in developing countries by the *Washington Post* also revealed "a booming, poorly regulated testing system dominated by private interests [which] far too often betrays its promises to patients and consumers" (Singer & Benatar, 2000, p. 747). Nyika et al. (2009) also pointed out the existence of non-holistic approaches to ethical review by RECs in developing countries. These works suggest that there is lack of general consistency in standards both between and among RECs, suggesting there is a need for worry about the cause of disagreement (Kaur, 2013).

A possible explanation for the persistence of these controversies, according to Emanuel, Wendler, Killen and Grady (2004), is partly due to the fact that current ethical codes and guidelines can be comprehended in many ways, are every so often inconsistent, or may rely on unstated, yet controversial, ethical principles. Kaur (2013) suggested that the key to providing a solution to these controversies is to provide REC members with sufficient training by providing them with the tools needed to participate in meaningful discussions. However, meaningful such discussions may be, such trainings might not address a particular ethical situation needing to be addressed. Also, the impact of training is expected to reflect in the quality of decision-making processes employed by RECs but there are very few or no studies evaluating the impact of training on REC members in terms of their decision-making process.

In view of the above controversies, and considering the fact that research involving human subjects in developing countries creates greater risk for exploitations, Emanuel, Wood et al., Fleischman, Bowen, Getz, Grady, Levine, Hammerschmidt, Faden, Eckenwiler, Muse and Sugarman (2004) believe that aside from training of REC members, there is also the need to review and evaluate the decision-making processes employed by RECs which has long been overlooked globally, and in Africa, thus, creating the opportunity to investigate some features and outcomes of REC deliberations and decisions.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

The origin of the term *bioethics* can be attributed to an American biochemist Van Rensselaer Potter (Jecker, Jonsen & Pearlman, 2012). According to Piarulli (2012) Van Rensselaer Potter (1970 in Piarulli, 2012, p. 8) proposed the term bioethics to describe his vision of a "new conjunction of scientific knowledge and moral appreciation of the converging evolutionary understanding of human nature". Because his meaning of bioethics was interconnected with the environment, public health and morality, it was adopted in 1971 when it became necessary to include bioethics as an area of study at the Kennedy Institute in Georgetown. This was in response to the ethical analysis of an array of moral issues presented by medical practices due to advances in biomedical science and technology.

In only a few short decades, bioethics has become a prominent part of the scientific landscape. Its emergence has been examined through the impact of various events, issues, biomedical technological advancement and cultural changes. The tremendous recognition and institutionalization of bioethics within this short time frame have made it interesting for many authors and academics who sought to write on the origin and evolution of bioethics.

The discussion on ethical issues can be tracked back to the post World War II era when various ethical dilemmas were brought to the public attention (Jonsen, 1998). However, Fox and Swazey (as cited in Piarulli, 2012) argue that there have been several divergent explanations of the emergence of bioethics: those driven by technology, those built around issues and events, those based on institutionalization, and those rooted in gradual multi-causal growth. Despite disagreements on the evolution of bioethics, the most common method used to describe the historical evolution of bioethics is connecting the origin to particular technological developments, controversial issues and landmark events, of which the Nazi medical experiments and the Tuskegee Syphilis Study remain the most crucial catalysts (Amdur & Bankert, 2011; Piarulli, 2012).

According to Piarulli (2012), the recorded controversies surrounding the historical evolution of bioethics could be attributed to the fact that the authors documenting and analyzing the events were not outside observers; therefore, their interpretation could be shaped by their personal experiences and contributions to the field. In addition to Piarulli's point, the controversies could also be shaped by their field of specialties since in the developmental phase of bioethics as a discipline and a discourse, many scholars moved from their parent

disciplines such as social sciences, psychology, medical science, theology and law (among others) to immerse themselves in the wide-ranging ethical controversies.

2.2 Human experimentations: The catalyst for bioethics discussion

Nationally and internationally, the well-being of humans has increased greatly through biomedical research. History has shown that the inclusion of humans in experimentation can be tracked back to the Eighteenth Century (Emanuel, Crouch, Arras, Moreno & Grady, 2003). According to this account, the first recorded inclusion of humans in research was in 1753 by a British surgeon James Lind. He conducted a six-year longitudinal study on scurvy in sailors aboard HMS Salisbury. In the study, he provided some of the sailors with a diet containing fruit and vegetables and others with no fruit or vegetables (control group) and observed that the 'interventional' group was more likely to remain free from scurvy compared to the other sailors. Nonetheless, despite the successes recorded with medical research, there have been many examples of studies that defied the rights and dignity of participants and in other instances cost health and lives. The accounts of some major studies follow.

The post-World War II era (Piarulli, 2012) marked the turning point in the history of human experimentation where 23 Nazi doctors and bureaucrats were tried by the Allies in Nuremberg for using 1,750 concentration camp prisoners as participants in various brutal experiments without their informed consent. These prisoners were forced to undergo horrifying and brutal procedures for research purposes. Some of the brutalities included the high-altitude (low-pressure) experiment where prisoners were put into low-pressure tanks to see how long they would survive; the freezing experiment where prisoners were immersed in freezing weather or in freezing water for long hours (between 9 to 14 hours) without clothing, as well as the malaria experiment, the mustard gas experiment, the sulfanilamide experiment, the typhus experiment, the poison experiment, the incendiary bomb experiment and the sterilization experiment (Amdur & Bankert, 2011).

In July 1963, the Brooklyn Jewish Chronic Disease Hospital study also sparked criticism and debate (Amdur & Bankert, 2011). During this study, chronically ill and mostly demented elderly patients were deliberately injected with live cancer cells without their informed consent. The aim of the study was to establish how the spread of cancer could be influenced by a weakened immune system. The major ethical flaw was non-disclosure in a physician-patient relationship.

Another notorious landmark was the famous Tuskegee syphilis study sponsored by the US Public Health Service between 1932 and 1972. This study was to establish the natural history of untreated syphilis in human beings, approximately 300 men, mostly illiterate sharecroppers living with syphilis, were recruited for the study (Amdur & Bankert, 2011). There was no meaningful disclosure of information to participants and their partners on their medical conditions, nature of study and its associated risks. Participants did not understand

that the purpose of the study was to document the course of their illness without treatment. Many years later, after penicillin became widely available and known to be beneficial in the treatment of syphilis, the participants were still denied treatment. This aroused public outrage in response to high-profile exploitation forcing investigators to stop the studies. In 1997, the Federal government led by President Bill Clinton rendered an apology to affected participants and this was followed by an award of $200,000 dollar grant which was used to create the Tuskegee University National Center for Bioethics in Research and Health (Amdur & Bankert, 2011).

Another important but infamous study was the Willowbrook study conducted in the 1950s to study the transmission of hepatitis virus in developmentally disadvantaged children (Beecher, 1966). These children were residents in the Willowbrook state school facility in New York State. The purpose of the research was to understand the course of the hepatitis epidemic in the institution and the study design involved infecting healthy children with hepatitis intentionally by feeding them with a solution made from faeces of children with active hepatitis. In addition, parents were told their children could only be cared for at the hospital when they participated in the study.

Other recorded unethical studies include the Guatemalan syphilis study which took place from 1946 to 1948 where highly vulnerable population (soldiers, prisoners and sex workers) were intentionally infected with syphilis or gonorrhoea in order to investigate/establish new prevention methods for sexually transmitted diseases (STDs). The study, as reported by the U.S. Department of Health and Human Services, was sponsored by the U.S National Institutes of Health to the Pan American Sanitary Bureau (currently known as the Pan American Health Organization. Other ethically unacceptable studies were the Wichita Jury Study of 1955, the thalidomide uncoordinated or monitored release of medication for the treatment of morning sickness (nausea) in pregnant women in 1962 which resulted in severe birth deformities in thousands of children, Milgram's studies of obedience to authority in the 1960s and the Tearoom Trade Study in the 1970s (Amdur & Bankert, 2011). These problematic studies resulted in the formulation of various codes and guidelines to govern all forms of research involving human participants. Many of these unethical incidents influenced the development of ethical guidelines in use today. Some of these guidelines are reviewed in the next section.

2.3 Codes, guidelines and oversight mechanisms: The formation of modern ethics review systems

Since the events described above, various ethical codes and guidelines have been formulated to inform and guide researchers and reviewers in the conduct of biomedical research involving human participants. Most of the earlier reported guidelines were 'born in scandals' responding to a specific controversy (Emanuel, Wendler & Grady, 2008). These authors believed that because the codes and guidelines were born out of scandals, they tend to focus on what was perceived to be the transgression of that scandal. However, the strength of these guidelines still remains relevant in their applicability to other situations.

The aftermath of the Nuremberg trial after World War II to bring justice to the Nazi doctors for the crimes committed against humanity resulted in the formation of the Nuremberg code in 1947. This code articulated the fundamental ethical requirements for carrying out ethical studies in a manner that respects the basic rights of human research participants (Amdur & Bankert, 2011). Informed consent, coupled with voluntary participation, favorable risk-benefit ratio as well as the freedom to withdraw without penalty constituted the basic fundamentals of the Nuremberg code. These basic elements have been incorporated into most subsequent ethical codes such as the Declaration of Helsinki.

The World Medical Association (WMA) was motivated after the Nuremberg code to draft ethical guidelines to govern physicians in carrying out their functions. The initial deliberation of research ethics guidelines was drafted in 1953, subsequently adopted in 1964, and later referred to as the Declaration of Helsinki (DoH). These guidelines have undergone several revisions with the latest version emerging in 2013. The fundamental resolutions of these guidelines require consent by all ill participants or their next of kin and informed consent in the case of healthy participants (Emanuel et al., 2003).

Henry Beecher's 1966 controversial citation of 22 atrocities committed against human participants such as the Tuskegee syphilis study led to the development of the Belmont report issued in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The above report contained three basic ethical principles: respect for persons, beneficence and justice. These three principles are believed to be generally applicable in all cultural traditions across the globe. However, according to Beauchamp and Childress (2013), the adoption of these principles as the three basic principles of biomedical research has resulted in various recent debates by various philosophers about their feasibility or applicability in non-Western countries. These authors claim that the interpretation of these principles was based on Western ideology which is not an exclusive reflection of their culture (Onuoha, 2007). Nevertheless, these principles can be interpreted differently to suit a particular culture in terms of what is done and best practiced and how they can solve situations with consultation with indigenes, rather than a prescription for what ought to be done.

After the formulation of these three earlier historical codes and guidelines, several other recognized ethical guidelines were promulgated. Below in table 2.1 are lists of some selected ethical guidelines in the history of biomedical research with humans. Judging from the years revised and amended, it can be concluded that most of these codes and guidelines shown in Table 2.1 below are outdated and have not been revised for the past 10 or more years to accommodate the changing research landscape and transition in global burden of disease.

Table 2.1: Selected guidelines on the ethics of biomedical research with humans

Guidelines	Source	Year Issued, Revised or Amended
45 CFR 46 (U.S. common Rule)	U.S. Department of Health and Human Services (DHHS) and 16 other U.S. federal agencies	DHHS guidelines: 1981 Common Rule: 1991
International Ethical Guidelines for Biomedical Research Involving Human Subjects	Council for International Organizations of Medical Science in collaboration with World Health Organization	1982 (draft) Revised:1993 with 2008 being the recent one
Good Clinical Practice: Consolidated Guidance	International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals of Human Use	1996
Resolution 196/96:Rules on Research Involving Human Subjects	National Health Council, Brazil	1996
Convention on Human Rights and Biomedical	Council of Europe	1997: revised 2005
Medical Research Council Guidelines for Good Clinical Practice in Clinical Trials	United Kingdom	1998
Guidelines for the Conduct of Health Research Subjects in Uganda	Uganda National Council for Science and Technology	1998
Tri-Council Policy statement: Ethical Conduct for Research Involving Human	Tri-Council Working Group, Canada	1998; amended: 2000, 2002, 2005
National Statement on Ethical Conduct for Research Involving Humans	National Health and Medical Research Council, Australia	1999
Ethical Guidelines for Biomedical Research on Human Subjects	Indian Council on Medical Research Council, New Delhi	2000
Guidelines on Ethics in Medical Research in Tanzania	Tanzania National Health Research Forum	2001

Guidelines on Ethics in Medical Research: General principles	Medical Research Council of South Africa	1977: revised 1987,1993 & 2002
Guidelines for Good Clinical Practice in the Conduct of Clinical Trials in Human Participants in South Africa	Department of Health, South Africa	2000
South African Research Ethics Guidelines	Department of Health-National Health Research Ethics Council (NHREC)	2015

Source: Adapted from Emanuel et al. (2004)

However, the increasing quantity of research both nationally and internationally made it very important to have an oversight body responsible for the overseeing of research studies that involved human participants (Kirigia, Wambebe & Baba-Moussa, 2005). As a result, in 1974 there was a declaration in the US Common Rule (45 CFR 46, 1991) in a Federal policy on the protection of human subjects requiring that:

> "All research that is conducted or supported by a Federal Department or Agency, whether or not it is regulated as defined must be reviewed and approved in compliance with the policy by an Institutional Review Board (IRB) that operates in accordance with the pertinent requirements of this policy". (Emanuel et al., 2003, p. 39).

This declaration formed the basis of the modern ethics review (REC) systems which are now a requirement for research with humans (Kass, Hyder, Ajuwon, Appiah-Poku, Barsdorf, Elsayed, Mokhachane, Mupenda, Ndebele, Ndossi, Sikateyo & Tindana, 2007).

"In the United States, these committees are called Institutional Review Boards (IRBs) while elsewhere they are generally referred as Research Ethics Committees" (RECs) (Kass et al., 2007, p. 26). The primary purpose of ethics review is to safeguard the dignity and protect the well-being of research engaging human participants so as to hopefully avoid exploitation of vulnerable individuals and populations. The exact functions, responsibilities and procedures of modern RECs have been well described in Amdur and Bankert (2011) and World Health Organization (WHO) (2011). Kirigia, Wambebe and Baba-Moussa (2005) pointed out that "in the present times of globalized biomedical research, good ethics stewardship mandates that every country, regardless of their level of economic development, should establish an efficient research ethics review system in order to protect the dignity, integrity and safety of its citizens who participate in research"(p. 7) This was in support of the World Medical Association (WMA) (2008) and WHO (2000) prerequisite that all biomedical research studies involving human participants must be scrutinised by an independent body (Ikingura, Kruger & Zelele, 2007). Social scientists were not an exception to this rule as in August, 1979, the Department of

Health, Education and Welfare (DHEW) promulgated some set of guidelines (44 FR 47688) binding all social research irrespective of funding source to undergo a comprehensive REC review as their counterparts in the biomedical fields were required to do. This, however, was not welcomed by social scientists who raised strong arguments and debates regarding the decree as a restriction to impede their work. Others raised the argument that the restriction did not accord with the risks of social research (Casell, 1980; Mosteller, 1980). This has been vigorously debated by Wassenaar and Mamotte (2012) who argue that social science research should be subjected to the same ethical scrutiny as biomedical research.

Although many countries have now made it a legal requirement, Ikingura et al. (2007) observed that until the 1980s, there were no RECs in many countries. In the United States, governmental agencies such as the Office of Human Research Protection (OHRP) now oversee the functions of the IRBs in the country.

In Africa, the earliest REC was set up by the University of Witwatersrand, Johannesburg, South Africa in 1966 (Cleaton-Jones, 2008). "The second oldest in Africa was formed in 1974 in Zimbabwe but had only intermittent functioning until 1992 when it became formally established" (Kass et al., 2007, p. 27). Since then, most of the RECs formed in Africa are institutionally based either in academic institutions, research institutions, or hospitals (Dixon-Woods, Angell, Ashcroft & Bryman, 2007) with very few countries having a National Ethics Committee (NEC). According to Ikingura et al. (2007), the main reason that led to the establishment of RECs in most countries was an increase in collaborative research which demands host country ethics approval for sponsors and scientific journals, and due to the complexities of new biomedical technologies. Langlois (2013, p. 6) also pointed out that "the extension of biomedical research beyond national borders renders international standards on bioethics necessary so that research participants are treated equally and fairly, which ever country they are in", thus driving the establishment of RECs in many countries.

In Ghana, although some research activities were ongoing in various health research institutions, it was only in 2000 when discussions and empirical studies on bioethical issues began to receive attention. In view of this, the first REC in Ghana was established in 2000 in response to the growing need to protect human participants in research and also to reposition Ghana for the increased number of international collaborative studies. By the year 2004, there were six RECs in Ghana located at the Noguchi Memorial Institute for Medical Research, Navrongo Health Research Centre, Kintampo Health Research Centre, Kwame Nkrumah University of Science and Technology, Ghana Health Service and Sunyani Hospital. Currently, Ghana can now boast of about fourteen (14) RECs but is still without a National Ethics Committee or Council (NEC).

The map below is an attempt to show the distribution of the RECs in Ghana. Ghana has ten regions and research is conducted in almost all ten regions. However, from the map it is clear that most of the RECs are based in the capital city Accra with very little representation in the other regions.

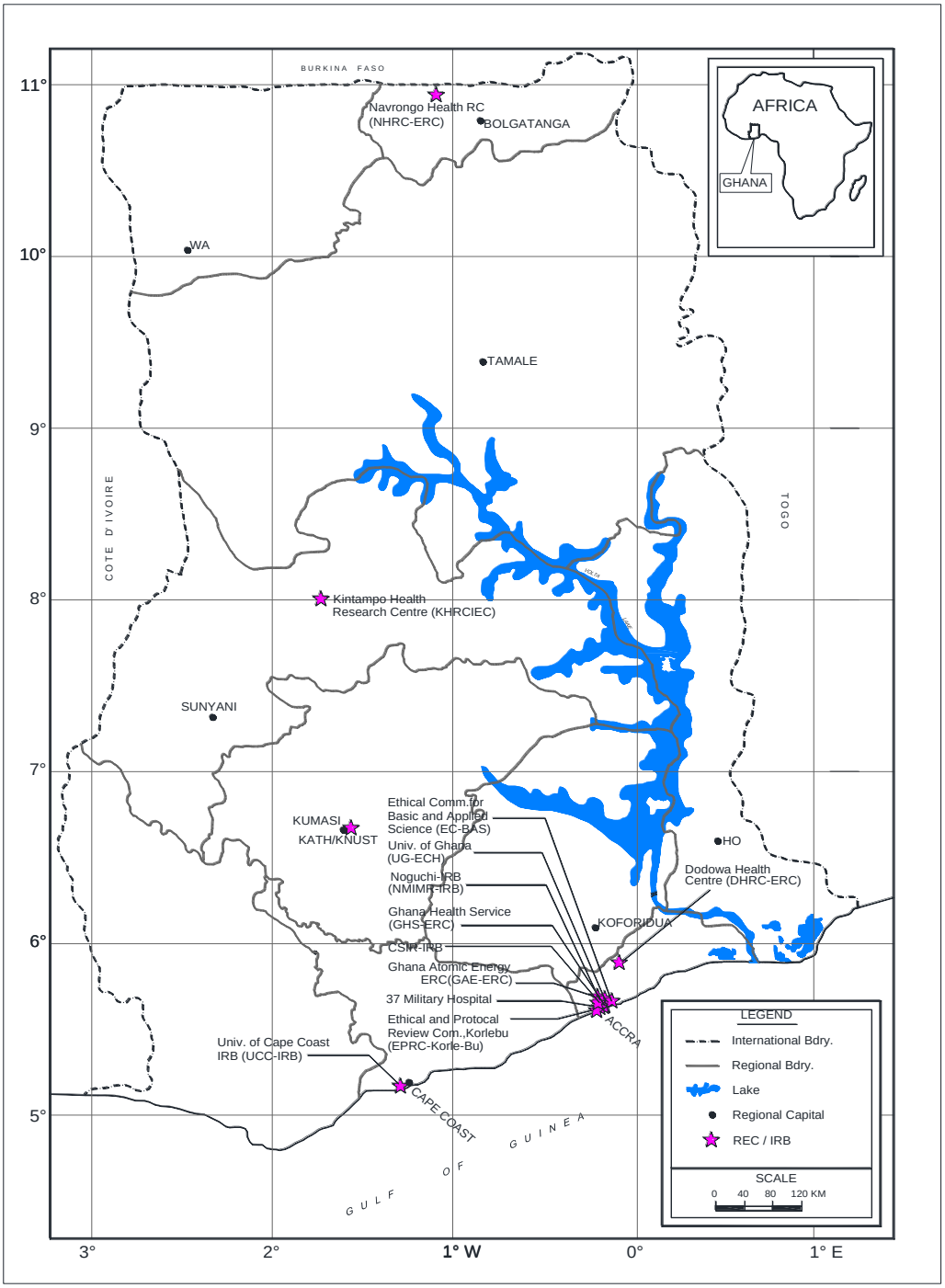

Figure 2.1: Map of Ghana showing the distribution of RECs

The absence of a national ethics committee (NEC) in Ghana compelled most RECs to comply with international codes and guidelines for their operations. However, in 2009, the Ghana National Bioethics Committee (GNBC) was inaugurated following the United Nations Educational, Scientific and Cultural Organization's (UNESCO) call on member states to set up National Bioethics Committees. However, the operation of GNBC has been faced with several challenges with the most pressing one being its identity and

legal status. This is because it is placed within the Ghana National Commission for UNESCO (which is hosted under the Ministry of Education). This creates problems for advocacy and policy advice on bioethical issues – the NEC's main responsibility (UNESCO, 2010).

Work has, however, commenced towards having a National Ethics Committee (NEC) spearheaded by the Noguchi Memorial Institute for Medical Research and some other key personnel from other institutions. This initiative has also faced some challenges. The latest was the Council for Scientific and Industrial Research-Ghana, through a European and Developing Country Clinical Trials Partnership (EDCTP) capacity-building grant to convene a meeting to identify some of the challenges and how to address them. Some of the major challenges that were identified as facing the establishment of the NEC in Ghana included: the inability to identify the right vehicle through which the whole concept should be channelled for its acceptance by the Government of Ghana and by parliament, as well as proper communication plans. Table 2.2 provides a list of some African countries with National Research Ethics Committees (NECs) and National Research Ethics Councils. Regardless of how they are referred to in each country, their status determines their functions. Some countries such as South African have a National Research Ethics Council; this council does not conduct reviews but publishes national guidance and registers and audits all RECs in South Africa (Langlois, 2013).

Table 2.2: ***List of African countries with a National Research Ethics Committee***

COUNTRY	NAME OF NATIONAL ETHICS COMMITTEE	YEAR OF ESTABLISHMENT
Algeria	Conseil National de l'Éthique des Sciences de la Santé	
Benin	National Ethics Committee for Research in Health	2004
Botswana	Ministry of Health Research and Development Committee	1992
Burkina Faso	Comité national d'éthique pour la recherche en santé (CNERS)	2002
Cape Verde	Comité National de Ética en Recherche Pour la Santé	
Congo	Comited'ethique de la recherche en sciences de la sante	2009
Cote d'lvoire	Comité Consultatif National de Bioéthique de la République de Côte d'Ivoire	
Dem. Rep. of Congo	Comité national de bioéthique	2009

Egypt	Egyptian National Bioethics Committee	2002
Ethiopia	National Ethical Clearance Committee (NECC) & National Bio-Ethics Committee	
Gambia	Gambia Government/MRC Joint Ethics Committee	2002
Gabon	Comité National d'Ethique pour la Recherche (CNER)	2009
Kenya	National Ethics Review Committee	
Madagascar	ComitéMalgached'Ethique pour les Sciences et les Technologies	
Malawi	National Health Sciences Research Committee	1988
Mauritius	National Ethics Committee of Mauritius	
Mali	Le Comitéd'Ethique, Institut National de Recherche en Santé Publique	2002
Nigeria	National Health Research Ethics Committee of Nigeria	2006
Rwanda	Rwanda National Ethics Committee	2003
Senegal	Conseil National de Recherche en Santé (CNRS)	
South Africa	National Health Research Ethics Council	2003
Togo	Comité Consultatif National de Bioéthique (National Bioethics Committee of Togo)	2007
Tanzania	National Health Research Ethics Committee	2002
Uganda	National Bioethics Committee of Uganda	
Zimbabwe	Medical Research Council of Zimbabwe	1974

Source: World Health Organization (2012)

2.4 Overview of the functioning, challenges and future developments of African RECS

The composition of most RECs usually consists of researchers, physicians, other institutional role-players, lay affiliates and representatives from the community (Silaigwana & Wassenaar, 2015; White, 1999). In addition, Kaur (2013) also pointed out that REC membership should reflect the diversity of the communities in which the research is carried out to enable different ideas during ethical review. In line with the mandate of RECs to approve, oversee and maintain ethical standards for human participants research, they must apply specific criteria which must be complied with by all studies in order to gain approval. These criteria must ensure that risks to subjects are minimized (reasonably in relation to anticipated benefits), subject selection is equitable,

and seeking voluntary consent and informed consent must be appropriately documented (Department of Health and Human Services, 2009).

Generally, REC review takes place in two phases. Firstly, REC staff members screen the initial submission including the consent form document and secondly, the reviewers examine the submission through rigorous review and identify ethical concerns using the criteria stipulated above. Thereafter, studies which satisfy all criteria are given approval. Nonetheless, studies with concerns may be 'approved with conditions' or deferred and re-reviewed at an appropriate convened meeting or expedited depending on the level of risks (Department of Health and Human Services, 2009). Even though not much empirical information exist on the number of studies approved or deferred by RECs, an internal review of a South African University based REC as reported by Cleaton-Jones & Vorster (2008) showed that a quarter to a third research proposals were approved at once at initial meetings, 60% required minor revisions and approximately 10% required major revisions, re-submission or were not approved. Another study reported by Chelbowski (1984) also revealed that 92.3% of studies were approved with approximately 70% containing contingencies, while 7.7% were deferred. RECs basically protect and support the welfare of research participants through the three principles illustrated in Figure 2.2.

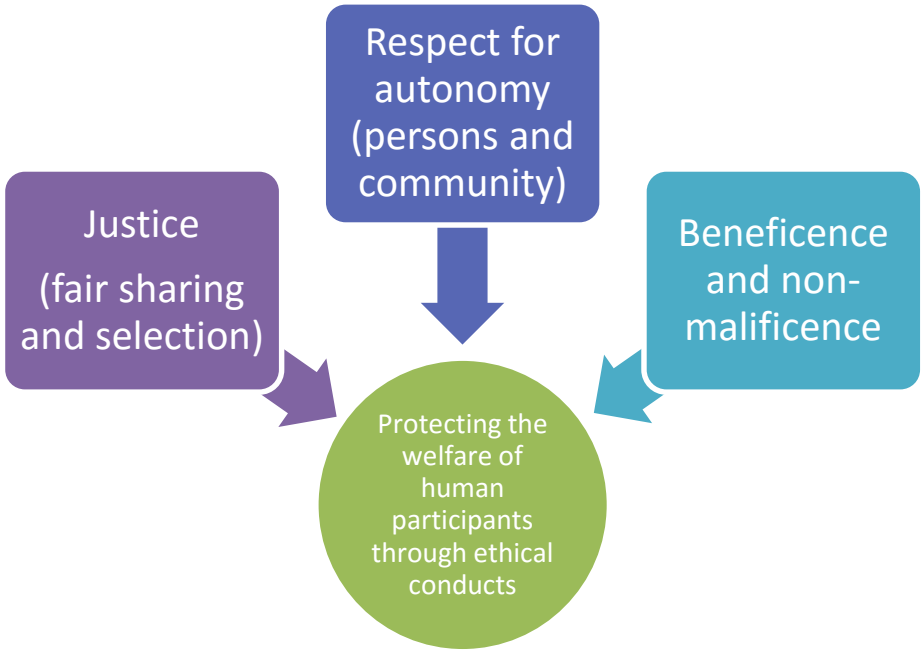

Figure 2.2: Illustration of the biomedical principles and their application

In the application of the above principles in the review of applications, REC members consider these basic principles of the ethical decision-making model:

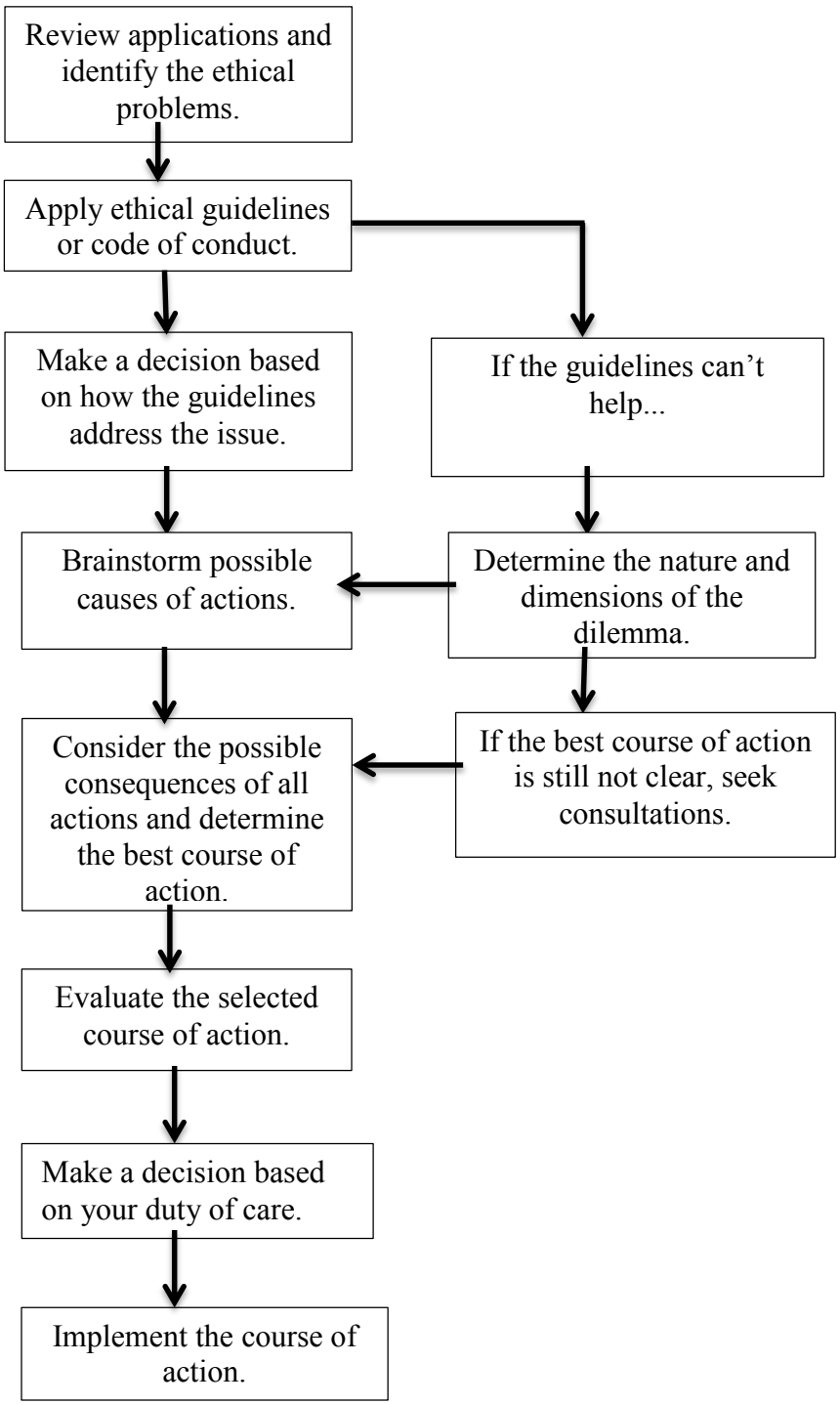

Figure 2.3: Principles of ethical decision-making model (Forester-Miller & Davis, 1996).

Though many countries have devoted significant resources to creating and strengthening RECs, these have been faced with numerous constraints and obstacles in achieving their goals to protect human participants (Silaigwana & Wassenaar, 2015). These include the distribution of appointed members, uncertainties about regulatory guidelines, procedures to follow and capacity development of their members are considered as the primary challenges to the functioning of RECs (Silaigwana & Wassenaar, 2015 and Ikingura et al., 2007). According to Kass et al. (2007), most literature examining the limitations of RECs only comes from the more developed countries. Most of the challenges as reported by Emanuel, Wood et al. (2004) to be facing RECs had to do with structural review procedure problems and performance-assessment problems.

Similar problems were reported by Kass and colleagues (2007) in developing countries especially in Africa. They identified inadequate training and funding, budget constraints and the tendency of a few RECs to 'rubber stamp' proposal approvals in order to secure international funding as peculiar challenges to African RECs. Meanwhile Ateudjieu et al. (2009) also observed that the composition of most RECs in Africa does not reflect an appropriate balance between different health academics and lay members. This raises critical questions about the competence and independence of most RECs. There have also been many controversies and debates on the ethics of 'standards of care' in research in developing countries (Emanuel, Wendler et al., 2004; Lavery, Grady, Wahl & Emanuel, 2007).

Even though there has not been any empirical study to document specific problems faced by RECs in Ghana, it is assumed that with Ghana's participation in Kass et al.'s (2007) research, the problems enumerated could apply to RECs in Ghana. An unpublished study by Mokgatla-Moipolai and Kasule (2013) reported that the major problems confronting most RECs in Africa have to do with inadequate work space, workload and improvement of RECs efficiency. For instance, the current situations of some RECs in Africa are well illustrated in Figure 2.4.These were also evidenced in the research work by Silaigwana & Wassenaar, 2015.

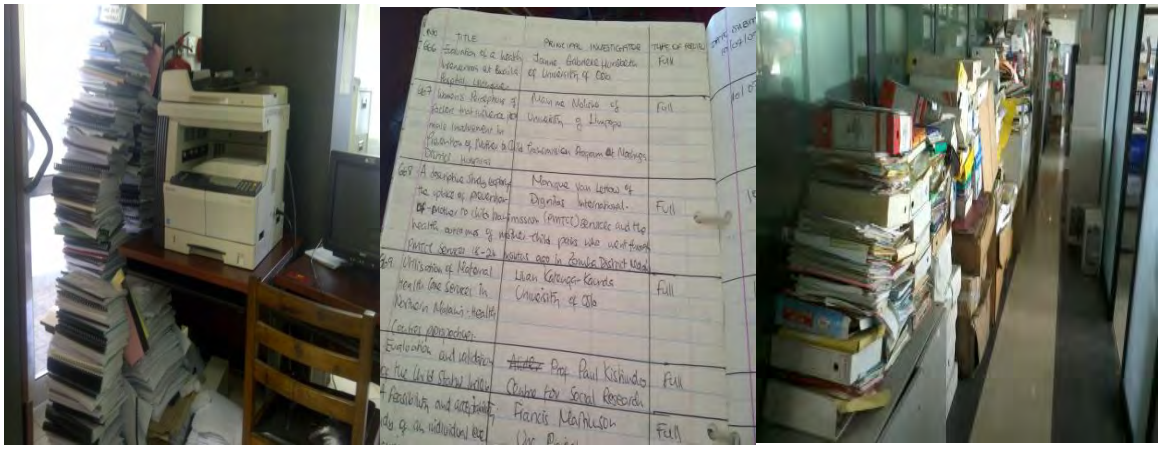

Figure 2.4: RECs in Africa face many backlogs and technological challenges (adapted from Council on Health Research for Development (COHRED) and Global Forum presentation, 2013)

Another pressing challenge facing the RECs is the resistance to ethical review of research by researchers. Considering the growing emphasis on ethics review and making it mandatory, this is worrying. According to Wassenaar and Mamotte (2012), this resistance can be grouped into principled and pragmatic objections. The main principled objection they cited was the impediment to academic freedom imposed by ethical review. However, this can only be true if academic freedom is regarded as the freedom to pursue any academic research regardless of the methodology and with no considerations to the welfare of research participants. Other reasons for resistance are the universalism of the three major ethical principles (Mattingly, 2005; Onuaha, 2007; Reissman, 2005, all cited in Wassenaar & Mamotte, 2012); however, these principles can be translated into practical use based on the context in which they are applied.

Despite all these challenges faced by RECs, Getz (2011) believes that REC systems are gradually hindering the protection of research participants through inconsistent guidelines and their interpretation, unnecessary wasteful expenditure and time on the part of research sponsors as they reconcile and coordinate wide variations in ethical review across multiple RECs, and over-arching roles and barriers where RECs regard themselves as gatekeepers. These observed obstacles are eventually leading to reform that could streamline and create a more harmonized review process. The US Common Rule (45 CFR 46) is currently under review (Emanuel, 2015).

In response to these reforms and to improve ethical review in developing countries, a number of governmental and non-profit organizations have been involved in various capacity-building activities such as training REC members and administrators and the provision of office equipment to improve REC operations (Hyder, Ali, Hallez, White, Sewankambo & Kass, 2015). Notable among these is the South African Research Ethics Training Initiative (SARETI), funded by the Fogarty International Center of the US National Institutes of Health. Similarly, organizations such as the African Malaria Network Trust (AMANET) and the European and Developing Countries Clinical Trial Partnership (EDCTP) have organized various capacity building initiatives

in Ghana and other African countries (Ndebele et al., 2014). A notable reason assigned to the increasing concern to strengthen RECs by these organizations suggested by Coleman and Bouesseau (2008) suggests that sponsors are conducting most of their research in low and middle income countries probably because it is less expensive and also becoming difficult to ensure notable number of research participants from the sponsor's country. However, this is highly debatable.

2.5 Strengths and weaknesses of the guidelines - their implications for RECs functioning

The increasing role of RECs has made them the implementers of international, national and local ethical guidelines on research with human participants. However, ethical reviews in recent years have been characterised by various controversies. Part of the problem was due to the fact that international guidelines are legally binding for countries that nevertheless chose not to abide by them. Thus, there is a need for national laws and guidelines. According to Coleman and Bouesseau (2008), some countries have no laws relating to research ethics and where such laws exist, they are either incomplete or unenforced.

The persistence of controversies, as Emanuel and colleagues (2004) also observed, are in part due to the fact that existing ethical guidelines can be interpreted in multiple ways. Sometimes they appear contradictory or rely on unstated yet controversial, ethical principles. White (1999) also pointed out that "in countries and societies where these values are understood differently or are not expressed in local culture and institutions, it may be impossible or of no practical value to insert them into their research setting" (p. 90). A typical example can be seen in informed consent in the United States, where individual informed consent is considered ethically imperative for research involving human subjects; however, this has been argued to be difficult in other societies that define persons by their relations to others, and important decisions are made by family heads (Onuoha, 2007). Even though contemporary biomedical studies may minimize the likelihood of historical atrocities and harms inflicted on humans, risks of manipulation or exploitation still persist in some settings. These possibilities are magnified in international collaborative research when subjects' social and cultural norms differ significantly from those of the sponsoring researcher, or when health care delivery is otherwise minimal or non-existent.

Even though various codes and guidelines delineate principles to guide the conduct of essential biomedical research, they offer no further comment on how to assess risk efficiently or on how RECs should conduct reviews effectively. For instance, the ten statements of the Nuremberg Code and the 32 principles of the Declaration of Helsinki, (originally with 22 principles) contain no elaboration on this (Emanuel, Wendler et al., 2004). The CIOMS guidelines, formulated by the Organization of Medical Sciences with the World Health Organization, are the most comprehensive guidelines with a number of recommendations for REC reviews. However, important though these initiatives may be, these recommendations are not specific enough to be used by RECs. As Emanuel and colleagues (2004) also pointed out, agreements can frequently be secured on

the broader principles by RECs but this often hides deep disagreement about how they should be interpreted and applied to a specific situation. Burke (2005) also proposed that much of the tension that exists between RECs and investigators is due to variability in the application of Federal regulations by RECs across institutions.

In another publication by Emanuel and colleagues (2004), the authors acknowledged that there is no effective mechanism for addressing fundamental and recurring ethical issues. Numerous national bodies have attempted to address these issues; however, mostly their efforts have been intermittent and unsystematic, and rarely implemented because most of these mechanisms have inherent limitations. Even though ethical decision making is not an exact science, one of the suggestions put forward is that regulations must be harmonized and they provide further guidance for REC reviews, thereby creating a flexible and fair application of these principles in complex social situations (Emanuel, Wendler et al., 2004).

Due to the existing deficiencies in ethical guidelines and regulations, Emanuel, Wendler et al. (2004) believed that there is a need for a broader, systematic and comprehensive framework that includes an ethical justification as well as specifications for how each principle is to be fulfilled in practice. To satisfy this desire, Emanuel, and colleagues (2004) re-analyzed the various ethical guidelines, incorporating overlapping concerns, and organized them into a coherent set of eight principles with accompanying benchmarks. Even though it may be claimed that these principles and benchmarks are obvious and do not add to existing guidance, Emanuel, Wendler et al. (2004) argued that these principles are distilled from existing guidance and make coherent the widely accepted sources of guidance including the Nuremberg code (Nuremberg Military Tribunals, 1949), Declaration of Helsinki, Belmont Report and the US Common Rule.

The main intention of these proposed frameworks (and their principles and benchmarks) is to improve the quality of work done by RECs by helping members participate in systematic and meaningful discussions so as to optimize protection of human subjects. Tsoka-Gwegweni and Wassenaar (2014) and Mark (2014) commented that the principles and benchmarks of the framework are inclusive, universal and applicable to all settings and contexts. They also pointed out that the ethical requirements are listed in sequence from the start to implementation and conclusion of any research. Due to the inclusive nature of this framework, many writers reference it in the literature. It has also been used to design training courses and other ethics review frameworks on research ethics, as well as to review both published and proposed research (Budin-Ljosne, 2012; Fakruddin, Chowdhury, Hossain & Mannan 2012; Miller & Brody, 2013; Miller & Shorr, 2002; Shaw & Elger, 2013; Union Graduate College & Vilnius University, 2012; Wassenaar, 2006). For instance, Carley (2006) reported that the United States Environmental Protection Agency used the framework to review a published study that investigated environmental exposure to chromium.

Hyder , Merrit, Ali, Tran, Subramaniam and Akhtar (2008) described the principle of collaborative partnership of the framework as relevant to public health intervention research in low- and middle-income countries (LMICs), stressing that it is an important tool. They encourage policy-makers to engage in research programmes to influence policy. As also reported by Tsoka-Gwegweni and Wassenaar (2014), the *Medecins San Frontieres* Ethics Review Board (ERB) reported that this framework was useful for both researchers and their ERB, and therefore adopted it to design their standard operating procedures. Wassenaar and Mamotte (2012) also recommended the framework for review of social science research. The work of Emanuel et al. (2004, 2008) has greatly influenced the structuring of a major Joint United Nations Programme on HIV/AIDS (UNAIDS, 2012) ethics guidance document for HIV prevention trials (Tsoka-Gwegweni & Wassenaar, 2014). A brief description of the principles and their benchmarks is presented below.

2.5.1 Collaborative partnership

Collaboration, as defined by Gray (1989), is a process through which parties who see different aspects of a problem can explore constructively their differences and search for solutions that go beyond their own limited vision of what is possible. Other experts have also defined it as the relationship or liaison between researchers, policy makers, communities in developing countries, sponsors and other researchers from developed countries (Emanuel, Wendler et al., 2004; Lavery et al., 2007). The goal of this liaison is to minimize possible exploitation by ensuring that developing countries are capable of evaluating for themselves the magnitude of importance of a particular research to their community needs (Emanuel, Wendler et al., 2004; Lavery et al., 2007).

With regard to the definitions above, particularly the latter version, collaborative partnerships always requires the inclusion of community representatives to help in the planning and conduct of the research, determination of results and use of the results to improve community health. Because research ideally should arise from express community need and be based on the community's values, circumstances, culture and social practices, community representatives are also able to make substantial inputs that enrich the research, so as to ensure fair benefit distributions (Emanuel et al, 2008). Lairumbi et al. (2008) believe this principle was derived from the need to reduce possible exploitation of research participants and communities, and ensuring fair participant benefit from the research. One viable challenge of this principle, identified by Marsh, Kamuya, Rowa, Gikonyo and Molyneux (2008), is the extent of balance and fairness of representation of each of the parties involved.

2.5.2 Social value

For a study to realize its full social value, the principles of beneficence, justice and respect for dignity should be employed in establishing the beneficiaries or prospective beneficiaries. Even though the value of research to society remains an endless debate, the problems under study should result in knowledge and/or

interventions that are of value to society and, ideally, the research participants. Mechanisms to enhance social value must also be defined in terms of dissemination of research findings and, lastly, the research must not undermine existing structures of the community (Emanuel,Wendler et al., 2004). The Nuremberg Code also emphasized that studies with social value should yield fruitful results for the good of society, be unprocurable by other methods or means of study and should not be randomly unnecessary in nature, since a study might be scientifically valid with a well-designed hypothesis but of no social value (Freedman, 1987).

The concept of social value normally brings into consideration who will benefit from the conduct and results of a research study, the potential value of the research for each prospective beneficiary, enhancing the social value of the research and, lastly, minimizing the adverse impact, if any. If the proposed research does not help in any of these ways, it tends to waste resources and money (Emanuel et al., 2006).

Another important component of social value is the ability of the researchers to share their results and findings with other researchers and the general public through the media in order to improve public health. As the role of research in developing countries is becoming of utmost importance, access to beneficial interventions, ancillary care and other research-related benefits will be developed (IJsselmuiden, Kass, Sewankambo & Lavery, 2010). Therefore, the Illinois White Paper (2003) cautioned that RECs cautiously address this principle in their review as it might be the one most likely to test IRB's/REC's role as research governing bodies.

2.5.3 Scientific validity

According to the Declaration of Helsinki (2013, Paragraph 11), medical research or any research involving humans must conform to generally accepted scientific principles and must be based on a thorough knowledge of the scientific literature and other relevant sources of information. It further noted that scientific review must consider, inter alia, study design, including provision for avoiding or minimizing risk and monitoring safety. In short, since the primary responsibility of RECs is to safeguard the rights, safety and well-being of the research subjects, scientific review and ethical review cannot be separated (CIOMS, 2002).

As mentioned earlier, when a study in itself is scientifically invalid, all other ethical considerations become irrelevant (Freedman, 1987). Research must be carefully planned to answer a specific question: a hypothesis to be tested, a control and controlled variables (Emanuel, Abdoler & Stunkel, 2006). This is achievable when the design, sample, methods and analysis are rigorous, justifiable and feasible (Emanuel et al., 2008). There is the need for REC to know if in ethical review, protocols are of sound scientific design so that good research can be replicated if necessary. Wassenaar and Mamotte (2012) also pointed out that irrespective of the research design used, methodology should be rigorous, appropriate and systematic. Thus scientific validity should be assured, and assessed using strategies appropriate to the research design.

2.5.4 Fair subject selection

Beauchamp and Childress (2013) defined fairness as that which is deserved, due or owed to a person. Fair selection of subjects should be related to the scientific goal of the study, and not necessarily to the vulnerability, privileges and other factors that might be related to the study (Emanuel et al., (2004, 2008). The decision on who to include or exclude must be based on the principle of justice and clearly spelt out in the inclusion and exclusion criteria of the study. The history of research involving human participants has shown that groups were recruited into studies with no potential benefit but for the reason that they were readily available or easily accessible and lacked the ability to protect themselves (Emanuel et al., 2000). It is therefore important to note that efficiency cannot override fair recruitment of subjects.

To ensure fair selection of subjects, the study population selected should ensure valid science, minimize risk and maintain social values; in election, familial coercion, social marginalization, political powerlessness and economic deprivation must be considered (Emanuel, Wendler et al., 2004). The practice of fair subject selection in research means to be fair both to the participants and the beneficiaries. Some people might enrol in research for the sake of benefits, nevertheless; such people should not be excluded without good scientific or safety reasons provided they satisfy the inclusion criteria. Intentionally targeting vulnerable participants such as prisoners, pregnant women, terminally ill people or children is considered ethically unfair (Emanuel, et al., 2008). In explaining the study to research participants, clarity and transparency should be of utmost consideration.

2.5.5 Favourable risk-benefit ratio

Research is regarded as ethical when the risk to the participant is balanced by benefit. The US Common Rule prescribed using procedures which are consistent with sound research design but do not expose participants to unnecessary risk, or to minimize risk to participants if any are reasonably acceptable in relation to anticipated benefits. The Nuremberg Code also emphasized the need for minimal risk such that the risks never exceed those determined by the humanitarian importance of the problem to be solved by the experiment. Weijer (2000) pointed out that in evaluating risks and benefits, RECs should consider only those risks and benefits that may result from the research as distinguished from risks and benefits of therapies that participants would receive even if they were not participating in the research.

Similar to the Nuremberg code and the USA Common Rule, the Belmont recommended that "it is commonly said that benefits and risks must be 'balanced' and shown to be 'in a favorable ratio'"(Emanuel, Crouch et al., 2003, p. 34). To achieve this, Wassenaar and Mamotte (2012) proposed that in determining the risk-benefit ratio, the probability of harm occurring and the anticipated severity of the harm should be considered.

Therefore, in reviewing proposals, RECs should identify all potential risks in order to ensure that within the context of good research, potential benefits to individual participants are delineated, relevant, enhanced available and complementary to the risks (Emanuel, Wendler et al., 2004). The riskier the research study, the more benefit it must offer to be considered ethical. In addition, the research burden should be as low as possible. Research burden is measured by the time taken for people to participate, and the inconveniences and the discomfort caused to participants (Emanuel et al., 2006).

Above all, the popular statement 'treat all equals equally and unequal's unequally'(Hume, 1987) is essential and should be considered by RECs when reviewing research proposals. However, RECs should be warned that identifying the worst case scenario does not necessarily equate to identifying the probability that it will occur (D'Agostino, 1995). With regard to social science, Wassenaar and Mamotte (2012) argue that no matter how altruistically studies may be packaged, they are often largely for the career of the researcher and have relatively few benefits for participants and society at large; this may also be the case for some biomedical research. Therefore RECs must consider this ratio carefully so as to prevent exploitation of research participants.

2.5.6 Independent review

The US Common Rule demands that all research involving human participants be passed through an independent review such as the REC (Amdur & Bankert, 2011). For this reason, Emanuel et al. (2008) placed on record the fact that researchers have inherently legitimate multiple interests. Some of these include the need to conduct high quality research, to complete the research expeditiously, to protect research participants, to obtain funding and to advance their careers, among other reasons. However, even though these intentions might be good, they can as well generate other conflicts of interest that may unwittingly distort or undermine their judgments regarding the design, conduct and analysis of research, as well as their adherence to ethical requirements.

Emanuel et al. (2000) argued that in order to promote public accountability, avoid conflict of interest and minimize risk, it is important to employ non-affiliated individuals on RECs to give an independent review of proposed research studies. This has the capacity to enhance transparency and increase public acceptance. In order to achieve the desired and high-quality independent review, Emanuel and his colleagues proposed four benchmarks which include:

- Are the procedures for independent review established by law and have the regulations being properly followed?
- Is the review body both independent and competent?
- Is the review process transparent and are reasons given for the review committee's decision?

- Are multiple reviews minimized, and reconciled if they conflict?

2.5.7 Informed consent

Virtually all ethical codes and institutional rules governing research involving human subjects require that all researchers obtain informed consent from participants prior to data collection. However, over the past decades, informed consent has mistakenly been regarded as the sole determinant of ethical research probably due to the events leading to the emergence of research ethics. However, Emanuel, Wendler et al. (2004, 2008) have shown that there are actually eight determinants of ethical research, of which informed consent is only one. Beauchamp and Childress (2013) point out that obtaining informed consent is required to protect autonomous choice and to ensure that individuals control whether or not to enroll in research. To provide informed consent, potential participants subjects must be accurately informed of the purpose, methods, risks, benefits and alternatives to the research. Individuals need to understand this information and its bearing on their own situation in order to make a voluntary decision to participate (Emanuel et al., 2000, 2004, 2008).

With regard to informed consent, Emanuel, Wood et al. (2004) propose that the community must be involved in the establishment of recruitment procedures and the determination of incentives, information and consent. These should be disclosed appropriately according to cultural and linguistic norms. Freedom to refuse or withdraw should be ensured. The mechanisms to symbolize consent should be consistent with the participant's culture and context (Emanuel et al., 2008). Some essential components of informed consent recognized by all the guidelines include: information disclosure, understanding of information, capacity to decide (legal and mental), voluntariness (personal agency) and explicit/formal consent.

According to the Declaration of Helsinki respect for persons requires that subjects are capable, and be given the opportunity to choose what shall and shall not happen to them. This opportunity is provided when adequate standards of informed consent are satisfied. Informed consent should therefore be a continuous process. According to Katz and Capron, (198,s reported by Emanuel, Wendler et al., 2000), informed consent promotes individual autonomy, encourages rational decision making, avoids fraud and duress, involves the public, encourages self-scrutiny by investigators and reduces the criminal liability of the investigator and his or her institution. However, particular care and precautions need to be employed in obtaining informed consent, both with vulnerable populations and capable/competent populations.

2.5.8 Respect for recruited participants and the study communities

Respect for recruited participants and a study community goes beyond mere informed consent (Emanuel et al., 2000, 2004, 2008). Respect begins when the person is seen as a possible participant, at enrolment and when the person decides to discontinue enrolment or withdraw from the study. It is important that researchers do not

see participants as a means to an end but rather as an end to themselves. The concept of respect for subjects is hinged on two principles namely the principles of beneficence (do good) and non-maleficence (do not harm). Respecting participants and study communities entails four main activities: developing and implementing procedures to respect the confidentiality of recruited and enrolled participants; making participants aware of their unrestricted freedom to withdraw without penalty; monitoring and providing interventions for research-related injuries; and providing information that may arise in the course of the research and the results thereafter (Emanuel et al., 2004, 2008). In order to uphold respect for participants, they should be told about any new information including risks that might have developed after the study has started, as well as benefits. In so doing, one shows the research participants that they are partners in the research (Emanuel et al., 2006).

The principle of respect goes beyond mere provision of adequate information but also entails the maintenance of confidentiality. To some, confidentiality may mean keeping sensitive information released by participants and others, avoidance of using participant names/institutional names and any information that could be easily linked to the participant to prevent stigmatization.

In view of this, Wassenaar (2006) cautioned researchers to fully inform participants about confidentiality risks prior to participation. Nonetheless, how much information is necessary for participants to make an informed decision? A debatable assertion is made by Guenther (2009) that naming participants may encourage them. This argument could be true for some research but can also be disastrous for other research; thus, the American Academy of Pediatrics (2004) warns that careful measures should be taken since participants wanting to be named may not comprehend anticipated/ potential harms of being named. As a result, RECs are charged to make such decisions on their behalf.

There is also a growing international concern about researchers' obligations to provide care for participants on health issues unrelated to the study aims and which fall outside the research budget (ancillary care), and whether or not researchers are obligated to meet those needs (Belsky & Richardson, 2004; Richardson, 2010).

Emanuel et al. (2000, 2004, 2008) warn that these principles and their benchmarks should not be seen as adding ethical requirements, but rather should be seen as distilled and coherently articulating the ethical norms underlying many of the prevailing guidelines. The eight principles and their benchmarks are not weighted; therefore, it is not known how they are distributed in the functioning of RECs (Tsoka-Gwegweni &Wassenaar, 2014).

Since the framework designed by Emanuel et al. (2008) is said to be applicable to all settings, this study could provide insightful information on its applicability and compatibility with the REC's operations in Ghana. The first attempt to prove this assertion was a study conducted by Tsoka-Gwegweni and Wassenaar, (2014) using a South African REC. The results from this study showed that the most frequent issues that emerged were

informed consent, scientific validity, fair participant selection, and ongoing respect for participants. The current study has therefore adapted the methodology employed by Tsoka-Gwegweni and Wassenaar, (2014) to see if the results would differ. Table 2.3 below summarises the eight principles and their benchmarks.

Ghana is a diverse country with diverse cultures, socio-economic and political status, educational background and disease burden. As it is involved in international collaborative research, it woud be useful to determine whether these principles are applied by a Ghanaian REC in its review of research protocols.

Table 2.3: Emanuel et al. (2004, 2008) Ethical principles and benchmarks for multinational clinical research

Principles	Benchmarks
Collaborative partnership	• Develop partnerships with researchers, makers of health policies, and the community. • Involve partners in sharing responsibilities for determining the importance of health problems; assessing the value of research; planning, conducting, and overseeing research; and integrating research into the health-care system. • Respect the community's values, culture, traditions and social practices. • Develop the capacity for researchers, makers of health policies, and the community to become full and equal partners in the research enterprise. • Ensure that recruited participants and communities receive benefits from the conduct and results of research. • Share fairly financial and other rewards of the research.
Social value	• Specify the beneficiaries of the research. • Assess the importance of the health problems being investigated and the prospective value of the research for each of the beneficiaries. • Enhance the value of the research for each of the beneficiaries through dissemination of knowledge, product development, long-term research collaboration, and/or health system improvements. • Prevent supplanting the extant health system infrastructure and services.
Scientific validity	• Ensure that the scientific design of the research realizes social value for the primary beneficiaries of the research. • Ensure that the scientific design realizes the scientific objectives while guaranteeing research participants the health-care interventions to which they are entitled. • Ensure that the research study is feasible within the social, political and cultural context or with sustainable improvements in the local health-care and physical infrastructure.
Fair selection of study population	• Select the study population to ensure scientific validity of the research. • Select the study population to minimize the risks of the research and enhance other principles, especially collaborative partnership and social value. • Identify and protect vulnerable populations.
Favourable risk-benefit ratio	• Assess the potential risks and benefits of the research to the study population in the context of its health risks.

	• Assess the risk-benefit ratio by comparing the net risks of the research project with the potential benefits derived from collaborative partnership, social value and respect for study populations.
Independent review	• Ensure public accountability through reviews mandated by laws and regulations. • Ensure public accountability through transparency and reviews by other international and Non-governmental bodies, as appropriate. • Ensure independence and competence of the reviews.
Informed consent	• Involve the community in establishing recruitment procedures and incentives. • Disclose information in culturally and linguistically appropriate formats. • Implement supplementary community and familial consent procedures where culturally appropriate. • Obtain consent in culturally and linguistically appropriate formats. • Ensure the freedom to refuse or withdraw.
Respect for recruited Participants	• Develop and implement procedures to protect the confidentiality of recruited and enrolled participants. • Ensure that participants know they can withdraw without penalty. • Provide enrolled participants with information that arises in the course of the research study. • Monitor and develop interventions for medical conditions, including research-related injuries, for enrolled participants, at least as good as existing local norms. • Inform participants and the study community of the results of the research.

Source: Emanuel et al. (2008)

2.6 Aim and rationale

The aim of this study was to evaluate the operations of a selected REC in Ghana by identifying ethical issues that were frequently raised during the protocol review process using the principles and their various benchmarks proposed by Emanuel et al. (2008). Available information shows that, this may be the second African study of its kind attempting to apply the framework to describe and analyze issues raised by an REC in its routine work. The first was published by Tsoka-Gwegweni and Wassenaar (2014), using a biomedical REC in South Africa. This study is another study of the concerns of an African REC based on the Emanuel et al. (2004, 2008) framework, and evaluating the applicability of the Emanuel model, in an African context. Other similar studies are currently underway in several African countries.

2.7 The general objectives

The principal goal for this research is to describe the ethical concerns raised by African RECs when reviewing protocols, find out if any patterns exist in ethical concerns raised by these RECs and if there are, to describe

the pattern. This research is part of an international collaboration involving the 2013 South African Research Ethics Initiative (SARETI) hosted at the University of KwaZulu-Natal, South Africa and Master's degree students. These countries and partners currently include: Ghana, Malawi, Nigeria and Zimbabwe. This is because demographic location and culture may contribute to variability in decision-making process of RECs. For this study to be able to contribute to the international group project, the same standard methodology and analytic framework was adopted across all four countries.

2.8 Specific objectives

- To study the minutes of a Ghanaian REC's review meetings in order to ascertain the pattern of ethical concerns raised in its reviews.
- To describe the pattern of ethical issues and concerns raised during the review of proposals.
- To analyse the ethical issues and concerns using a specific proposed framework.

2.9 Key questions

- Is there a systematic prioritization of some ethical issues over others?
- Is there an observable pattern to the ethical concerns raised by committee members? If so, what is the pattern?
- Are the concerns raised consistent with the proposed framework?
- Does any feature of the framework dominate the concerns? If so, which one?

2.10 Justification

This study is significant because it will uncover how much attention ethics committees place on each one of the principles of the Emanuel et al. (2004, 2008) framework. The Emanuel et al. (2004, 2008) framework was derived from a content analysis of the major ethical guidelines which have been criticized for inconsistencies and repackaged into a simpler form to enable RECs to conduct thorough review and application of ethical review criteria. This study therefore may provide useful information on the functioning of a Ghanaian REC as part of a broader pan-African study to describe the key concerns raised by several African RECs in the course of their review work.

CHAPTER THREE

METHODOLOGY

3.1 Data collection approach

This research has employed a qualitative content analysis approach because it aimed at interpreting meaning from text data. In recent years, content analysis has found wide use in health studies and it is among one of the five research themes approved by the US National Institutes of Health (NIH) (Hsieh & Shannon, 2005). Three types of content analysis have been recognized: conventional, directed and summative (Hsieh & Shannon, 2005; Morgan, 1993). In conventional content analysis, "coding categories are derived from the data, with a directed approach; analysis starts with a theory or relevant research findings as guidance for initial codes" (Hsieh & Shannon, 2005, p. 1279) while summative analysis "involves counting and comparisons, usually of keywords or content, followed by the interpretation of the underlying context" (p. 1283).

According to Barcus (1959, in Hsieh & Shannon, 2005), content analysis was first used as an analytic technique in the United States at the beginning of the 20th century as either a qualitative or quantitative method in research depending on the research design. However, it was later used as a qualitative research method with text data coded into categories and reported using statistics. The use of content analysis has been well recognized recently, contributing to its increased application and popularity (Nandy & Sarvela, 1997; Sparkes, 2001). For the purpose of this research, summative content analysis was used because the research involves identifying and quantifying content of text with the purpose of understanding its use.

3.2 Validity, reliability and rigour

According to Hammersley (1990), validity in research is defined as 'truth' and may be interpreted as "the extent to which an account accurately represents the social phenomena to which it refers" (p. 57). Cook and Campbell (1979) developed a taxonomy of potential threats to research validity: statistical conclusion validity; construct validity; external validity; and internal validity. Internal validity refers to "whether the inferences made from the collected data are accurate (i.e., valid)" (p. 463) and "external validity to the ability to generalize from the results of the study to other environments and populations" (p. 466).

For both practical and logistical reasons, it was not possible to incorporate all of the above strategies into this study; however, the strategies of peer review of methods (with fellow researchers working in other countries on the same topic), as well as clarifying researcher bias were considered in the design and conduct of this study from the outset. Furthermore, Silverman (2013) identifies a specific potential threat to overall validity as

'anecdotalism' which is a specific threat to this study. According to Silverman (2013), anecdotalism refers to the disposition of some researchers to convince the reader that their findings are genuine and unbiased.

During the design process of this study, other possible threats to both the internal and external validity were also identified. Acknowledgement is given to Cook and Campbell's (1979) taxonomy of threats to validity and recognizes that because the research was a desk review, carried out on specific documents kept for specific purposes with a specific group of people working in a specific environment, it is possible that a) the study will not return results that have external validity (i.e. that it will not be possible to generalize the results to other populations and/or to other environments) and b) that because the sample population was primarily selected using purposive methods, the element of randomness was not present in the selection process. This may, therefore, impact upon the internal validity of the study's results.

3.3 Study site/selection of study site

For this study to be able to contribute to the international group project, the same standard methodology and analytic framework were adopted across all countries. This international collaboration involved the 2013 South African Research Ethics Initiative (SARETI) Master's degree students from the University of KwaZulu-Natal, South Africa. These countries and partners include: Ghana, Malawi, Nigeria and Zimbabwe.

The research reported here was carried out at one REC in Ghana. The sample site for this study was conveniently and purposively selected based on availability, without any prior rationale attached (Terre Blanche, Durrheim & Painter, 2006). The sample size for the research was not limited as it depended on the workload of the REC under study within the stipulated time frame.

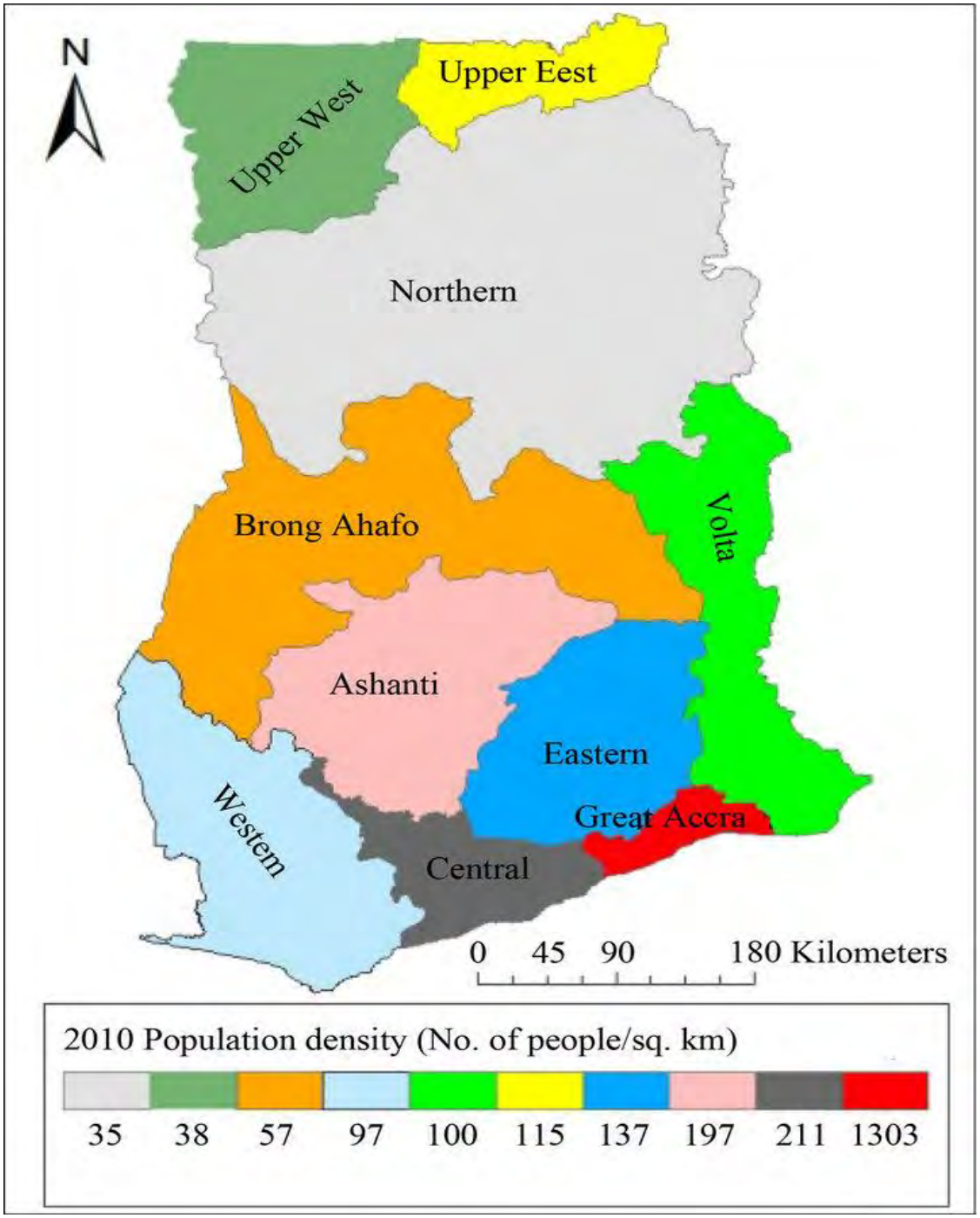

Figure 3.1: Ghana provinces and population

Ghana is a West African sovereign nation located along the Gulf of guinea and the Atlantic Ocean. Fig 3.1 above shows the area covered by Ghana, its ten (10) provinces and population. The country spans a land mass of 238,535 km^2 and its bordered by the Ivory Coast in the West, Burkina Faso in the North, Togo in the East and the Gulf of Guinea and Atlantic Ocean in the South. Ghana is a multicultural nation with a 2010 population census of approximately 25 million with an annual average inter-census growth rate of 2.5%; Ghana incorporates a variety of ethnic, linguistic and religious groups (Ghana Statistical Service, 2012). Its diverse geography and ecology range from coastal savannahs to tropical jungles. The World Bank has

categorized Ghana as a middle-income country with a GDP of USD 38.65 billion growing at 0.90% and a GDP annual growth rate of 3.90% (World Bank Ghana Home, 2015).

Accra is both the political and commercial capital city of Ghana with a population density of 1,303 persons per square kilometres. It is the most densely populated region while the least densely populated is the Northern region with a population density of 35 persons per sq. km (Ghana Statistical Service, 2012).

By the year 2010, Ghana had ten administrative regions with 170 districts (Ghana Statistical Service, 2012). The 2010 census results also showed that Ghana has a youthful population consisting of a larger portion of children under 15 years and a small portion of elderly person (65 years and above). Research also showed that the majority (74.1%) of the population is literate with 67.1% able to read and write English.

At the last census in 2010 (Ghana Statistical Service, 2012), Ghana had 55.3% of its population economically active while 6.9% were unemployed. The main economic activities in the districts are agriculture, commerce, service, manufacturing and processing, with agriculture being the leading economic activity. Ghana is categorized as one of the top-ten fastest growing economies in the world and the fastest-growing economy in Africa; however, Ghana is heavily reliant on international financial and technical assistance. Health care infrastructure is still patchy and inadequate especially outside Accra. Even though hospitals and emergency services are available in the cities, these cannot be matched with Western standards; likewise, there is limited availability of health institutions and even doctors in rural areas. According to a WHO (2015) report, the leading causes of death in the country are lower respiratory infection, stroke, malaria, ischaemic heart disease, HIV/AIDS, preterm birth complications, diarrhoeal diseases, birth asphyxia and birth trauma, meningitis, protein energy malnutrition. Below are the Millennium Development Goals (MDGs) indicators for the country (WHO 2015):

Millennium Development Goals (MDGs)

Indicators	Statistics	
	Baseline*	Latest**
Under-five mortality rate (per 1000 live births)	128	78
Maternal mortality ratio (per 100 000 live births)	760	380
Deaths due to HIV/AIDS (per 100 000 population)	89.1	40.8
Deaths due to malaria (per 100 000 population)	98.7	68.7
Deaths due to tuberculosis among HIV-negative people (per 100 000 population)	30	4.4

*1990 for under-five mortality and maternal mortality; 2000 for other indicators
**2012 for deaths due to HIV/AIDS and malaria ; 2013 for other indicators

3.4 Data collection

This study was based on a content analysis of archived written documents. These were the minutes for a period of two years (2012-2013) of a Ghanaian REC's review meetings was assessed. Approval from relevant authorities was obtained to access and analyse the documents (REC minutes). Bearing in mind that the REC have five planned meetings in a year, there were ten set of minutes for this period of review. These minutes provided the basis of the review feedback letters that were sent to respective applicants. Because this REC was newly established and therefore did not have a large throughput, all ten sets of minutes were selected and analysed. Only minutes recorded on newly submitted applications reviewed at full REC meetings between the two year periods were considered, without any consideration of the type of study (clinical trial, biomedical, epidemiological, social research, behavioral, implementation research, or operational research or studies). All continuing reviews, annual reports and final reports were excluded because they had already been reviewed. The data were collected using a specifically designed data collection sheet drawn from the Emanuel et al. (2008) framework (see Appendix 1).

Once the relevant and available minutes (2012-2013) were accessed, a summary of reviewed comments were obtained and categorized using the Emanuel et al. (2004, 2008) framework. This was done by two independent coders who identified, coded and ranked the most frequent issues raised by the committee during its meetings; this was done in accordance to the framework recommended by Emanuel et al. (2004, 2008). The second independent classifier was thoroughly trained to fully understand the principles and identify them.

Where necessary provision for 'other' categories of reviewed comments recorded in the minutes but not covered by the Emanuel et al. framework were created. The number of comments per category/principle per proposal was recorded. All counts of ethical issues raised in relation to each proposal mentioned in the REC minutes were also recorded. The frequencies of occurrence of other issues recorded in the minutes but not covered by the Emanuel et al. (2004, 2008) framework were also recorded.

Data were also collected for the year of review, number of protocols, area of research, study designs and source of data. Only recorded issues that were minuted by this particular REC were coded, though other issues may have been deliberated by the REC but not recorded in the minutes. The other issues considered which may not be part of the Emanuel et al. (2008) framework will be described in the Results section of this thesis.

3.5 Data analysis

The data obtained were captured on Microsoft Excel. The data consisted of counts of the number of issues per proposal and for analysis, these were considered as scores. How frequently particular issues arose was analyzed using configural frequency analysis (which reveals very rarely used classifications, as well as extremely highly used classifications) as well as through more conventional categorical data analysis. Because each proposal would be classified in terms of a dominant problem, chi-square (χ^2) was calculated to determine the relationship between the dominant issues raised. In addition, other frequency analysis such as percentage frequency was also applied to the data.

Measures such as Cohen's Kappa were also calculated to show that an independent classifier can reach the same conclusions as the original classifier (Viera & Garrett, 2005). These were carried out using STATA software. The results have been presented graphically (see Chapter 4). Eventually, and in a later work, the results from all five African countries will be compared and combined and analyzed together, to generate a broad picture of concerns raised by RECs in selected African countries when reviewing health research proposals.

3.7 Ethical considerations

3.7.1 Collaborative partnership

This principle requires that a researcher develop studies in collaboration with the population and relevant stakeholders so as to reduce possible exploitation (Emanuel, Wendler et al., 2008). Putting this into consideration, the REC was selected based on consultation with relevant stakeholders. In view of that, gatekeeper permission was also obtained from the relevant authorities in charge (see appendix 3 below). Because this study did not reveal any destructive process, the exception to this principle, as pointed out by Wassenaar and Mamotte (2012), does not apply to the study.

3.7.2 Social value

Social value is relevant component of every research such that the research must address questions that are of value to a particular participant (Emanuel, Wendler et al., 2008). The aim/purpose of this research is evidence that the findings of this research will help improve ethics review which will eventually benefit both that REC and researchers. Also, Wassenaar and Mamotte (2012) pointed out that it is an ethical obligation of social researchers to include interventional actions or advocacy efforts, as part of this study, the findings will be communicated to the REC through a presentation during a session of their review with relevant recommendations.

3.7.3 Scientific validity

As part of the ethical consideration of scientific validity, rigorous attention was given to the choice of methodology putting into consideration its feasibility to answer valid research question outlined in the objectives of the study. All issues of validity, reliability and rigour were addressed under 3.2 above. In order to obtain high quality and scientifically valid research results as recommended by Wassenaar and Mamotte (2012), the second independent rater/coder was thoroughly trained on the Emanuel et al. (2004, 2008) framework. Care was taken not to influence her rating decisions.

3.7.4 Fair selection of participants

Even though Wassenaar and Mamotte (2012) argued that convenience samples should be avoided unless in pilot research studies, for this study, the sample site was conveniently and purposively selected based on availability, without any prior rationale attached. The site was considered based on the willingness of the REC without and undue inducements offered. More so, the benefits of this research even though will improve REC review, recommendations are open to other RECs to adapt the framework during review. There was no direct benefit accrued to this study but provision of useful information.

3.7.5 Favourable risk/benefit ratio

There was no direct risk associated participating in this study rather generation of useful information that will help formulate good policy and enhance harmonise ethics review.

3.7.6 Independent ethics review

As per requirements of the US Common Rule (45 CFR 46, 1991) and also to satisfy the sixth principle of independent ethical review of the Emanuel et al. (2008) framework and other international declarations, that all research works should be reviewed by an independent body, ethical approval was obtained from the REC under investigation (see Appendix 4) and from the UKZN Humanities and Social Sciences REC approval number HSS/1450/014CA (see Appendix 5 and Appendix 6).

3.7.7 Informed consent

This study was exempted from informed consent. However, gatekeeper's permission and local permission to access the records were obtained. To preserve confidentiality, these permissions and approvals are not included in the appendices but are available on request.

3.7.8 Ongoing respect for participants and study communities

According to Wassenaar and Mamotte (2012), it is best practice to consider keeping the identity of participants as well as institutions confidential in order to prevent stigmatization and discrimination. In view of this, to ensure confidentiality in this study, all identifiers for the institution, the biomedical IRB, protocols and investigators were removed. Emanuel, Wendler et al. (2004) & (2008) uphold confidentiality as the key prerequisite for ongoing respect. Wassenaar and Mamotte (2012) again pointed out that "there is increasing international concern about what happens to participants once the study is over" (p. 278). Addressing this, the results from this study will be communicated to the REC under review so as to help them review decision making. To address the ethical problems associated with making findings available to the institution (distress by self-identification in publications), care will be taken to taken to avoid wording that could be construed as critical or distressing.

3.8 Problems encountered and resolved

The major problem foreseen with this study was the willingness of the REC to allow the student researcher to access and use its meeting minutes for research purposes, since these are confidential and private. In addition, the REC chair may also feel that this is a way of probing them and exposing credibility issues. However, to resolve this, a confidentiality agreement (see Appendix 2) was signed between the student researcher and the various parties involved. In addition, the REC and host institution were not reported by name, thereby

respecting their privacy. In addition, in future publication of results, the REC name or any identifying information will be omitted.

Another problem was the potential for incomplete or inaccurate minutes; for example, some of the issues identified, debated and/or resolved may not have been reflected in the minutes. According to Atkinson, Delamont and Coffey (2004), documents such as minutes may have a distinctive ontological status. They form a separate reality which they refer to as 'documentary reality' and they should not be taken to be 'transparent representations' of an underlying organizational or social reality. Thus, Atkinson et al. (2004) argue that even 'official' records may not be firm evidence of what is contained in them. In addition, according to Bryman (2008, p. 15), well-known people may "have one eye firmly fixed on the degree to which they really reveal themselves in their writings, or alternatively ensure that they convey a 'front' that they want to project". In addition, considering that it was necessary to engage a second coder in order to verify the coding, the second coder and I maintained an attitude of healthy scepticism regarding the accuracy with which the REC reported their true concerns through their minutes. Where there were disagreements in coding, these were resolved through discussion (see table 4.4 below).

The minutes to be reviewed were only those for new and recent applications but not for recertification of ongoing studies or amendments. Fourthly, it was not necessary to include one of the benchmarks during the content analysis of the minutes of meetings as the 'independent review' component should already have been satisfied by being considered by the REC. However, researchers whose proposals were reviewed by the REC in question and who were also members of the REC would have had to declare conflicts of interest and these could be coded under this principle.

CHAPTER FOUR

RESULTS

4.1 Summary of protocols selected

Minutes for a total of 22 protocols submitted to the REC from 2012 to 2013 were available for this study, nine (9) from 2012 and thirteen (13) from 2013. On average, the REC reviewed 3.5 protocols at each meeting, ranging from one (1) to five (5). Of the 22 protocols sampled, ten (10) of the proposed research studies involved adult participants and 12 involved both adult and child participants. The proposed research studies were mainly biomedical (10) and social behavioural research (10), while two (2) proposed research studies focused on a combination of both biomedical and social sciences. All the proposed research sought to collect primary data.

Table 4.1: Summary of protocols reviewed by the REC

Year	Total	Percentage
Protocols (N=22)		
2012	*9*	*40.91*
2013	*13*	*59.09*
Study design		
Biomedical	*10*	*41.67*
Social/Behavioural	*10*	*41.67*
Biomedical/Social	*2*	*8.33*
Participants		
Children	*0*	*0*
Adults	*10*	*41.67*
Adults and children	*12*	*50.00*
Data sources		
Primary	*22*	*100*
Secondary	*0*	*0*

Table 4.2: Ethics queries raised by the REC 2012-2013 (N=232)

Emanuel et al. (2004, 2008) principles and benchmarks	**Frequency *(n)* of queries**	**Percentage**
Principle 1: Collaborative partnership	**0**	**0.00**
Community representatives	0	0.00
Responsible sharing (collaboration)	0	0.00
Respect for local context (environment)	0	0.00
Fair research benefits for community	0	0.00
Sharing research products	0	0.00
Principle 2: Social value	**2**	**0.86**
Research beneficiaries	1	0.50
Research benefits	0	0.00
Enhancing research benefits	1	0.50
Impact on health systems	0	0.00
Principle 3: Scientific validity	**57**	**24.57**
Appropriate design and methods	56	98.25
Applicability of results	1	1.75
Impact on provision of health care service	0	0.00
Study design feasibility	0	0.00
Principle 4: Fair participant selection	**9**	**3.88**
Suitable study population	1	11.11
Risk minimization	5	55.56
Benefits to participants	1	11.11
Vulnerability	2	22.22
Principle 5: Favourable risk-benefit ratio	**6**	**2.59**
Risk identification and minimization	6	100.00
Type, probability and magnitude of benefits	0	0.00
Comparison of risks and benefits	0	0.00
Principle 6: Independent ethics review	**70**	**30.17**
Regulatory compliance	22	31.43
REC members' conflicts of interest	4	5.71
Transparent review	22	31.43
Minimization and reconciliation multiple reviews	22	31.43
Principle 7: Informed consent	**79**	**34.05**
Recruitment/incentives applicability to local context	13	16.46
Appropriate disclosure documents and processes	60	75.95
Presentation and accuracy of information	3	3.80
Legally authorized representatives	1	1.27
Gatekeeper's permission	1	1.27
Context of consent process	1	1.27
Respect for autonomy	0	0.00
Principle 8: Respect for participants	**9**	**3.88**
Monitoring health and well-being	0	0.00
Confidentiality and privacy	3	33.33
Voluntariness	2	22.22
Research results dissemination	4	44.44
Post-research obligations	0	0.00

4.2 Most frequent ethical issues considered by the REC as identified by the Emanuel et al. (2004, 2008) framework

A total of 232 queries were counted and coded in the minutes of all 22 protocols reviewed by the REC during the two-year period using the principles and benchmarks proposed by Emanuel et al. (2004, 2008). Assessment of data from the review meetings revealed that Principle 7 (informed consent) was the most frequent issue considered by this REC, scoring 79 of the 232 queries (34.05%). Of 79 queries about informed consent, appropriate disclosure documents and processes in terms of language, context and comprehension of required information was the most frequently discussed benchmark (60 queries; 75.95%), followed by recruitment and incentives' applicability to local context (13 queries; 16.46%) and presentation and accuracy of information sensitive to local context using of local language, culturally appropriate idioms and analogies that are easily comprehensible to prospective participants (3 queries; 3.80%). Others such as legally authorized representatives, gatekeeper's permission, context of consent process and respect for autonomy were weighted equally as shown in Table 4.2.

The second most frequent issue was Principle 3 (scientific validity) which recorded 57 queries (24.57%). Under this principle, the REC paid particular attention to the appropriate design and methods which attracted 56 queries of the total 57 (98.52%) where they interrogated the researcher's strategies for data collection (such as randomization), participant selection criteria and control procedures. Throughout the two-year period, only one query (1.75%) was recorded for applicability of results. No issue was raised on the impact of the research on the provision of health care service through improvement of sustainable health care infrastructure and study design feasibility; alternatively, if such issues existed, they may have been resolved in REC discussion.

Principle 4 (fair participant selection) and Principle 8 (respect for participants) were equally weighted by the REC, as the two principles emerge as the third most considered principles with nine (9) queries each, representing 3.88% of the total queries raised. Risk minimization, a benchmark under Principle 4, received more discussion, scoring 5 queries (55.56%), followed by the vulnerability benchmark 2 queries (22.22%). Under Principle 8, however, the REC acknowledged the importance of research result dissemination with four (4) queries (44.44%), followed by confidentiality and privacy with three (3) queries (33.33%) and voluntariness with two (2) queries (22.22%) respectively.

Other issues considered but with low frequency included Principle 5 (favourable risk-benefit ratio) with only 6 queries (2.59%). Within this category risk identification and minimization received the unanimous (100%) weighting of the REC by scoring all six (6) queries. Principle 2 (social value) received two (2) queries (0.86%) as the least important principle that featured in the minutes of the REC meetings. Principle 1 (collaborative partnership) was the only principle under the Emanuel et al. (2008) framework that received no weighting by the REC as no queries were recorded in the minutes.

There were 48 issues considered by the REC that could not be accommodated within the Emanuel et al. (2004, 2008) framework (see table 4.3). These were administrative and clerical errors such as grammatical errors and omissions (missing signature, addresses, incomplete forms, among others), scientific technical committee review (STC), regulatory approvals and signed material transfer agreements, respectively (see table 4.3 below). These represented 20% of all queries raised. This means that 80% of all issues raised by the REC could be coded using the Emanuel et al. (2004, 208) framework. The other issues not considered throughout the two-year period under review were good clinical practices (GCP) certificates, data safety monitoring board (DSMB) issues, insurance cover for research participants, investigational brochures, and responsible conduct of research.

Table 4.3: Other issues considered outside of the Emanuel et al. (2004, 2008) framework (*n*=48)

Issues	**Number**	**Percentage**
Data/Material transfer agreement (MTA)	*1*	*2.08*
Good Clinical Practices (GCP certificates)	*0*	*0.00*
Data safety monitoring board	*0*	*0.00*
Insurance cover for research participants	*0*	*0.00*
Investigational brochure	*0*	*0.00*
Scientific Technical committee review approval (STC)	*22*	*45.83*
Responsible conduct of research	*0*	*0.00*
Regulatory approvals pending	*2*	*4.17*
Admin issues (e.g. signatures missing)	*23*	*47.92*
Total	**48**	**100**

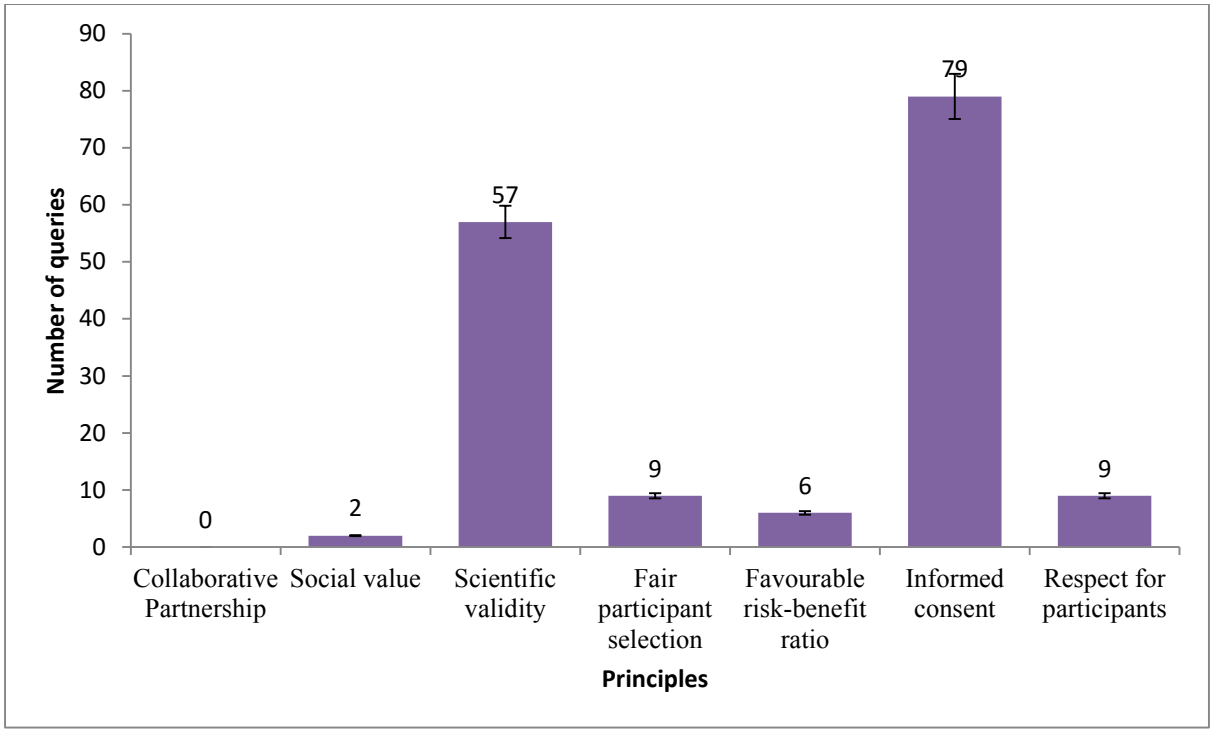

Figure 4.1: Ethical queries considered by the REC during 2012-2013 (N=232) (frequencies)

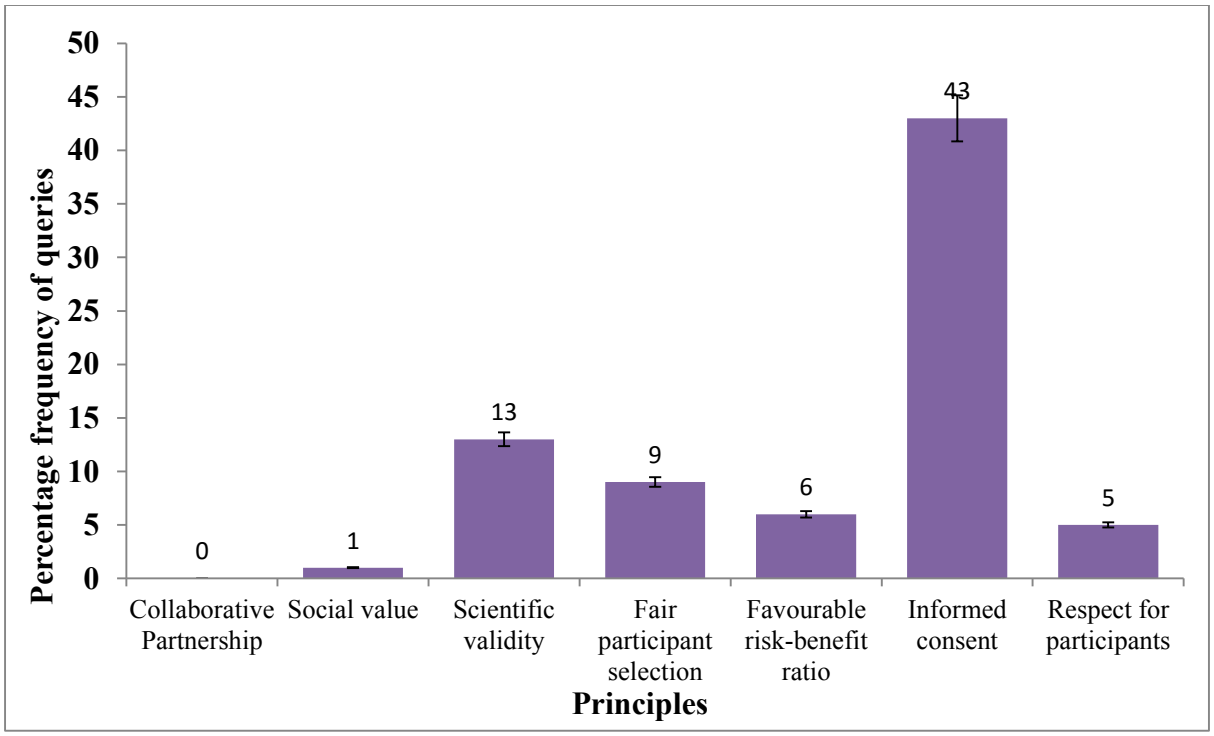

Figure 4.2: Ethical queries considered by the REC during 2012-2013 (N=232) (percentages)

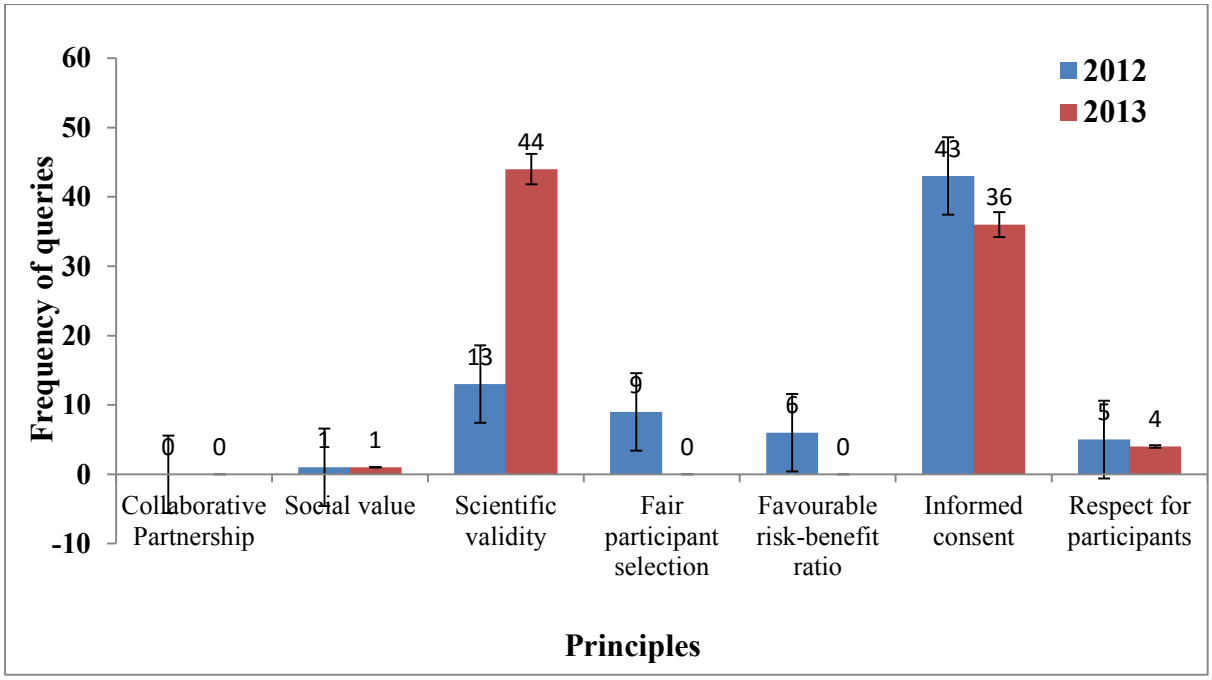

Figure 4.3: Comparison of ethical issues raised by the REC during 2012-2013

Comparing the data from the two years under review (2012 and 2013) revealed that in 2012, Principle 7 (informed consent) was the most predominant principle considered, whereas Principle 3 (scientific validity) was the most considered in 2013. In 2013, however, there were no issues recorded on Principles 4 and 5 (fair participant selection and favourable risk-benefit ratio) respectively even though they were both considered in 2012.

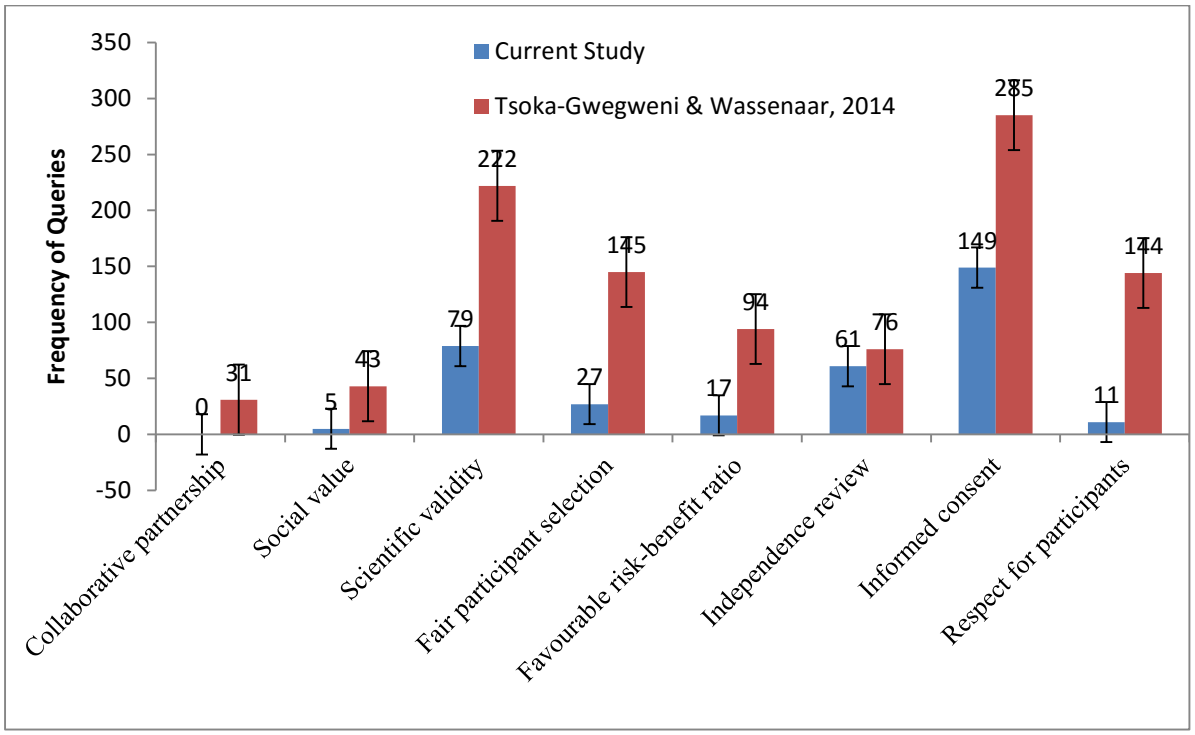

Figure 4.4: Comparison of frequency of queries raised by REC in Tsoka-Gwegweni & Wassenaar (2014) and the current study. (Note: Denominators differ)

Fig 4.4 shows that when comparing the current study to that of Tsoka-Gwegweni and Wassenaar (2014), informed consent and scientific validity came out as the two most considered issues by both RECs. Exceeding independent review, the third most considered issue in both studies was fair participant selection which was more frequently raised in Tsoka-Gwegweni and Wassenaar (2014), than the current study. Again no issues were raised on collaborative partnership in the current study. Below is a graph showing how these issues compared as a percentage of the queries raised by each REC.

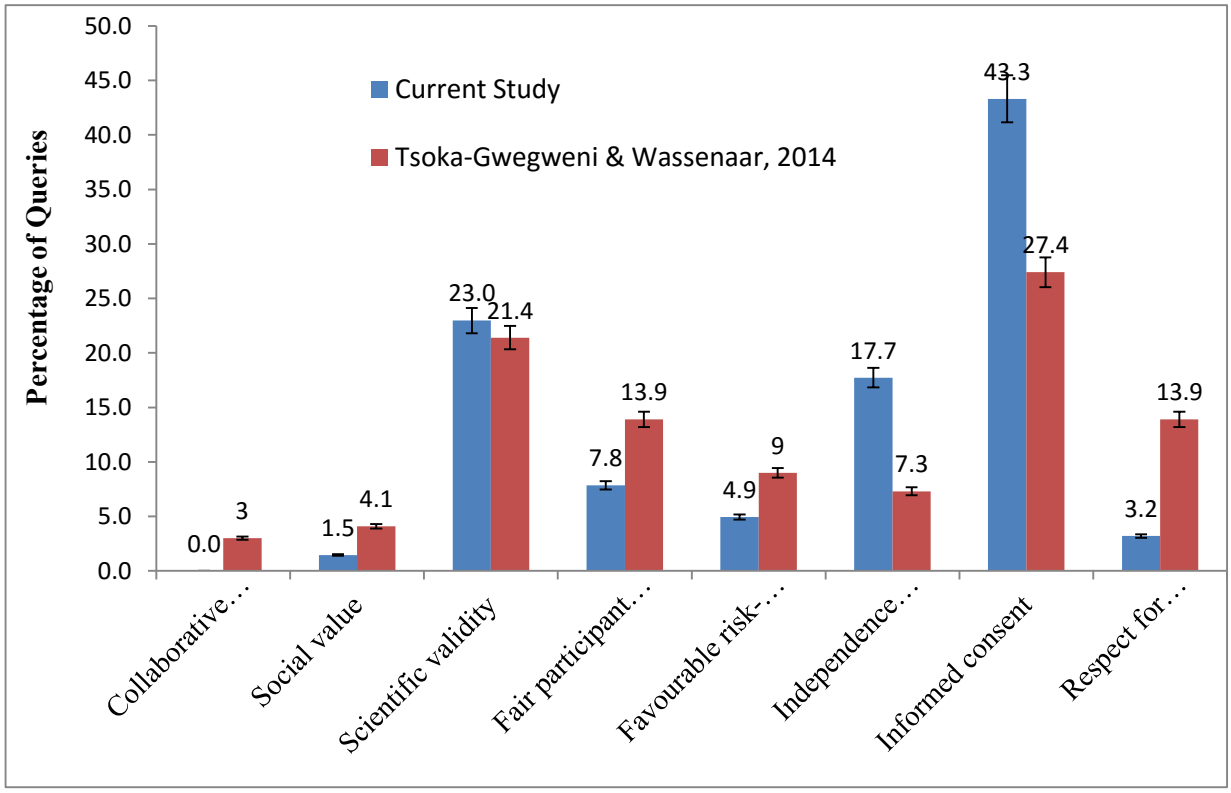

Figure 4.5: Comparison of percentage of queries raised by REC in Tsoka-Gwegweni & Wassenaar (2014) and the current study.

Table 4.4: Test of agreement between two classifiers/coders

Variables	Agreement	Expected agreement	Kappa	Std. Err.	Z	Prob.>Z
Collaborative partnership	-	-	-	-	-	-
Social value	100.00	83.47	1.0000	0.2132	4.69	0.000
Scientific validity	95.45	20.87	0.9426	0.0988	9.54	0.000
Fair participant selection	100.00	75.62	1.0000	1.1705	5.86	0.000
Favourable risk-benefit ratio	100.00	75.62	1.0000	0.1705	5.86	0.000
Independent review	100.00	7.025	1.0000	0.2132	4.69	0.000
Informed consent	72.73	11.78	0.6909	0.0744	9.28	0.000
Respect for participants	90.91	52.48	0.8087	0.1686	4.80	0.000
Overall agreement	72.73	11.98	0.6901	0.6901	9.39	0.000

The test of agreement analysis assessed between the first and second independent classifiers/coders revealed a 100% agreement for social value, fair participant selection, favourable risk-benefit ratio, and independent review, while scientific validity had 95.45% agreement. There was 72.73% agreement for informed consent, whilst respect for participants had 90.91% agreement. Because both classifiers noted that there was no mention in the minutes of collaborative partnership, it forms a good ground to draw a 100% agreement conclusion between the two classifiers. The overall initial agreement for all the principles and benchmarks for the entire study was 72.73%.

Table 4.5: Chi-square ($\chi^{2)}$ test of relationships among dominant issues

Variables	X^2	*P*-value
Scientific validity vs. Fair participant selection	*10.42*	*0.73*
Scientific validity vs. Respect for participants	*11.21*	*0.67*
Scientific validity vs Informed consent	*49.30*	*0.73*
Fair participant selection vs. Respect for participants	*8.05*	*0.09*
Fair participants selection vs. Informed consent	*11.04*	*0.79*
Informed consent vs. Respect for participants	*20.59*	*0.20*

Chi-square tests were conducted among the dominant issues under review to explore if any relationship existed among them, as shown in Table 4.5 above. At a significant level of 0.05 and confidence level (95%), the analysis showed that there was no significant relationship or association between the four most frequently considered principles.

4.3 Summary of results

The findings from this study revealed that during the two-year period under review:

- The REC met five (5) times in each year, reviewed about 22 protocols with an average of 3.5 protocols per meeting ranging from one (1) to five (5).
- In descending order, principles 7, 3, 4, and 8 (informed consent, scientific validity, fair participant selection, and respect for participants) were the most prioritized issues during the period under review by the REC.
- Principle 7 (informed consent) (34.05%) emerged as the most dominant issue considered by the REC.
- Most of the concerns raised by the REC (80%) could be easily accommodated by the Emanuel et al. (2008) framework for ethical review.
- In 2012, informed consent was the highest weighted ethical principle while in 2013, scientific validity was the most considered issues. However, the percentages varied considerably in both years.
- From the chi-square results, there was no significant relationship between the four most weighted principles, suggesting that they were independent principles.
- About 20% of issues raised, including scientific technical committee (STC) review, administrative issues, and material transfer agreement (MTA) and regulatory approval pending were also considered by the REC; these largely administrative issues were not accommodated by the Emanuel et al. (2004, 2008) framework.

- The overall initial agreement between the two coders or classifiers for all the principles and benchmarks for the entire study was 72.73%. Consensus on all of these was reached through discussion.

CHAPTER FIVE

DISCUSSION, CONCLUSION & RECOMMENDATIONS

5.1 Systematic prioritization and dominant ethical concerns

The Association for the Accreditation of Human Research Protection Programs (AAHRPP, 2010) and Byerly (2009) have pointed out that a well-prepared consent document which meets all standards and best informs research subjects is often necessary to prevent delays in approval of research proposals, thus indicating that informed consent is pivotal in review process. This assertion lends credence to several research studies which showed that the RECs studied focused predominantly on informed consent documentation during review processes (Blackwood et al., 2015; Dixon-Woods, 2008; Flory & Emanuel, 2004; Kass et al., 2007; Lidz et al., 2012; Lilleyman, 1995; Pokorny, Jason, Schoeny, Townsend & Curie, 2011; Raich, Plomer & Coyne, 2001; Tsoka-Gwegweni & Wassenaar, 2014, see figures 4.4 & 4.5 above).

Similarly in this study, informed consent was the most dominant ethical query considered by the REC. Critical attention was, however, paid to language of communication, with particular reference to the use of technical terms and local context, study participants' comprehension of required information and appropriate incentives (in the local context) to avoid undue inducement of participants. The REC also focused specifically on indications of possible risk and benefits associated with the research. This was to help participants make a well-informed decision to be included or excluded from the research, so as to minimize the exploitation of unsuspecting participants. These are the key prerequisites for the informed consent process (Beauchamp & Childress, 2013).

In an attempt to analyse the nature of REC contingencies required for informed consent document approval, Blackwood et al. (2015) and Geisser, Alschuler and Hutchinson (2012) reported that "better clarity" (p. 240) scored an appreciable 24% as the second most frequent issue interrogated by most RECs. The findings of Blackwood et al. (2015) and Geisser et al. (2012) are in broad agreement with the current REC under study, often requiring 'better clarity' of information presentation to inform decision-making by study participants. This result was also in agreement with Biggs and Marchesi (2015), who pointed out that informed consent forms were often too long and difficult to understand. The findings of Jones, White, Pool and Dougherty (1996), though not using the Emanuel et al. (2004, 2008) framework, and as well as those of Cleaton-Jones (2010) and Tsoka-Gwegweni and Wassenaar (2014), employing the principles and benchmarks of the Emanuel et al. (2008) framework, all made similar findings albeit with different orders of priority.
Kass, Dawson and Loyo-Berrios (2003) are of the view that when RECs focus predominantly on informed consent, little or no time is spent on examining voluntariness, selection of participants and risk, but Burke

(2005) argued that the work of RECs is not helped when protocols and consent forms do not meet minimal standards. Therefore, RECs cannot overlook consent issues but must also focus on issues raised by Kass et al. (2003). Data from the present study suggest (table 4.2) that this REC also paid attention to the other key principles and benchmarks of the Emanuel et al. (2004, 2008) framework, including scientific validity (24.57%), fair participant selection (3.88%) and respect for participants (3.88%) in descending order of priority. This was a way of ensuring that investigators provided adequate information to participants without underestimating the risks involved (Dixon-Wood, 2008). The results from this study are, however, contrary to the findings of Lidz et al. (2012), which attributed 98% of reviews and questions raised to informed consent, paying little or no attention to the other (Common Rule) criteria. This information is significant and gives an indication that the said REC has been weighing the principles of the framework fairly, depending on the type of study involved, as seen in the following excerpt:

The informed consent form/sheet was unsatisfactory and should be written in lay terms simplifying the language and reduce the use of technical terms

Scientific validity, which was found to be the second most dominant principle considered, was also reported by Dixon-Wood (2008) to be one of the most frequent issues of concern likely to be raised by RECs. Issues such as appropriate design and method, which were considered by reviewers under scientific validity, are also compatible with what Freedman (1987) proposed as a core prerequisite for ethical research. An excerpt from the issues raised on this ethical principle follows:

The committee advised that the proposal be re-submitted with a clearly outlined objectives and methodology.

Furthermore, comparing the results from this study with Tsoka-Gwegweni and Wassenaar (2014), the four dominant issues considered were similar and consistent except that in the current study, fair participant selection and ongoing respect for participants received equal weighting. In addition, collaborative partnership (3.0%), which was given some consideration in Tsoka-Gwegweni and Wassenaar's (2014) study received no weighting in the current study (0%) (see figures 4.4 &4.5 above). The reason for this could be either that this issue was well dealt with by all applicants, or deliberated and resolved or the REC did not review collaborative works; it is also possible that these issues were overlooked by the REC. Collaborative partnership is an important ethical issue which, if overlooked, could result in research being conducted without appropriate consultation with local communities and possibly without considering national health priorities and issues. In future research, a further examination of the actual protocols by an experienced coder and comparison with REC minutes will be helpful in determining why collaborative partnership was not considered by the REC. Also, an interview with the chair or members of the REC would help with some explanation of the above issues. Levine (1986) argued that the importance of scientific validity is retained. He further explained that determination of the importance of the knowledge to be gained and the likelihood of gaining that knowledge requires close consideration of the adequacy of research designs. Social value received 0.87% of the queries raised by the REC.

Assuring respect for confidentiality and participants' privacy was also considered to be very important by Dixon-Wood (2008) and Geisser et al. (2012). In general, even though such concerns are captured under informed consent, for the purposes of this study, confidentiality and respect for participants' privacy was grouped under Principle 8 and respect for participants received the highest weighing under this grouping, showing that the results from this study are in agreement with Dixon-Woods (2008) and Tsoka-Gwegweni and Wassenaar (2014).

In application of the principles of the framework, Emanuel et al. (2008) stressed that depending on a study's objectives and context, a particular principle or benchmark may be given greater weight than others. Data from the present study suggest that collaborative partnership was weighted low by the REC. This is possibly either because the submissions addressed these issues or because the REC did not consider them. The only way to verify this would be to conduct a further expert review of each protocol after the minutes were evaluated, as recommended earlier. Even though independent review was regularly considered by the REC in this study, it was earlier noted that it was not necessary to include it as one of the benchmarks during the content analysis of the minutes of meetings as the 'independent review' component should already have been satisfied by the activities of the REC in question.

With regard to issues in the minutes not accommodated by the Emanuel et al. (2004, 2008) framework (20% of responses), scientific technical committee review (STC) and administrative issues were other issues considered by the REC. STC was frequently considered because this REC doubles as a scientific technical committee (STC) since the STCs within the home institution of the REC selected for this study were not functional. A requirement that researchers submit material transfer agreements (MTAs) and obtain export permits from relevant state agencies before the export of any human tissues for analysis or other purposes was also considered by the REC, which is in line with the requirements of the National Health Research Ethics Council (NHREC) (Department of Health 2015). Good clinical practice (GCP certificates), data safety monitoring board and charter of work, insurance cover for research participants and investigational brochures were not considered by this REC, most likely because the REC did not review any clinical trials. Even though these latter issues are not captured by the Emanuel et al. (2008) framework, they were considered by the REC, showing that some issues could not be accommodated in the Emanuel et al. (2004, 2008) framework.

With the exception of collaborative partnership, which did not come up in this study, all other principles of the Emanuel et al. (2008) framework were represented in this study, ranked similarly in frequency to those found in the Tsoka-Gwegweni and Wassenaar (2014) study. It is unknown how the distribution of issues raised in the study can be generalized for other RECs in the same country over a similar period. Consequently, a

parallel study which is currently being conducted by a fellow SARETI student on another Ghanaian REC may help interpretation of the data. However, it is also very important to note that ethical concerns raised may be affected by characteristics of the membership of a particular REC; examples are background, experience with research and review, research ethics training, ethics review tools used, and review processes employed.

5.2 An observable pattern to the ethical concerns raised by committee members

Throughout the two-year review period under study, the most dominant issues considered by the REC, in descending order, were informed consent forms, scientific validity, independent review, fair participant selection, and respect for participants. However, in 2012, informed consent was the highest weighted ethical principle compared to scientific validity in 2013. The apparent change in which principle was prioritized might have resulted from a change in focus of interest by members of the REC, or different quality and type of applications, or based on reviewers' experiences acquired over the years. It should be borne in mind that the sample for this study is small and that a longer time period sampled would yield more valid and reliable data. Researchers might also have been well informed about what was required of them, leading to a change in the trend of proposals submitted for reviews.

5.3 Are concerns raised consistent with the proposed framework?

One criticism levelled against the Emanuel et al. (2008) framework is that it serves as a set of rules that may not allow engagement and discussion (Médecins Sans Frontières, 2013). However, the results from this study have shown that the framework is applicable and appears to be compatible with the work of the REC studied here.

5.4 Limitations of the study

The limitations of this study are similar to those identified byTsoka-Gwegweni and Wassenaar (2014), most probably because a largely similar methodology was adopted to generate comparable results. Beyond description, further interpretation of the data presented in this study is beyond the scope of this study. Moreover, apart from some studies in progress or in press, the very first part of this research work in Africa was carried out in 2014. Another limitation was that this research work was done on the basis of the assumption that the minutes of the REC were a true reflection of their review meetings. However, some equally relevant issues debated amicably and normally resolved at review meetings may not be included in the minutes and thus there is a probability that the results might have been different if an audio recording of the meeting was used rather than the minutes. However, the letters that applicants are asked to respond to are based on the minutes, suggesting that unminuted comments are irrelevant. Without such verification, it is nevertheless assumed that those issues requiring a response from the applicant/PI are adequately reflected in

the meeting minutes that were coded for this study. The quality and nature of the research applications submitted are also likely to influence the frequency of issues raised and the importance attributed to them by the REC, as pointed out by Tsoka-Gwegweni and Wassenaar (2014).

There was an overlap of some of the benchmarks as they appear under more than one principle. In order to improve upon the reliability of coding by researchers in future studies, it is important the benchmarks are arranged and placed where they best fit. For example, vulnerability was originally placed under fair selection of participants; however, it was moved to social value. This was because, in determining the social value of any research, RECs should first consider the beneficiaries and in so doing, might have already addressed issues on vulnerability. Finally, the study focused on only one REC and this makes it difficult to generalize the findings to other RECs in Ghana and beyond Ghanaian jurisdiction. A second Ghanaian study is currently underway and it would be useful to compare results with those of this study and with Tsoka-Gwegweni and Wassenaar (2014).

5.5 Conclusion and recommendations

The results of this study suggest that the Emanuel et al. (2008) framework can be used to code the majority (80%) of issues raised by an African REC. The frequencies of ethical issues raised by the REC largely resemble those by data reported by Tsoka-Gwegweni and Wassenaar (2014) from a South African biomedical REC. Depending on the type of research protocol, not all the principles need be fulfilled before a research study can be regarded as ethical (Wassenaar & Mamotte, 2012), and it therefore requires a careful assessment so as not to appear to be 'picking or choosing'. Even though the framework did not accommodate some largely administrative issues raised by the REC, it accommodated the vast majority of issues raised by the REC, so can thus be said to be an appropriate framework to use for the analysis of REC minutes.

The limitations of the methodology and sample employed in this study, and factors affecting reliability of the data, have been identified and should be refined for future consideration. Overall, however, the Emanuel et al. (2004, 2008) framework appears to be useful as a way of coding the outcomes of REC reviews, and can possibly be adapted by future researchers and RECs for review processes. Overlap of some ethical issues such as benefits and risk minimization appearing under multiple principles, indicating a need for threshold points across principles since this may be a contributing factor for the differences recoded in the level of disagreement between two coders – and between data from different RECs.

In practical evaluation of protocols by the REC, ethical issues such as favourable risk-benefit ratio, confidentiality and privacy, among others, are mostly scrutinized on informed consent forms. 'Research beneficiaries' under social value and 'suitable study population' under fair participant selection appear to mean the same and may be confusing when coding. It could be argued that the principle of fair participant

selection be merged with social value. Similarly, the benchmark 'research benefits' should be synonymized with 'benefits to participants' and likewise, 'risk minimization' and 'risk identification and minimization' appear confusing and could result in disagreement between two raters. It is also not clear if the arrangement (in terms of order) of the principles in the framework by Emanuel et al. (2004, 2008) has any relation to the order in which they should be used to evaluate research proposals. Further comparative research is needed where some expert coders/raters re-review research applications considered by the REC and compare their coding using the Emanuel et al. (2004, 2008) framework with the coding of the reviews of the REC. This will also present a better picture of REC review outcomes.

To conclude, the Emanuel et al. (2004, 2008) framework has been shown to accommodate the majority of issues raised by a Ghanaian REC.

Nevertheless, RECs need to be constantly re-trained and be abreast with current happenings both locally and internationally to be able to apply the framework optimally. Although the peculiarities of the applications considered were not studied, it would appear that the REC in question raised a spread of issues largely compatible with the Emanuel et al. (2004, 2008) framework, and resembling in some respects the results from Tsoka-Gwegweni and Wassenaar (2014) from another African REC.

With regard to recommendations, an attempt to place the overlapping benchmarks where they best fit, based on the practicality of using the principles during ethical review process is suggested below:

Table 5.1: An attempt to place overlapping benchmarks where they best fit.

Principle	Proposed Benchmarks	Old Benchmarks
Collaborative partnership	Community sharing (collaboration)	Community representatives
	Respect for local context (environment	Responsible sharing (collaboration)
	Fair research benefits for community	Respect for local context (environment)
	sharing research products	Fair research benefits for community
		Sharing research products
Social value	Research beneficiaries	Suitable research beneficiaries
	Research benefits	Vulnerability
	Enhancing research benefits	Research benefits
	Impact on health systems	Enhancing research benefits
		Impact on health systems
Scientific validity	Appropriate design and methods	Appropriate design and method
	Applicability of results	Applicability of results
	Impact on provision of health care services	Impact on provision of health care service
	Study design feasibility	Study design feasibility
Favourable risk-benefit ratio	Synonymized with other benchmarks	Risk identification and minimization
		Type, probability and magnitude of benefits
		Comparison of risks and benefits
Independent review	Regulatory compliance	Regulatory compliance
	REC members conflicts of interest	REC members conflicts of interest
	Transparent review	Transparent review
	Minimization and reconciliation of multiple reviews	Minimization and reconciliation multiple reviews
Informed consent	Recruitment & incentives applicability to local context	Recruitment & incentives applicability to local context
	Appropriate disclosure documents and processes	Appropriate disclosure documents and processes
	Presentation and accuracy of information	Presentation and accuracy of information
	Legally authorized representatives	Legally authorized representatives
	Gatekeeper's permission	Gatekeeper’s permission
	Context of consent process	Context of consent process
	Respect for autonomy	Respect for autonomy
	Confidentiality and privacy	Confidentially and privacy

Principle	Proposed Benchmarks	Old Benchmarks
Professional integrity	Participants' competence	Participants' competence
	Researcher competence	Researcher competence
	Research team	Research team
Respect for participants	Monitoring health and well-being	Monitoring health and well-being
	Voluntariness	Voluntariness
	Research results dissemination	Research results dissemination
	Post-research obligations	Post-research obligations

Note: This can be compared to the originally proposed framework in Appendix 1.

In Table 5.1, principle 4 has been removed and its benchmarks distributed where they best fit, such as principle 2 (selection of study population to ensure scientific validity would have been satisfied by specific benchmarks of the study under principle 2). Also, a new principle 7 (professional integrity) has been suggested.

REFERENCES

45 CFR 46. (1991). Federal policy for the protection of human subjects. *Federal Register*, *56*, 28003-28018.

Abbott, L., & Grady, C. (2011). A systematic review of the empirical literature evaluating IRBs: What we know and what we still need to learn. *Journal of Empirical Research on Human Research Ethics*, *6*(1), 3-19.

Amdur, R., & Bankert, A. E. (2011). *Institutional review board: Member handbook* (3rd ed.). Sudbury, Ontario: Jones & Bartlett.

American Academy of Pediatrics. (2004). Policy statement: Ethical considerations in research with socially identifiable populations. *Pediatrics, 113*(1), 148-151.

Association for the Accreditation of Human Research Protection Programs (AAHRPP). (2010). Information for benchmarking now available. *Advance: Enhancing protection for research participants*, *7*(3). Retrieved July 31, 2013 from https://admin.share.aahrpp.org/Website%20Documents/AAHRPP_Advance_2010_Vol_07%20No_03 Summer

Ateudjieu, J., Williams, J., Hirtle, M., Baume, J. I., Niaré, A., & Sprumont, D. (2009). Training needs assessment in research ethics evaluation among research ethics members in three African countries: Cameroon, Mali and Tanzania. Developing World Bioethics, *10*(2), 88-98. doi: 10.1111/j.1471-8847.2009.00266.x

Atkinson, P., Coffey, A., & Delamont, S. (2004). *Key themes in qualitative research: Continuities and changes*. Walnut Creek, CA: Altamira.

Beauchamp, T. L., & Childress, J. F. (2013). *Principles of biomedical ethics* (7th ed.). New York: Oxford University Press.

Beecher, H. K. (1966). Ethics and clinical research. *New England Journal of Medicine*, 274(24), 1354-1360

Belsky, L., & Richardson, H. (2004). Medical researchers' ancillary clinical care responsibilities. *British Medical Journal*, *328*, 1494-1496.

Belmont Report, (1979). Ethical *principles and guidelines for the protection of human subjects of research*. *Retrieved: ori.dhhs.gov/education/products/RCRintro/c03/b3c3.html*

Biggs, J. S. G., & Marchesi, A. (2015). Information for consent: Too long and too hard to read. *Research Ethics*, *11*(3), 1-9. doi: 10.1177/1747016115583381

Blackwood, R. A., Maio, R. F., Mrdjenovich, A. J., VandenBosch, T. M., Gordon, P. S., Shipman, E. L. & Hamilton, T. A. (2015). Analysis of the nature of IRB contingencies required for informed consent document approval. *Accountability in Research*, *22*, 237-245.

Bryman, A. (2008). The end the paradigm wars? In P. Alasuutari, L, Bickman, & J. Brannen, J. (Eds.), *The SAGE handbook of social research methods* (pp. 13-25). London: Sage.

Budin-Ljosne, I. (2012). A review of ethical frameworks for the disclosure of individual research results in population-based genetic and genomic research. *Research Ethics*, *8*, 25-42.

Burke, G. S. (2005). Looking into the Institutional Review Board: Observations from both sides of the table. *Journal of Nutrition*, *135*, 916-917.

Byerly, W. G. (2009). Working with the Institutional Review Board. *American Journal of Health-System Pharmacy*, *66*(2), 176-184.

Carley, J. M. (2006). *Initial ethical review of hexavalent chromium human sensitization study* (Office of Prevention, Pesticides and Toxic Substances). Washington, DC: United States Environmental Protection Agency.

Casell, J. (1980). Red herrings and anecdotes. *Society*, *15*, 32-33.

Chelbowski, R. T. (1984). How many protocols are deferred? One IRB's experience. *IRB: A Review of Human Subjects Research, 6*(5), 9-10.

Cleaton-Jones, P. (2008). Workload of a South African university-based health research ethics committee in 2003 and 2007. *South African Journal of Bioethics & Law*, *1*(2), 38-42.

Coleman, C. H., & Bouesseau, M. C. (2008). How do we know that research ethics committees are really working? The neglected role of outcomes assessment in research ethics review. *BMC Medical Ethics*, *9*(1), 6. doi:10.1186/1472-6939-9-6

Cook, T. D., & Campbell, D. T. (1979). *Quasi-experimentation: Design and analysis issues for field settings*. Boston, MA: Houghton Mifflin Company

Council for International Organizations of Medical Sciences (CIOMS). (2002). *International ethical guidelines for biomedical research involving subjects.* Geneva: Author.

D'Agostino, F. (1995). The ethics of social science research. *Journal of Applied Philosophy*, *12*(1), 65-76.

Davison, R. M. (2000). Professional ethics in information systems: A person perspective. *Communications of the AIS*, *3*(8) 1-34

Department of Health, Education and Welfare (1979). Protection of Human Research Subjects. *Federal Register,* 44(158): 47688-47729, August 14/proposed rules.

Department of Health and Human Services. (2009). *45 CRF 46*, *Subpart E*. Retrieved from http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46

Department of Health and Human Services. (2005). National Institutes of Health and Office for Human Research Protections. *The Common Rule Title 45 (Public Welfare). Code of Federal Regulations, Part 46, (Protection of Human Subjects).* http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm.

Department of Health. (2015). *Ethics in health research: Principles, processes and structures*. Pretoria, South Africa: Author.

Dixon-Woods, M. (2008). What troubles research ethics committees? *Research Ethics*, *Clinical Discovery*, 3(5), 14-15.

Dixon-Woods, M., Angell, E., Ashcroft, R. E., & Bryman, A. (2007). Written work: The social functions of research ethics committee letters. *Social Science & Medicine*, *65*(4), 792-802.

Emanuel, E.J. (2015). Reform of clinical research regulations, finally. *New England Journal of Medicine,* Nov 4th 20-15. Doi: 10.1056/NEJMp1512463

Emanuel, E. J., Abdoler, E., & Stunkel, L. (2006). *Research ethics: How to treat people who participate in research*. Bethesda, MA: National Institutes of Health (NIH).

Emanuel, E. J., Crouch, A. R., Arras, D. A., Moreno, D. J., & Grady, C. (2003). *Ethical and regulatory aspects of clinical research: Readings and commentary*. Baltimore, MA: Johns Hopkins University Press.

Emanuel, E. J., Wendler, D., & Grady, C. (2008). An ethical framework for biomedical research. In E. J. Emanuel, C. Grady, R. A. Crouch, R. K. Lie, F. G. Miller & D. Wendler (Eds.), *The Oxford textbook of clinical research ethics* (pp. 123–133). New York: Oxford University Press.

Emanuel, E. J., Wendler, D., & Grady, C. (2000). What makes clinical research Ethical*? Journal of the American Medical Association, 283*, 2701-2711.

Emanuel, E. J., Wendler, D., Killen, J., & Grady, C. (2004). What makes clinical research in developing countries ethical? The benchmarks of ethical research. *Journal of Infectious Diseases*, *189*(5), 930-937.

Emanuel, E. J., Wood, A., Fleischman, A., Bowen, A., Getz, A. K., Grady, C., Levine, C., Hammerschmidt, D. E., Faden, R., Eckenwiler, L., Muse, C. T., & Sugarman, J. (2004). Oversight of human participants research: Identifying problems to evaluate reform proposals. *Annals of Internal Medicine*, *141*(4), 282-291.

Fakruddin, M., Chowdhury, A., Hossain, M. N., & Mannan, K. S. B. (2012). Ethics in clinical research. *Bangladesh Journal of Bioethics*, *3*(3), 16-20.

Flory, J., & Emanuel, E. (2004). Interventions to improve research participants' understanding in informed consent for research: A systematic review. *Journal of the American Medical Association, 3(3), 16-20.*

Freedman, B. (1987). Scientific value and validity as ethical requirements for research: A proposed explication. IRB: *Ethics & Human Research*, *9*(6), 7-10. doi: 10.2307/3563623

Geisser, M. E., Alschuler, K. N., & Hutchinson, R. (2011). A Delphi study to establish important aspects of ethics review. *Journal of Empirical Research on Human Research Ethics*, *6*(1), 21-24.

Getz, K. A. (2011). Frustration with IRB bureaucracy and despotism: doing more harm than good will ultimately force human subject protection system reform. *Applied Clinical Trials.* http://www.spectroscopyonline.com/spectroscopy/article/articleDetail.jsp?id=703033

Ghana Statistical Service. (2012). 2010 Population and Housing Census*:* Summary reports of final results. *Accra*: Author.

Gray, B. (1989). Collaborating: Finding common ground for multiparty problems. *San Francisco*, CA: Jossey Bass.

Gray, B., & Crooke, R. (1980). The impact of IRBs on research. *Hastings Center Report*, *10*(1), 36-41.

Guenther, K. M. (2009). The politics of names: Rethinking the methodological and ethical significance of naming people, organizations and places. *Qualitative Research, 9*(4), 411-421.

Hammersley, M. (1990). *Reading ethnographic research: A critical guide*. London: Longman.

Forester-Miller, H. & Davis, T. (1996). *A practitioner's Guide to ethical decision making*. Alexandria, VA: American Counselling Association.

Hsieh, H. F. & Shannon, E. S. (2005). Three approaches to qualitative content analysis. *Qualitative Health Research*, *15*(9), 1277-1288. doi: 10.1177/1049732305276687

Hume, D. A. (1987). *A treatise of human nature*. London: Penguin.

Hyder, A. A., Ali, J., Hallez, K., White, T., Sewankambo, N. K., & Kass. N.E. (2015). Exploring institutional research ethics systems: A case study from Uganda. *AJOB Empirical Bioethics*, *6*(3), 1-14.

Hyder, A. A., Merritt, M., Ali, J., Tran, N. T., Subramanian, K., & Akhtar, T. (2008). Integrating ethics, health policy and health systems in low- and middle-income countries: Case studies from Malaysia and Pakistan. *Bulletin of the World Health Organization*, *86*, 606-611.

IJsselmuiden, C. B., Kass, N. E., Sewankambo, K. N., & Lavery, J. V. (2010). Evolving values in ethics and global health research. *Global Public Health*, *5*, 154-163.

Ikingura, J. K. B., Kruger, M., & Zeleke, W. (2007). Health research ethics review and needs of institutional ethics committees in Tanzania. *Tanzania Health Research Bulletin, 9*(3), 154-158.

Illinois White Paper. (2003). Improving the system for protecting human subjects: Counteracting IRB "Mission creep". *Qualitative Inquiry*, *13*(5), 617-649. doi: 10.1177/1077800407300785

Jecker, S. N., Jonsen, R. A., & Pearlman, A.R. (2012). *Bioethics: An introduction to history, method and practices* (3rd ed.). Jones and Bartlett Learning.

Joint United Nations Programme on HIV/AIDS. (2012). *Ethical considerations in biomedical HIV prevention trials*. Geneva: Author.

Jones, J. S., White, L. J., Pool, L. C., & Dougherty, J. M. (1996). Structure and practice of institutional review boards in the United States. *Academic Emergency Medicine*, *3*(8), 804-809.

Jonsen, R. A. (1998). *The birth of bioethics*. New York: Oxford University Press.

Kass, N., Dawson, L., & Loyo-Berrios, N. (2003). Ethical oversight of developing country research: Results of a survey of US investigators. *IRB: Ethics and Human Research*, *25*, 1-10.

Kass, N. E., Hyder, A. A., Ajuwon, A., Appiah-Poku, J., Barsdorf, N., Elsayed, D. E., Mokhachane, M., Mupenda, B., Ndebele, P., Ndossi, G., Sikateyo, B., Tangwa, G., & Tindana, P. (2007).The structure and functional of research ethics committees in Africa: A case study. *PLos Medicine 4*(3), e136.

Kaur, S. (2013). How IRBs make decisions: should we worry if they disagree? *Journal of Medical Ethics, 39*, 230. doi: 10.1136/mediethics-2012-100965

Kirigia, J. M., & Wambebe, C. (2006). Status of national health research systems in ten countries of the WHO African Region. *BMC Health Service Research*, *6*, 135. Doi:10.1186/1472-6963-6-135.

Kirigia, J. M., Wambebe, C., & Baba-Moussa, A. (2005). Status of national research bioethics committees in the WHO African region. *BMC Medical Ethics*, *6*, 10. doi:10.1186/1472-6939-6-10

Lairumbi, G. M., Molyneux, S., Snow, R. W., Marsh, K., Peshu, N., & English, M. (2008). Promoting social value of research in Kenya: Examining the practical aspects of collaborative partnerships using an ethical framework. *Social Science & Medicine*, *67*(5), 734-747.

Lavery, J. V., Grady, C., Wahl, E. R., & Emanuel, E. J. (2007). *Ethical issues in international biomedical research: A Casebook*. Oxford: Oxford University Press.

Levine, R. J. (1988). *Ethics and regulation of clinical research* (2nd ed.). New Haven, CT: Yale University Press.

Lidz, C. W., Appelbaum, P. S., Arnold, R., Candilis, P., Gardner, W., Myers, S., & Simon, S. (2012). How closely do Institutional Review Boards follow the Common Rule? *Association of American Medical Colleges*, *87*(7), 969-974. doi: 10.1097/ACM.0b013e3182575e2e

Lilleyman, J. S. (1995). Informed consent: How informed and consent to what? *Pediatric Hematology and Oncology*, *12*(6), xiii-xvi.

Langlois, A. (2013). *Negotiating bioethics*. Abingdon, UK: Routledge.

Mark, A. (2014). *What is ethical? A presentation of bioethical concerns and cases for clinical research.* Retrieved from http://www.bc.edu/clubs/mendel/ethos/archives/2007/mark.shtml

Marsh, V., Kamuya, D., Rowa, Y., Gikonyo, C., & Molyneux, S. (2008). Beginning community engagement at a busy biomedical research programme: Experience from the KEMRI CGMRC-Wellcome Trust Research Programme, Kilifi, Kenya. *Social Science & Medicine*, *67*(5), 721-733.

Mattingly, C. (2005). Toward a vulnerable ethics of research practice. *Health, 9*(4), 453-472.

Médecins Sans Frontières. (2013). *MSF research ethics framework - guidance document*. Brussels, Belgium: Author.

Milford, C., Wassenaar, D., & Slack, C. (2006). Resources and needs of Research Ethics Committees in Africa: Preparation for HIV vaccine Trials. *IRB Ethics and Human Research*, *28*(2), 1-9.

Miller, F. G., & Brody, H. (2013). A critique of clinical equipoise: Therapeutic misconception in the ethics clinical trials. *Hastings Center Report*, *33*(3), 19-28.

Miller, F. G., & Shorr, A. F. (2002). Ethical assessment of industry-sponsored clinical trials: A case analysis. *Chest Journal*, *121*, 1337-1342.

Morgan, D. L. (1993).Qualitative content analysis: A guide to paths not taken. *Qualitative Health Research*, *3*, 112-121.

Mosteller, F. (1980). Regulation of social research. *Science*, *208*(4409), 1219.

Nandy, B. R., & Sarvela, P. D. (1997). Content analysis re-examined: A relevant research method for health education. *American Journal of Health Behavior*, *21*, 222-234.

Ndebele, P., Wassenaar, D., Benatar, S., Fleischer, T., Kruger, N., Adebamowo, C.,….Meslin, E. (2014). Research ethics capacity building in Sub-Saharan Africa: A review of NIH Fogarty funded programs 2000-2012. *Journal of Empirical Research on Human Research Ethics*, *9*(2), 24-40.

Nicholls, S. G., Hayes, T. P., Brehaut, J. C., McDonald, M., Weijer C., Saginur, R., & Fergusson, D. (2015). A scoping review of empirical research relating to quality and effectiveness of research ethics review. *PLoS One*, *10*(7), e0133639. doi:10.1371/journal.pone.0133639

Nuremberg Military Tribunals. (1949). *Trials of war criminals before the Nuremberg Military Tribunals under Control Council law no. 10*. Washington, DC: US Government Printing Office.

Nyika, A., Kilama, W., Chiliengi, R., Tangwa, G., Tindana, P., Ndebele, P., & Ikingura, J. (2009). Composition, training needs and independence of ethics review committees across Africa: Are the gate-keepers rising to the emerging challenges? *Journal of Medical Ethics*, 35, 189-193. doi:10.1136/jme.2008.625189

Onuoha, C. (2007). *Bioethics across borders: An African perspective* (unpublished doctoral thesis). Uppsala University, Uppsala.

O'Reilly, M., Dixon-Woods, M., Angell, E., Ashcroft, R., & Bryman, A. (2009). Doing accountability: A discourse analysis of research ethics committee letters. *Sociology of Health & Illness*, *31*(2), 246-261.

Piarulli, A. (2012). Forming bioethics. *Momentum*, *1*(1), Art. 16.

Pokorny, S. B., Jason, L. A., Schoeny, M. E., Townsend, S. M., & Curie, C. J. (2001). Do participation rates change when active consent procedures replace passive consent. *Evaluation Review*, *25*(5), 567-580.

Raich, P. C., Plomer, K. D., & Coyne, C. A. (2001). Literacy, comprehension, and informed consent in clinical research. *Cancer Investigation*, *19*(4), 437-445.

Reissman, C.K. (2005). Exporting ethics: A narrative about narrative research in South India. *Health*, 9, 473-490.

Richardson, H. S. (2010). Ancillary-care obligations. *Public Health Ethics*, 3, 63-67.

Silaigwana, B., & Wassenaar, D. (2015). Biomedical research ethics committees in Sub-Saharan Africa: A collective review of their structure, functioning, and outcomes. *Journal of Empirical Research on Human Research Ethics*, *10*, 169-184. doi: 10.1177/155626461557551.

Silverman, D. (2013). *Doing qualitative research*. (4th ed.) New York: Sage.

Singer, P. A., & Benatar, S. R. (2000). Beyond Helsinki: A vision of global health ethics. *British Medical Journal*, *322*, 747-748.

Shaw, D., & Elger, B. S. (2013). The relevance of relevance in research. *Swiss Medical Weekly*, *7*(143), w13792. doi:10.4414/mw.201313792

Sparkes, A. C. (2001). Myth 94: Qualitative health researchers will agree about validity. *Qualitative Health Research*, *11*(4), 538-552.

Terre Blanche, M., Durrheim, K., & Painter, D. (Eds.) (2006). *Research in practice: Applied methods for the social sciences*. Cape Town: University of Cape Town Press.

Tsoka-Gwegweni, J., & Wassenaar, D.R. (2014). Using the Emanuel framework to examine ethical issues raised by a biomedical research ethics committee in South Africa. *Journal of Empirical Research on Human Research Ethics*, *9*(5), 36-45.

UNAIDS Joint United Nations Programme on HIV/AIDS. (2012). *Ethical considerations in biomedical HIV prevention trials*. Geneva, Switzerland: Author.

UNESCO (United Nations Educational, Scientific and Cultural Organization). (2010). *Assisting bioethics committees* (ABC). Retrieved from http://www.unesco.org/new/en/social-and-human-sciences/themes/bioethics/assisting-bioethics-committees/

Union Graduate College & Vilnius University, (2012). *International Research Ethics 1, Week 1: Conceptual and regulatory aspects of human subjects research*. Course notes for the Advanced Certificate Program for Research Ethics in Central and Eastern Europe. New York: Center for Bioethics and Clinical Leadership.

Viera, A. J., & Garrett, J. M. (2005). Understanding inter-observer agreement: The Kappa statistic. *Family Medicine*, 37(5): 360-3.

Wassenaar, D. R. (2006). Commentary: Ethical considerations in international research collaboration: The Bucharest early intervention project. *Infant Mental Health Journal*, *27*, 577-580.

Wassenaar, D. R., & Mamotte, N. (2012). Ethical issues and ethical reviews in social science research. In M. M. Leach, M. J. Stevens, G. Lindsay, A. Ferrero & Y. Korkut (Eds.). *The Oxford handbook of international psychological ethics* (pp. 268-282). Oxford: Oxford University Press.

Weijer, C. (2000). The ethical analysis of risk. *Journal of Law, Medicine & Ethics*, *28*(4), 344-361.

White, T. M. (1999). Guideline for IRB review of International collaborative medical research: A proposal. *Journal of Law, Medicine & Ethics*, *27*, 87-94.

World Bank Ghana Home (2015). Retrieved October 2, 2015 from http://www.worldbank.org/en/country/ghana

World Health Organization. (2015). *Ghana: WHO statistical profile*. Retrieved December 8, 2015 from http://www.who.int/gha/en/

World Health Organization. (2011). Standards and *Operational guidelines for ethical review of health related research with human participants*. Geneva: Author, WHO document production services.

World Health Organisation (2012). Lists of National Ethics Committees. Who.int/ethics/national committees/NEC

World Medical Association. (2008). *Declaration of Helsinki*. Retrieved from http://www.wma.net/e/policy/b3.htm.

APPENDICES

Appendix 1*: *Criteria for identifying particular ethical issues raised by the RECs

The following benchmarks were used to extract the needed information as per the principles provided by Emanuel et al. These criteria were developed from the benchmarks of Emanuel and were re-phrased.

Principles	Benchmarks Old
Collaborative partnership:	Community representatives Responsible sharing (collaboration) Respect for local context (environment) Fair research benefits for community Sharing research products
Social value:	Research beneficiaries Research benefits Enhancing research benefits Impact on health systems
Scientific validity:	Appropriate design and methods Applicability of results Impact on provision of health care services Study design feasibility
Fair selection of study population:	Suitable study population Risk minimization Benefits to participants Vulnerability
Favorable risk-benefit ratio:	Risks identification and minimization Type, probability and magnitude of benefits Comparison of risks and benefits
Independent review:	Regulatory compliance REC members conflict of interest Transparent review Minimization and reconciliation of multiple reviews
Informed consent:	Recruitment & incentives application to local context Appropriate disclosure documents and processes Presentation and accuracy of information Legally authorized representatives Gatekeeper's permission Context of consent process Respect for autonomy

Respect for recruited participants:	Monitoring health and well-being Confidentiality and privacy Voluntariness Research results dissemination Post-research obligations

Appendix 2: Confidentiality Agreements

This information is withheld to maintain confidentiality; available on request.

Appendix 3: *Gatekeeper's Approval*

This information is withheld to maintain confidentiality; available on request.

Appendix 4*: Ethical Approval from CSIR-IRB*

This information is withheld to maintain confidentiality; available on request.

***Appendix 5**: Ethical Approval Final Letter- HSS UKZN*

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

17 December 2014

Ms Pamela Emefa Selormey (213569685)
School of Applied Human Sciences – Psychology
Pietermaritzburg Campus

Protocol reference number: HSS/1450/014CA
Project title: An evaluation of the ethical concerns raised by a Ghanaian Research Ethics Committee (REC), using the Emanuel et al. (2004) principles and benchmarks

Dear Ms Selormey

Full Approval – Expedited

This letter serves to notify you that your application in connection with the above has now been granted full approval.

Any alterations to the approved research protocol i.e. Questionnaire/Interview Schedule, Informed Consent Form, Title of the Project, Location of the Study, Research Approach/Methods must be reviewed and approved through an amendment /modification prior to its implementation. Please quote the above reference number for all queries relating to this study. Please note: Research data should be securely stored in the discipline/department for a period of 5 years.

The ethical clearance certificate is only valid for a period of 3 years from the date of issue. Thereafter Recertification must be applied for on an annual basis.

Best wishes for the successful completion of your research protocol.

Yours faithfully

.....
Dr Shenuka Singh (Chair)

/px

cc Supervisor: Professor Doug Wassenaar
cc Academic Leader Research: Professor D McCracken
cc School Administrator: Mr Sbonelo Duma

Humanities & Social Sciences Research Ethics Committee
Dr Shenuka Singh (Chair)
Westville Campus, Govan Mbeki Building
Postal Address: Private Bag X54001, Durban 4000
Telephone: +27 (0) 31 260 3587/8350/4557 **Facsimile:** +27 (0) 31 260 4609 **Email:** ximbap@ukzn.ac.za / snymanm@ukzn.ac.za / mohunp@ukzn.ac.za
Website: www.ukzn.ac.za