

CHAPTER I

INTRODUCTION AND BACKGROUND

1.1 INTRODUCTION

The ethical review system in South Africa has been in existence for few decades with a small number of research ethics committees in operation. There are 34 health research ethics committees (RECs) operating in South Africa currently (Department of Health, South Africa (DOH), 2004). Research Ethics Committees constitute the first line protection of human participants in health research, while the National Health Research Ethics Council (NHREC) makes up the second line of protection.

Ethical integrity in health research involving human participants is critical to ensure that the rights and safety of participants are protected. To this end, a number of regulations, structures and processes have been put in place. The NHREC established in 2006 in terms of section 72 (1) of the National Health Act No. 61 of 2003 (NHA), has the responsibility to promote, ensure and monitor compliance by research ethics committees with regulations (DOH 2001 and 2007) and guidelines (DOH 2004 and 2006). For this purpose, the NHREC is authorized to register and audit research ethics committees in South Africa (National Health Act (NHA), 2003). On the basis of the NHREC responsibility, this study intends to determine the compliance levels of registered RECs with the Department of Health (DOH) national guidelines on health research ethics.

Health Research Ethics Committees (RECs) play a significant role of protecting potential research participants from risks associated with health research when assessing research protocols. Risks in research studies range from minor injuries to fatality.

RECs are therefore well placed to allow health research to take place and contribute to generalizable knowledge and towards addressing health problems without compromising the safety, respect and justice of potential health research participants. In order to ensure that RECs protect the safety, respects and justice of potential research participants, NHREC requested RECs to register with it. Thus far 22 of the 34 (65%) RECs known to DOH have registered with NHREC. The registered RECs are therefore expected to comply with the national research ethics guidelines published in 2004 by the DOH.

This study is the first to determine the level of compliance with DOH 2004 national guidelines ethics in health research: principles, structures and processes by RECs registered with NHREC. It is also one of the first studies in South Africa to examine RECs composition and internal operating procedures set out by the national guidelines in health research ethics.

In the past, one study looked at 12 RECs in South Africa comparing their operations to international standards (Moodley and Myer, 2007). The other study looked at 3 RECs, which could give a distorted picture because of its

sample size (Strugo, 2007). Therefore the DOH needs a relatively bigger study to determine the level of compliance to its national research ethics guidelines and level of protection to research participants involved in health research studies.

1.2 PROBLEM STATEMENT

The rationale for this study is to fill the gap in research literature on health research ethics committees registered with NHREC and their compliance to the South African (SA) 2004 national guidelines ethics in health research: principles, structures and processes related to composition and operating procedures. This gap has arisen because most studies focus on comparing operations of SA RECs to international standards (Moodley and Myer, 2007).

Some (Moodley and Myer, 2007) affirm that this gap arose from lack of data to document whether RECs in SA are constituted according to the DOH national guidelines. This study therefore provides baseline information on composition and procedures of RECs registered with NHREC and operating procedures to fill the identified gap.

1.3 RESEARCH QUESTIONS

The main research question is whether health research ethics committees (RECs) registered with the NHREC in SA comply with existing DOH national

research ethics guidelines on composition and internal operating procedures. In relation to composition, the question covers membership, population demographics, gender, lay, legal representatives and profession. While operational procedures cover, documentation of meeting deliberations, proposed agenda, distribution of papers prior to meeting, review of research protocols, written response to researchers, documentation to monitor approved research and reporting adverse events.

In particular, there are three questions namely;

- What are levels of compliance of health research ethics committees based at universities and government statutory agencies to national guidelines;
- What are compliance levels of compliance of health research ethics committees based at other institutions except universities and government statutory agencies to national guidelines;
- What are the commonalities between health research ethics committees based at universities and government statutory agencies?

1.4 STUDY OBJECTIVES

The goal of the study is to determine the level of compliance of the health research ethic committees (RECs) registered with NHREC to the DOH 2004 national ethics guidelines in health research: principles, structures and processes. For the purpose of this study compliance with the standard specified

in the DOH ethics guidelines in health research is examined according to the following three categories namely; systematic compliance, non-systematic compliance and non-compliance (Valdez-Martinez, 2005). Systematic compliance occurs when the requirement is followed in conformity to the DOH guidelines and it is documented. Non-systematic compliance occurs when the requirement is carried out in conformity to DOH guidelines in some but not all times. Non-compliance occurs when the requirement was never followed (Valdez-Martinez, 2005). Specifically the objectives are:

- To establish the level of compliance by RECs registered with NHREC to the DOH guidelines on ethics in health research related to composition
- To establish the level of compliance by RECs registered with NHREC to the DOH guidelines on ethics in health research related to their operational procedures.
- To examine commonalities and differences in composition and operating procedures of RECs registered with NHREC.

1.5 JUSTIFICATION FOR THE STUDY

The results of this study could be useful to DOH research policy manager for the review and update of relevant research and ethics policies. It will also

contribute to the planned annual report of NHREC registered REC database. The DOH and NHREC could use these study results to inform evaluation of national guidelines determined for the functioning of RECs and to set national norms and standards for conducting health research on humans as mandated by the National Health Act of 2003. This study will also help to raise the profile of NHREC as required by health research capacity building in Africa (Whitworth, Kokwaro, Kinyanjui, et al, 2008). The NHREC could also use this information as part of the procedures to prepare for the planned REC audit.

The results may also encourage registered RECs to increase their compliance level to the DOH national guidelines. Furthermore unregistered RECs may realize the importance to register with NHREC and compliance to DOH guidelines.

Researchers, health professions and potential research participant may realize from the results of this study, the level of ethical protection they have from registered RECs, NHREC and DOH. Once they understand that increased levels of compliance by RECs to DOH national guidelines could translate to increase their ethical protection in research studies.

CHAPTER II

LITERATURE REVIEW

2.1 INTRODUCTION

This chapter provides a context for the study by discussing selected literature on the functioning of RECs including their composition and operational procedures internationally and particularly in SA. The literature firstly shows the diversity of ethics and what ethics refers to and its importance. It also provides a brief historical background of health research ethics and the different health research ethics oversight systems in developed and developing countries.

2.2 WHAT IS ETHICS

There are many definitions of ethics which include the following: ‘a critical reflection on morality with intent to safeguard human dignity, and promote justice, equity, truth and trust www.sahealthinfo.org/ethics/book1preface.htm). Brasel (2005) defines ethics as “ a set of moral principles or values, the principles of conduct governing an individual or group, or, a guiding philosophy. Some authors described ethics to be in vogue because it cuts across many sectors and areas such as environmental ethics (Hatcher T, 2004), advertising ethics, developmental ethics, ethical tourism, investment ethics and professional ethic (Kessel, 2003) as well as public health ethics (Kass, 2004).

Other authors indicate that ethics is included in human resources programmes (Weaver and Trevino, 2001).

For instance environmental ethics was depicted as “the study of moral relations between human beings and nature and also the value and moral status of the environment” (Hatcher, 2004). From this perspective environmental ethics upholds and focuses on the principle of beneficence. For example in this instance, clean water is valued because of the benefit it brings to human safety and health (Hatcher, 2004).

Regarding ethics in the area of human resources, companies introduced programmes to manage ethical behaviour of their employees (Weaver and Trvino, 2001). In this instance ethics is focused on the principle of distributive justice. For example fairness in allocation of organizational resources such as salaries, performance bonus, discipline ect (Weaver and Trvino, 2001).

The information above highlight principles of ethics namely respect for persons, beneficence and justice. These principles are applicable in different sectors and areas of operation as already indicated. The principles are contained in the 1979 Belmont Report (National Institute of Health, 2004). These principles provide a framework for ethical decision-making in research involving human subjects (National Institute of Health, 2004).

Bioethics in health research is based on the same principles of respect for the person's autonomy, beneficence and justice (Brasel, 2005). The principle of autonomy has a requirement to acknowledge a person's independence and to provide special protection for those with diminished autonomy such as children and mentally disabled (Brasel, 2005). According to the principle of beneficence, the potential treatment must not harm participants and the study must maximize possible benefits for the majority of the community at large (Brasel, 2005). Application of this principle is based on a fine balance between benefits and risks involved in a health research study. The principle of justice necessitates that advantages and success achieved from research study be available for all including those who did not participate in the study (Brasel, 2005). RECs are expected to protect the rights and wellbeing of research participants by applying these principles.

2.3 IMPORTANCE OF RESEARCH ETHICS

Research ethics play an important role of striking the balance between researches intended for contribution to generalizable knowledge and protecting the human dignity of participants. In the absence of research ethics, unethical research takes place including scientific misconduct (<http://www.sahealthinfo.org/ethics/ethicspolicy.htm>). The misconduct used to be wide spread. For example, the 1932 -1947 Tuskegee research study in the United States (US), wherein African-American men were recruited without true informed consent (Brasel, 2005). These men were also misinformed about research taking place

and were denied treatment even after it was available (Brasel, 2005; <http://od.nih.gov/guidelines/GrayBooklet82404.pdf> and National Institute of Health, 2004)

In the SA context, unethical research includes studies such as the Bezwoda study in which a prominent scientist based at university of Witwatersrand conducted a clinical trial assessing the efficacy of chemotherapy in women with metastatic breast cancer. Among others it was later discovered that Dr. Bezwoda did not have signed informed consent documents from study participants and his study proposal were not approved a local REC (Weiss, 2000; Cleaton-Jones, 2000; Horton, 2000).

The above examples indicate types of research risks involved in unethical research studies in the absence of research ethics. It also shows the importance of research ethics in protecting the human dignity and promoting justice for research participants.

2.4 HISTORY OF RESEARCH ETHICS

The history of research ethics dates back just over six decades since the first international ethics document was initiated in 1947. The document is known as the Nuremberg code. It was developed based on the Nuremberg trial where in 22 doctors were tried for conducting unethical research on prisoners without their consent during World War II. In trying to correct the unethical behaviour of

the 22 doctors involved, the Nuremberg code guides researchers to get voluntary consent from prospective participants in research. It also emphasizes on minimizing risks and maximizing benefits in research (Harris, 1992; Cho et al, 2008 and Fletcher and Siegler, 1996).

In 1964 World Medical Association (WMA) launched a medical ethics document known as Ethical Principles for Medical Research Involving Human Subjects (www.wma.net). The document is referred to as the Declaration of Helsinki because it was adopted at Helsinki. Among others it re-affirms the Nuremberg principle of voluntary participation in research studies. The document has been revised several times, most recently in 2008 (www.wma.net; Brasel, 2005).

In 1966 Henry Beecher reported that unethical misconduct is still happening in the conduct of research (Beecher, 1966 and Brasel, 2005). Beecher also reported that violation of ethical principles still take place in research and some violations are committed by prominent researchers (Beecher, 1966 and Brasel, 2005).

In 1982 the Council for International Organizations of Medical Sciences (CIOMS) published a manual known as "Proposed International Ethics Guidelines for Biomedical Research Involving Human Subjects". The aim of the manual was to translate the 1964 Declaration of Helsinki to be used as a guide for World Health Organization (WHO) member countries, particularly developing countries. The CIOMS guidelines have evolved to what is known today as the

2002 International Guidelines for Biomedical Research Involving Human Subjects.

European countries through the European Federation of Pharmaceutical Industries and Associations, US and Japan agreed on standardizing requirements for approval of pharmaceuticals. This agreement resulted in the creation of International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (www.ich.org). The harmonization focused mainly on safety, quality and efficacy. Within the harmonization documents, an important document pertinent to this research study is “The guidelines for Good Clinical Practice (GCP)” published in 1966. Among others the GCP restates the importance of informed consent. It also re-emphasizes research ethics principles in the Declaration of Helsinki. Notably, according to GCP “the rights, safety and wellbeing of clinical trial subjects are the most important consideration and should prevail over interest of science and society (www.ich.org)”.

In the SA perspective the GCP were developed based on the International Conference on Harmonization (ICH) guidelines and were published in 2000 and revised in 2006. However, the SA framework to regulate clinical trials apart from RECs includes the Medicines Control Council (MCC) established through the prescripts of the Medicines and Related Substances Act, 1965 (Act No. 101 of 1965) and the South African Clinical Trials Register (SACTR). All these

international and national historical documents contribute towards the idea of what research ethics is about and its significance.

2.5 INTERNATIONAL PERSPECTIVE ON RESEARCH ETHICS

COMMITTEES (REC)

The review of research protocols by RECs is a foundation of international guidelines on health research with human participants (Coleman and Bouesseau, 2008). For instance, according to the Council for International Organizations of Medical Sciences (CIOMS) all research proposals to conduct research involving human participants must be submitted to at least one independent REC for ethical and scientific review (CIOMS, 2002; and 1991).

The same responsibilities for RECs are echoed in guidelines published by International Conference on Harmonization (ICH), the Council of Europe and United Nations Educational, Scientific and Cultural Organization (UNESCO) (Coleman and Bouesseau, 2008). According to these guidelines RECs are expected to ensure that risks of proposed studies in relation to anticipated benefits are reasonable, researchers meet their obligations when obtaining informed consent, ethical matters like confidentiality of participants are sufficiently addressed (Coleman and Bouesseau, 2008).

The above-mentioned international guidelines become mandatory through national laws and policies (Coleman and Bouesseau, 2008) after being adopted by countries. For example many developed countries like the United States (Coleman and Bouesseau, 2008) United Kingdom and Australia (Langlosi, 2008) have made REC review mandatory for research involving human participants. Conversely, the scenario in developing countries is such that there are no laws requiring REC oversight, or existing laws are incomplete or under-enforced (Caniza, 2008) and (Hyder, 2004).

However, it is beginning to emerge in literature that developing countries have started developing or strengthening RECs through legislation and policy. For example Kenya has adopted national guidelines referred to as “Guidelines for Ethical Conduct of Biomedical Research Involving Human Subjects in Kenya” (Langlosi, A 2008). While South Africa through the Department of Health and in collaboration with relevant stakeholders developed “Ethics in Health Research: Principles, Structures and Processes” (Langlosi A, 2008).

2.6 RESEARCH ETHICS COMMITTEES (REC) IN SOUTH AFRICA

In a SA perspective, research without informed consent is disallowed (NHA, 2003 and Slack, Strode, Fleischer, Gray, and Randchod, 2007). Research ethics committee (RECs) are charged with the responsibility to ensure protection of rights, safety and well-being of human participants involved in research studies (DoH, 2006). Unlike in some developing countries where

RECs might not promote high standards of protecting research participants due to lack of financial and adequately trained human resources (Moodley & Myer, 2007), the SA perspective is backed by the legislative framework. This legislative framework entails the national health research system, National Health Act No. 61 of 2003, Health Research Policy in SA published in 2001, Regulations related to human subjects in health research publicized in 2007, Regulations related to establishment of National Health Research Ethics Council and national guidelines in good clinical practice of 2006 as well as those related to ethics in health research of 2004.

Following the principle of international law to provide special legal protection to protect a person as early as childhood (<http://www.un.org/oversight/rights.html>), SA like other countries has developed special laws to protect vulnerable populations (Slack, et al, 2007). For instance, the SA Sexual Offence Act has particularly protected children from being involved in sexual act at the age of 16 and prostitution (Department of Social Development and http://ci.org.za/depts/ci/plr/pdf/bills/_chuldrensAct38-2005pdf). The same law also compels any person to identify children needing care and protection to refer them to a social worker (Slack, et al, 2007). Based on these, some argue that researchers and any person involved in health research is legally obliged to report abuse or ill-treatment disclosed by an adolescent in a research study (Slack, et al, 2007).

This array of legislative tools form part of the World Health Organization (WHO) Regional Committee for Africa resolution passed in 1998 which urged member states to develop national research policies and strategies and build national health research capacities and establish research coordination mechanisms (Kirigia and Wambebe, 2006). RECs in other less developed countries are challenged by the environment where they are expected to execute their functions in the absence of well-developed regulatory structures or a culture which lacks compliance to procedural requirements (Coleman and Bouesseau, 2008).

2.7 EXISTING OVERSIGHT MECHANISMS FOR RECS

Research regulation in developed countries has become complex, bureaucratic and expensive (Noor, 2009). This approach is reported to place a huge burden on researchers related to compliance, documentation and training (Noor, 2009). Conversely, RECs in Africa operate on weak health systems and wide spread social disparities. Most African countries are now reported to have at least some form of ethical review process in place (Noor, 2009). These processes are however challenged by limited resources including human and finance, insufficient training, and inadequate standard operating procedures (Noor, 2009; Kirigia et al, 2005; Effa, Massougbojji, and Ntouil, 2007; and Kilama et al, 2007).

2.7.1 Systems in developed countries

The responsibility of oversight in many countries lies with national government agencies (Coleman and Bouesseau, 2008). For instance there are several role players in the United States (US) oversight and review system. In this case the oversight regulatory framework is based on the code of Federal Regulations Title 45, Part 46 (45CFR46) and (Fischer, 2006). The Food and Drug Administration and the Office for Human Research Protections (OHRP) are responsible to oversee Institutional Review Boards (IRBs, equivalents of RECs elsewhere (Fischer, 2006) and (Straight, 2009). OHRP is mandated to monitor and promote compliance with Federal Regulations 45 CFR 46 promulgated by the US Department of Health and Human Service (DHHS) which relates to research ethics standards. OHRP monitors compliance through establishing assurance or contract with institutions involved in research funded by or subjected to DHHS regulations (DHHS and OHRP, 2004).

According to Fischer, 2006 among others US oversight expects IRBs to comply with the following composition requirements: every IRB

- Must have a minimum of 5 members.
- Must have men and women
- Should represent different races, cultural backgrounds and “community attitudes”
- Must have written procedures for scheduling initial reviews of research projects for the frequency of monitoring ongoing projects

and for researchers to report newly determined risks or harms not originally reviewed by the board.

- Must have at least one member who is independent of the institution, one chiefly concerned with science, one chiefly concerned with areas other than science.

Unlike the FDA which at regular intervals (every four years) plans and audit IRBs conducting drug related (clinical trials). “The OHRP does not routinely evaluate or audit institutional IRBs” (Straight, 2009).

The Central Office for Research Ethics Committees (COREC) oversees RECs in United Kingdom (UK) (Rustam, 2005) and (DOH London, 2001). The National Research Ethics Service is responsible for accreditation of RECs. While the United Kingdom Ethics Committee Authority (UKECA) is responsible for regulation (recognition) of RECs reviewing clinical trials of investigational medicinal products (CTIMPs), in accordance with The Medicines for Human Use (Clinical Trials) Regulations of 2004, for the class of research and geographical area indicated (Ashcroft, 2005) and (<http://www.nres.npsa.nhs.uk/aboutus/what-are-recs/>).

Recognition by the UKECA distinguishes between three types of RECs namely, type 1 RECs which are recognised for review of phase I Clinical Trials of Investigational Medicinal Products (CTIMPs) in healthy volunteers only. Some

type 1 RECs are independent ethics committees. Type 2 RECs are recognised for review of Clinical Trials of Investigational Medicinal Products (other than phase I trials in healthy volunteers) taking place within a single domain. While type 3 RECs are recognised for review of Clinical Trials of Investigational Medicinal Products (other than phase I trials in healthy volunteers) and all other research taking place in more than one domain anywhere in the UK (<http://www.nres.npsa.nhs.uk/aboutus/what-are-recs/>).

2.7.2 Systems in less developed countries

Noor 2006, and other authors mentioned that the 2006/2007 World Health Organization (WHO) report on status to provide oversight to vaccine research in Africa shows that only SA Regulatory Authority (RA) was found to have the capacity to adequately regulate vaccines. Six other countries including Nigeria, Senegal, Morocco, Tunisia, Algeria, and Zimbabwe had functional national RAs which needed strengthening. Other countries like Ghana, Egypt, Uganda and Ethiopia had the potential to quickly become functional. While the remaining countries had limited or weak RAs or no information was available (Kirigia and Wambebe, 2006; Chima, 2006 and Noor, 2009).

Unlike in the US, IRBs in Mexico are referred to as Local Committees of Medical Research or Local Research Ethics Committees (LREC) (Valdez-Martinez, et al, 2005). The Mexican system to regulate LRECs is based on the General Law of Health of 1984 and the Regulations regarding health research

of 1987 (Valdez-Martinez, et al, 2005). Mexican Institute of Social Security (IMSS) is responsible for the regulation of LRECs except for those based at health government institutions which are still in the process of being formally structured. Like the FDA in the US, the National Commission for Scientific Research (NCSR) in Mexico among others is mandated to approve drug related research studies (Valdez-Martinez, et al, 2005).

Like other developing countries, no study was ever done in Mexico to evaluate the IMSS LREC regulation system prior to 2001 (Valdez-Martinez, et al, 2005). Other authors are of the opinion that little or nothing is done to evaluate RECs (Coleman & Bousesseau, 2008).

The equivalent of DHHS, OHRP and FDA in SA is the Department of Health (DOH), National Health Research Ethics Council (NHREC) and Medicines Control Council (MCC) respectively. The National Health Research Ethics Council (NHREC) is mandated to execute the oversight role (NHA, 2003; Slack, 2007).

The NHREC functions on the basis of section 72 (6) of the National Health Act No. 61 of 2003. The NHREC is in the process of establishing an REC registration process which is equivalent to an assurance system in the US. Unlike the OHRP, the NHREC plans to regularly audit RECs every 3-5 years. The first of these planned audits will take place during 2010. However, in order

for the audits to enhance the work of RECs, they (audits) should be carefully designed, constructed and implemented (Valdez-Martinez, et al, 2005).

2.8 EVALUATION OF RESEARCH ETHICS COMMITTEES

In the US many role players evaluated strengths and weaknesses of systems in place to protect research participants (Fischer, 2006). However, little data published are available on effectiveness of Institutional Review Boards (Straight, 2009). For example one of the first studies in Croatia was in 2006 which aimed to explore the structure and function of ethics committees in healthcare institutions excluding pharmacies and homecare institutions (Borovecki, et al, 2006). Regulation of healthcare institution in Croatia is based on the Law on the Health Protection (Borovecki, et al, 2006). Borovecki et al study found that 46% of healthcare institutions in Croatia have ethics committees (ECs); 89% of ECs have 5 members, 3 of whom are from the medical professions and 2 of whom are from other fields; 49% of the committees mentioned that their main duty is to analyse research protocols; only a small number of EC sent in standard orders (SOPs), working guidelines or other documents that are connected with their work (Borovecki, et al, 2006).

The study concluded that there is a need to separate between the networks of healthcare institutions EC and IRBs; that “although there are legal provisions for ECs in the healthcare institutions in Croatia, there is evidence of discrepancies between practice and the Law on the Health Protection” (Borovecki, et al,

2006). Additional conclusions are that compared to other countries the development of EC in Croatia has some similarities with other transitional societies in Europe and additional research work should be undertaken in relation to the work of ECs (Borovecki, et al, 2006).

In 1992 a research study in Japan found that composition of Ethics Committees (ECs) based at medical schools was inappropriate such that few women participated and review processes were limited to medical schools (Saito, 1992).

In 2002, an eight-year follow-up study in Japan was undertaken to describe the characteristics and developments of ethics committees (ECs) established at medical schools (n=1457) and general hospitals with 300 beds (n= 1491). It was a follow-up study to the 1992 study which aimed to describe the composition and function of ECs in Japan. In particular, the 2002 study described the committee structure, frequency of annual meetings, committee functions.

Compared to the 1992 findings, the study found that ECs structure was overall interdisciplinary; frequency of annual meetings increased significantly between the two types of ECs; primary focus of ECs was to review protocols and policy development. The study concluded that there is a greater recognized degree of responsibility. Lastly, like Croatian ECs in Japan experienced increased workload indicating the need for more access to ECs (Akahayashi, Slingsby, Nagao, Sato, 2007).

In Latin America 20 RECs were examined and 45% had standard operating procedures, while members had limited research ethics training (Rustam, 2005). On the other hand, Cocker examined RECs in central and Eastern Europe and only 10 countries had national committees (Kass, Adnan, Ademola, 2004 and 2007).

Like in the 2002 Japanese study and 2006 Croatian study, in Israel, a study of hospital based ethics committees (ECs) was conducted, focusing on the structure, function and heterogeneity (Wenger, Molan, Shalev, and Glick, 2002) and (Ministry of Health in Israel, 1996). Notably the ECs are regulated through the Patients' Rights Act of 1996 (Wenger, et al, 2002). The study found that 33% of general hospitals have ECs and concentrated in large facilities; Hospitals without ECs tended to lack structures to handle ethics related issues; Committees tended to be interdisciplinary and gender mix; 33% of ECs never had a meeting; Some ECs attempted to solve cases while some refused to do so. The study concluded that there is lack of access to ECs; there is also an indication of discrepancies between practice and Patients' Rights Act Regulations (Wenger, et al, 2002).

This indicates the need for more studies to examine RECs in developing countries. Research examining RECs in developing countries should among others focus on procedures, strengths and challenges (Moodley & Myer, 2007). The world of Local Research Ethics Committees (LRECs) is under researched

Valdez-Martinez, et al (2005). Most of the current publications on this matter come from developed countries. While very little come from middle and less developed countries (Valdez-Martinez, et al, 2005).

For instance, in Mexico no study was ever done to evaluate the Mexican Institute of Social Security (IMSS) LREC regulation system prior to 2001 (Valdez-Martinez, et al, 2004; Valdez-Martinez, et al, 2005). In 2001 the first study was conducted to identify problems in the IMSS LRECs. Three hundred thirty-five (335) local research ethics committees took part in the national postal survey Valdez-Martinez, et al, 2004) & (Valdez-Martinez, et al, 2005). The study results were as follows:

- Most LRECs were operational for at least 10 years.
- LREC Composition
 - LREC membership was dominated by men and physicians
 - Lay persons were absent from LREC deliberations.

The second study was conducted in 2002. It took a qualitative approach to look at how LRECs perceived research ethics (Valdez-Martinez, et al, 2005). Eleven focus groups were conducted for this study and the results were as follows:

- LRECs emphasised rules and regulations rather than research ethics
- LRECS considered that the law provided a powerful tool through which to determine whether a decision was right or wrong.

Lastly, the third study was conducted which took an approach of LREC auditing where in 60 LRECs were audited (Valdez-Martinez, et al, 2005). The aim of the study was "to determine to what extent the LRECs performance conform to the standards of the IMSS regulation handbook; by showing frequency of conformity to the following:

- (i) the assessment of proposed research projects and
- (ii) continuing review of research previously authorised.

Compliance to the standard of the IMSS handbook was evaluated according to three categories namely; systematic compliance, non-systematic compliance and non-compliance. Systematic compliance occurred when the procedure was followed in conformity to the handbook and it was documented. Non-systematic compliance occurred when the procedure was carried out in conformity to the handbook in some but not at all times during the period subject to review. Non-compliance occurred when the procedure was never done during the period subject to review (Valdez-Martinez, et al, 2005).

The study results were as follows:

- Research Projects Assessment Process
 - In 60% (54/60) of LRECs executive directors reviewed submitted research protocols as required by the handbook.
 - In 10% (6/60) of the remaining LRECs research proposals were reviewed by committee secretaries research protocols received were of descriptive studies.

- In 38% (38/60) of LRECs reviewers did not issue a written report with the results of their evaluation.
 - Seventy-two percent (43/60) LRECs convened plenary meetings.
 - In 88% (38/43) of LRECs that held meetings the chairperson never presided over the plenary committee.
 - In 63% (27/43) LRECs the meeting was held in the presence of the principal researcher of the project; although they did not evaluate their own projects. This practice was generally followed in committees that had staff in training.
- Continuing Review Process
 - In 85% (51/60) of LRECs follow-up of research they had approved was confined to the six-monthly collection of verbal or written reports about progress of research from principal investigators.
 - In the remaining 15% (9/60) of LRECs follow-up was never conducted.
 - Overall Assessment per type of Compliance
 - Seventy percent (42/60) of LRECs displayed systematic compliance with the procedures of allocation of reviewers to research projects. While 20% (12/60) complied in a non-systematic manner.
 - Seventy-two percent (43/60) of LRECs held meetings for assessing research protocols submitted but only 38% (23/60)

carried out this process in a systematic manner and 33% (20/60) made it in a non-systematic manner.

- Even though 85% of (51/60) LRECs carried out a six-monthly follow-up of research they had approved, only 10% (6/60) committees showed a systematic compliance; and 75% (45/60) committees followed a non-systematic approach.

Apart from studies in Mexico, another study by Moodley and Myer (2007) similar to the ones described above was conducted in South Africa. This particular study aimed to investigate the composition, operations and training needs of health RECs in South Africa against the backdrop of national and international guidelines (Moodley and Myer, 2007). Twelve health RECs in South Africa were surveyed and the results were as follows:

- Composition of RECs
 - Ten of the 12 committees had been in operation for at least 10 years, with the oldest established more than 30 years previously. The other 2 committees were a year old at the time of the survey.
 - On average each REC had 16 members. REC membership ranged from 7 – 29.
 - REC members were predominantly male with a range of 46% to 82%.

- Representation of women members in committees ranged from 18% to 54%. In 83% of RECs, less than half the members were female
- Majority of members in the committees were white.
- Majority of members (56%) were scientists or clinicians who were affiliated to the same institution as the health REC.
- Eight percent (8%) of REC members were community representatives. However, the community representative did not come from the communities being research as per definition of the national guidelines on research ethics.
- Training Needs
 - Training needs for health REC members varied widely.
 - Of the 12 RECs surveyed, 17% had all their members trained in research ethics. At other committees none of the members had been trained at the time of the interview.
 - Most of the training had been attendance of Good Clinical Practice workshops.
 - Some RECs provide in-house training, time permitting, at meetings.
 - Others circulate articles on Research Ethics to members.
- Efficiency of RECs

- Total number of protocols reviewed by the 12 RECs in 2002 was estimated at 1600. Protocols reviewed per REC averaged at 133 with a range of 30 – 360.
- The average number of protocols reviewed per meeting varied from 4 to 30.
- The average time from protocol submission to response was five weeks with a range from ten days to ten weeks.

The research studies in Mexico indicated a strengthened structure of LRECs with 70% compliance level to the Mexican Institute Social Security (IMSS) regulation (Valdez-Martinez, et al, 2005). They (studies) also highlighted problems in the understanding and work of LRECs managed by IMSS. On the other hand the SA study demonstrated inadequacy of diversity of REC membership and the variability in operations, infrastructure and training needs amongst the various RECs (Moodley and Myer, 2007).

The commentary above indicates some similarities between the Mexican studies and the South African study. Similarities relate to composition of RECs and procedures followed when RECs execute their functions in relations to the regulatory requirements. Differences relate to diverse research methodologies used by the studies which make it a bit difficult to make direct comparison between the studies.

This study focuses mainly on compliance by RECs to the requirements of national regulatory authorities. During analysis comparison with the Mexican studies by Valdez- Martinez, et al (2004 and 2005) and the South African study by Moodley and Myer (2007) will be indicated. The researcher focuses on describing the findings on registered RECs in SA. SA is yet to audit RECs registered with NHREC.

2.9 COMPOSITION OF RESEARCH ETHICS COMMITTEES IN SOUTH AFRICA (SA)

Literature examining nine countries in the African region including SA shows that 36% did not have RECs (Kass, et al, 2004 and 2007) and (Benatar, 2007). This led to the question that who protects the rights of research participants in those countries. Of those remaining, the REC membership ranged from 9 to 31 (Kass, et al, 2004). In SA, it is recommended that RECs should have at least 9 members (DOH, 2006). Collectively they should have qualifications and experience to review and evaluate the science, medical aspects and ethics of the proposed research study.

National guidelines recommend that composition of REC in SA should meet the following minimum requirements: have at least nine members with 60% representing a quorum; be representative of the community they serve and reflect the demographic profile of the population of South Africa; include members of both genders, and not more than 70% of its members must be men

or women; must have a chairperson; include at least two lay persons who have no affiliation to the institution, are not currently involved in medical, scientific or legal work and are preferable from the community in which research is taking place; include at least one member with knowledge of, and current experience in areas of research that are likely to be regularly considered by the REC; include at least one member with knowledge of, and current experience in the professional care, counselling or treatment of people for example medical practitioner, psychologist, social worker or nurse; include at least one member who has professional training in both qualitative and quantitative research methodologies; include at least one member who is legally trained (DOH, 2004).

2.10 RESEARCH ETHICS COMMITTEES OPERATING PROCEDURES IN SOUTH AFRICA (SA)

Some REC procedures in SA are in line with the international standards. For example the Declaration of Helsinki; International Guidelines for Ethical Review of Epidemiological Studies; Council for International Organisations of Medical Sciences (CIOMS, 1991) and World Health Organization, 2000) Operational Guidelines for Ethics Committees that Reviewed biomedical Research, to mention a few. RECs are required to meet the following minimum requirements outlined by national guidelines related to operating procedures: frequency of meetings; preparation of agenda and minutes; presentation of protocols; presentation of all documents and other materials used to inform potential

research participants; timely review and notification of decisions to researchers; recording in writing decisions made by the REC and reasons for the decisions; confidentiality of the content of the protocols and REC's proceedings (DOH, 2004).

The goal of this study is to determine the level of compliance of RECs registered with NHREC to the DOH national guidelines. The study will focus mainly on REC composition and operating procedures.

CHAPTER III

METHODOLOGY

3.1 INTRODUCTION

In this section we introduce how research was conducted. The study examines the levels of compliance by RECs registered with NHREC to the requirements of the 2004 national guidelines ethics in health research: principles, structures and processes. Compliance level with the standard specified in the DOH guidelines ethics in research is examined according to the following three categories namely; systematic compliance, non-systematic compliance and non-compliance. The examination focuses particularly on the REC composition and operational procedures as indicated in Chapter 1 (Section 1.1). The study also identifies common elements and differences in the RECs internal procedures.

RECs are expected to be independent, multi-disciplinary and multi-sectoral. Regarding REC composition, the study examines compliance to the following requirements, that REC: Is representative of the community it serves and reflects the demographic profile of SA; Includes both genders with not more than 70% for either male or female; Has at least 09 members; Has at least 02 lay persons who have no affiliation to the institution and are not currently involved in medical, scientific or legal work; At least one members has

knowledge of and current experience in areas of research likely to be considered by REC; Representative with knowledge and current experience in professional care or treatment of people (e.g. nurse or social worker); At least one members with training in both qualitative and quantitative research methodologies; Includes at least one member with legal training, as mentioned in Chapter 2 (section 2.9).

On the other hand the study examines the level of compliance to operational procedures as required by the SA national guidelines ethics in health research outlined below:

Frequency of meetings; preparations of agenda and minutes; distribution of documents prior to meetings; consideration and review of research protocols; methods of decision making; prompt notification of decisions; reporting of adverse events and monitoring safety.

3.2 STUDY DESIGN

The study uses secondary data form the National Health Research Ethics Council (NHREC) database. The data comes from the completed questionnaires of RECs registered with the NHREC. The study uses quantitative research methods to retrospectively review the NHREC database of registered RECs for the period 2008 to 2009. For this reason, unregistered

RECs are excluded in the study since they did not complete questionnaire as requested by NHREC.

3.3 STUDY POPULATION AND SAMPLING PROCEDURE

The target population is RECs registered with NHREC between 2008 and 2009. During this period 22/34 (65%) RECs responded positively to the call by NHREC and registered. They have since been allocated unique identity numbers which is used in this study to uphold the principle of confidentiality.

All RECs registered with NHREC are included in the study. While unregistered RECs are excluded in the study because they did not complete the questionnaires which could have been captured into the NHREC database. This study analysis data for all 22 RECs registered with NHREC.

3.4 DATA COLLECTION

For the purpose of this study, secondary data is used for analysis. In this study secondary data refers to completed questionnaire submitted by RECs to NHREC during registration. Completed questionnaires were captured into NHREC database from July 2009 – August 2009. DOH is the custodian of the registered REC database. The researcher is the DOH employee and serves as secretariat to the NHREC. He is also responsible for the management of this

database. Hence the data will be retrieved by the researcher from NHREC database.

The database has information on 22 RECs registered with NHREC. It broadly covers information on REC composition and procedures. After completion of the first phase of REC registration in August 2009, data was captured into the database in September 2009. The researcher retrieved REC information relevant to his study from the NHREC database in January 2010. The data was coded within 01 week.

3.5 STUDY LIMITATIONS

The study is constrained by the data source mainly the NHREC database. Because of its secondary nature, the data is limited to the framework within which it is assembled. For example variables in analysis are predetermined.

This implies that the researcher has had to adapt the concepts and definitions as provided by the NHREC database and questionnaire. Among others the questionnaire is limited to only 8 of 20 REC operational procedures required by the 2004 South African national guidelines ethics in health research: principles, structures and processes. Finally this study is only limited to RECs registered with the NHREC. The indicated limitations have been unavoidably incorporated into the study.

3.6 DATA ANALYSES

Data master sheets have been developed to cater for all variables of interest. This study uses secondary data for analysis. The secondary data utilizes the dataset of RECs registered with the NHREC between 2008 and 2009.

Data was analysed using Statistical Package for Social Scientists (SPSS) version 17. Data was summarized as follows; frequency tables and multiple bar graphs was used to summarize REC information on composition and internal operating procedures as already indicated in Chapters 1 (section 1.1) and 2 (sections 2.5 – 2.6).

3.7 ETHICAL CONSIDERATIONS

The researcher sought permission and ethical clearance from the Medunsa Research Ethics Committee (MREC) of the University of Limpopo Medunsa Campus. The researcher was granted permission in writing by the Director of Health Research Directorate, National Department of Health to access NHREC database of registered RECs which completed the questionnaires for registration. Confidentiality and integrity of RECs is observed by using unique identification numbers instead of names indicated on the data collection form.

CHAPTER IV

PRESENTATION OF RESULTS

4.1 INTRODUCTION

This chapter provides an analysis of data on 22 RECs registered with NHREC as required by the National Health Act. Once again, the main objective is to establish the level of compliance by registered RECs to the DOH national guidelines of health research ethics. The objectives of the study are: to establish the level of compliance by RECs registered with NHREC to the DOH guidelines on ethics in health research related to their composition; to establish the level of compliance by RECs registered with NHREC to the DOH guidelines on ethics in health research related to their operational procedures.; and lastly, to examine commonalities and differences in composition and operating procedures of RECs registered with NHREC.

For the purpose of this study compliance with the standard specified in the DOH ethics guidelines in research is examined according to the following three categories namely; systematic compliance, non-systematic compliance and non-compliance. The analysis will follow the order of the research questions as presented in chapter 1 (section 1.3). The questions are as follows: what are levels of compliance of RECs based at universities and government statutory agencies to national guidelines; what are compliance levels of research ethics

committees based at other institutions except universities and government statutory agencies to national guidelines; what are the commonalities between RECs based at universities and government statutory agencies?

Generally, the analysis firstly focuses on compliance to DOH guidelines related to composition and procedures. In particular types and levels of RECs are associated to composition and procedures to determine compliance levels. Data are processed using SPSS. The analysis takes the form of frequency tables and cross tabulations. The results are presented by charts and tables.

4.2 COMPOSITION OF RECS

Table 1. REC Membership

Composition	Min	Max	Sum	Mean
No. Members	6	35	345	16.41
Males	3	19	187	8.50
Females	2	16	158	7.45
REC_Chair_P	1	1	22	1.00
Prof_Scient	0	30	237	10.77
Prof_Non_Scient	1	23	114	5.45
Lay-Rep	0	3	30	1.36
Leg-Rep	0	3	23	1.05

According to Table 1 and figure 1, all RECs had a chairperson, men and women, and members from other professional fields than science. The total number of members of the 22 RECs registered with the National Health

Research Ethics Council was estimated at 345, with an average of 16 members per REC. REC membership ranged from 6 – 35.

REC members in SA were male dominated with a range of 3 -19 and averaged at 09 men per REC. Fifty-three percent of REC members were men while 47% were women with a slight percentage difference (6%). The percentage difference on gender of REC membership is viewed to be minimal considering the requirement of not more than 70% of either male or female by the DOH guidelines. This result was not expected.

About 5% (1/22) of RECs did not have a scientific or clinician professional. Majority (68%) of REC members were scientists or clinicians who were affiliated to the same institution as the health REC. Non-scientists or non-clinicians members constituted about 33%. Eighty two percent (18/22) of RECs have lay persons as members while 18% (4/22) did not comply with this composition requirement. Seventy seven percent of RECs (17/22) had legal representative while 23% (5/22) did not comply with the requirement.

Figure 2 indicates that 63% of RECs registered with NHREC are based at universities and government statutory agencies. A further breakdown shows that 54% of RECs are classified as operating within university structure. The 63% RECs are expected to have high compliance to the DOH guidelines and have more commonalities because of their access to both to resources financial and human resources as well as post graduate training programmes at

universities which include research ethics. While only 19% of RECs operate either from a public hospital or government department. These RECs are expected to have more diverse approaches because of their categories and challenges of limited resources.

According to Figure 3 most (83%) RECs applied to be registered as level 2 RECs. Of the 83%, eleven percent is from public hospitals, 28% public universities, 33% private universities, 11% government statutory institutions, 6% private non-profit institutions and 11% private for-profit institutions. Level 1 RECs are those deemed to “have capacity to assess straightforward research designs that involve minimal risk to human participants. They include health research proposals that do not involve drug research, biomedical research involving human tissues, high-budget research (more than R 250 000 per annum), and high technology research” (DOH, 2004). While level 2 RECs refer to those “may review all types of health research proposals” (DOH, 2004).

Similarly to Figure 2, majority of RECs (68%) operate from under organizations such as universities, government statutory agencies and private for profit institutions. Because of the efficiency of the institutions, RECs operating from these organizations experience high workload of reviewing protocols compared to the other types. That is 54% of RECs based at universities reviewed 85% of the all research protocols for a twelve months period.

The reverse, that most 14% of level 1 RECs are based at public hospitals and government department and private non-profit organizations should also be expected. There is a huge (66%) percentage difference between types of REC stratified by level 1 and 2.

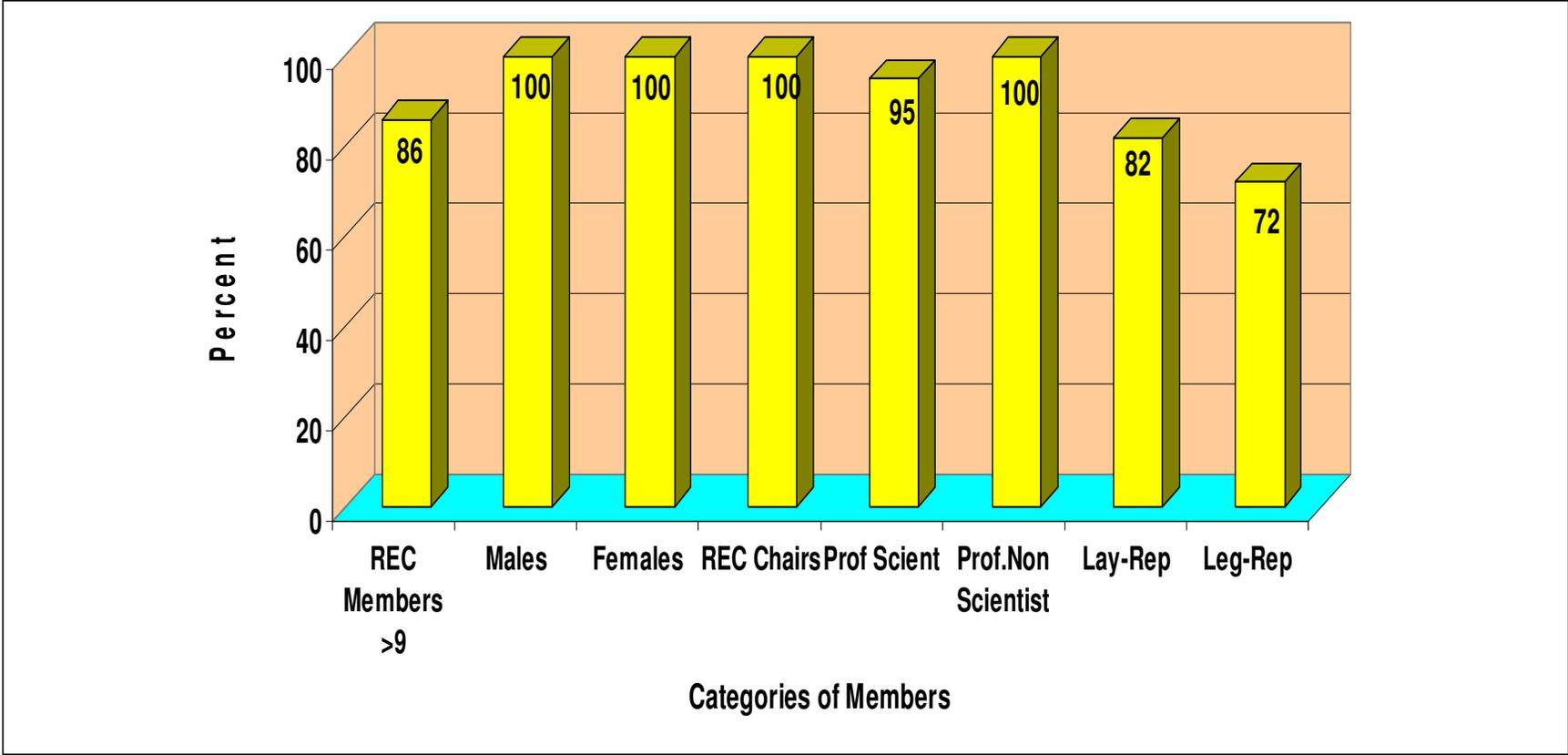


Figure 1. Percentage of Composition of REC Members by categories.

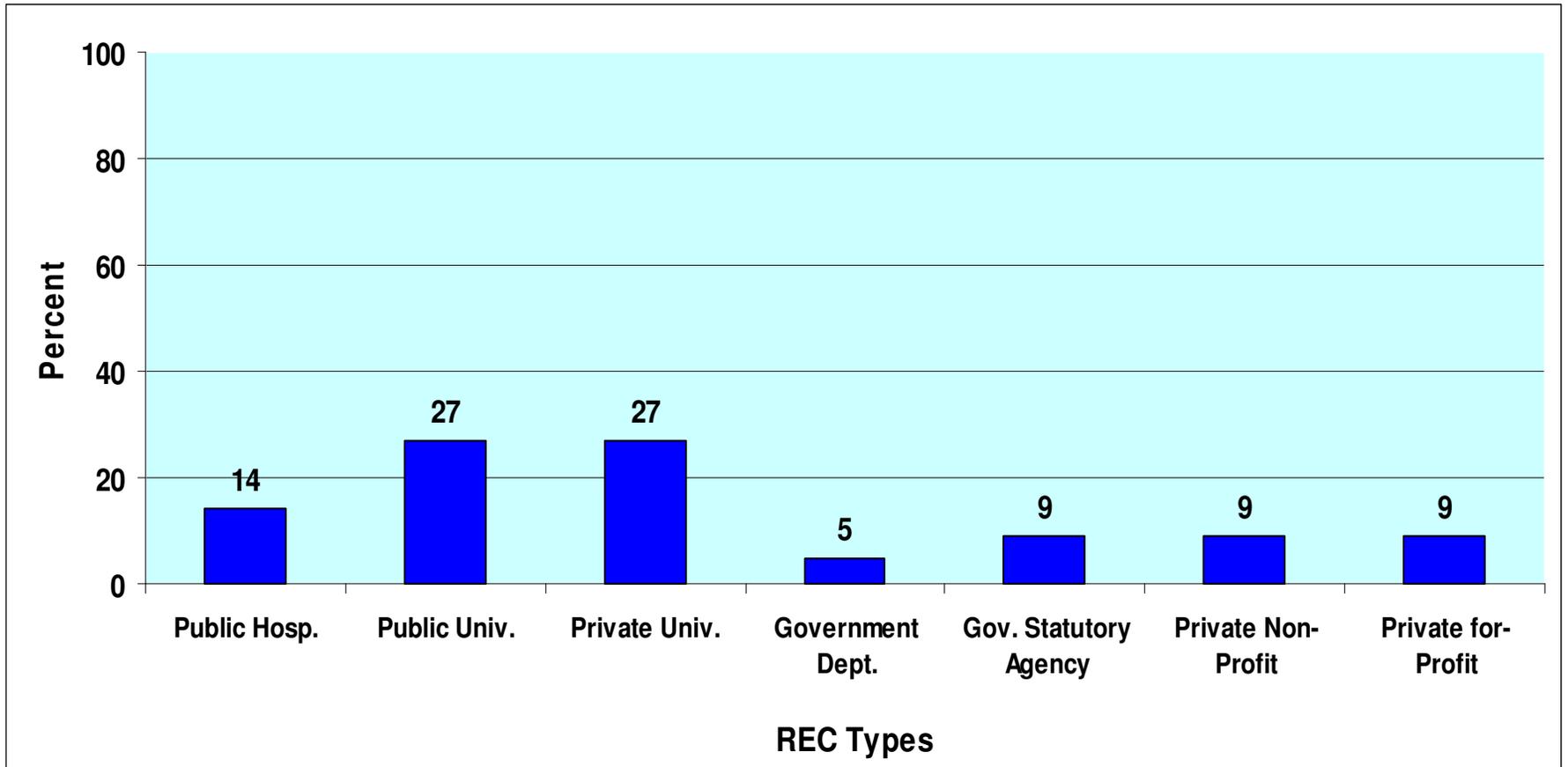


Figure 2: Percentages of REC types.

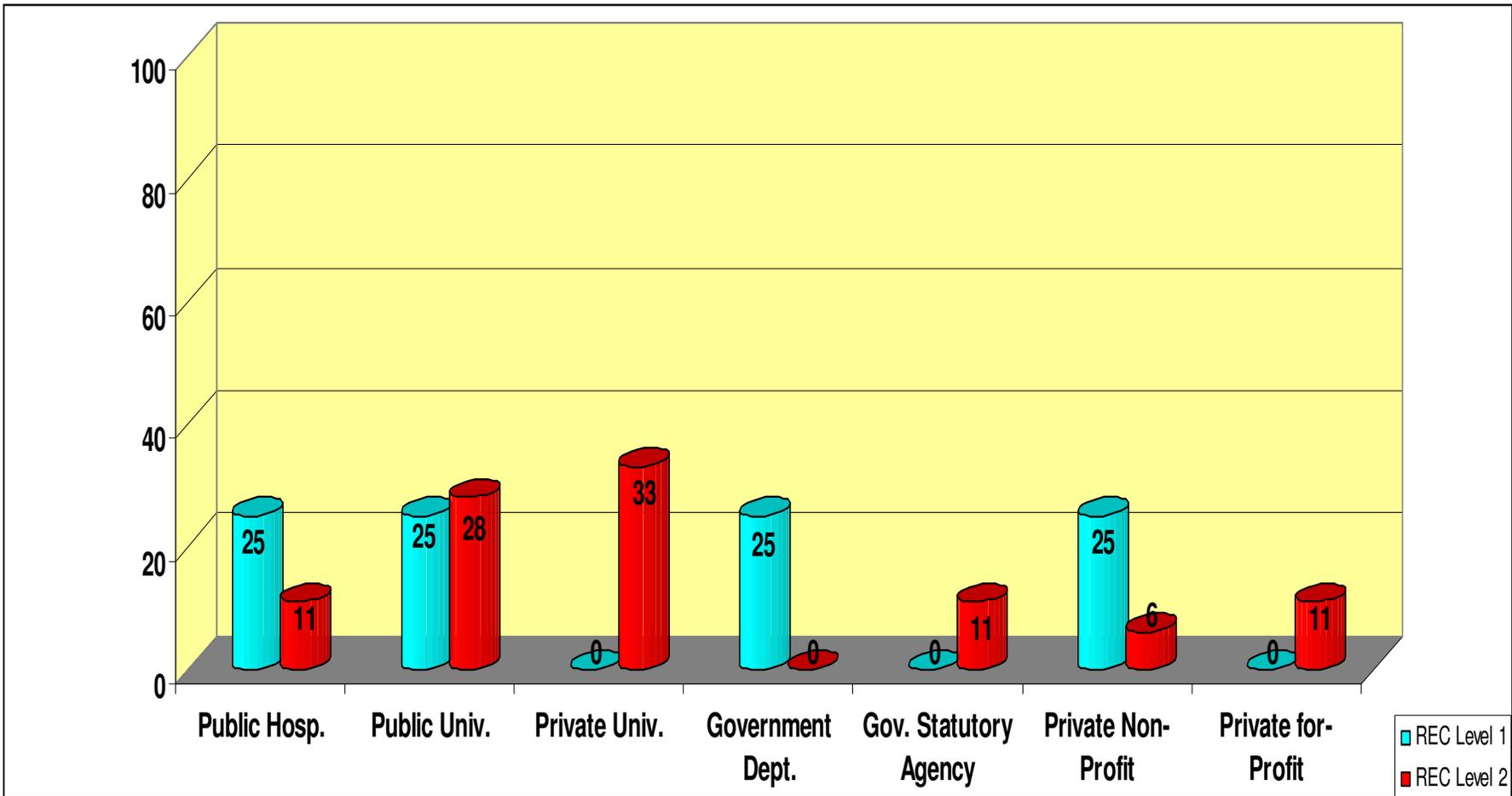


Figure 3: Percentage of REC type by level

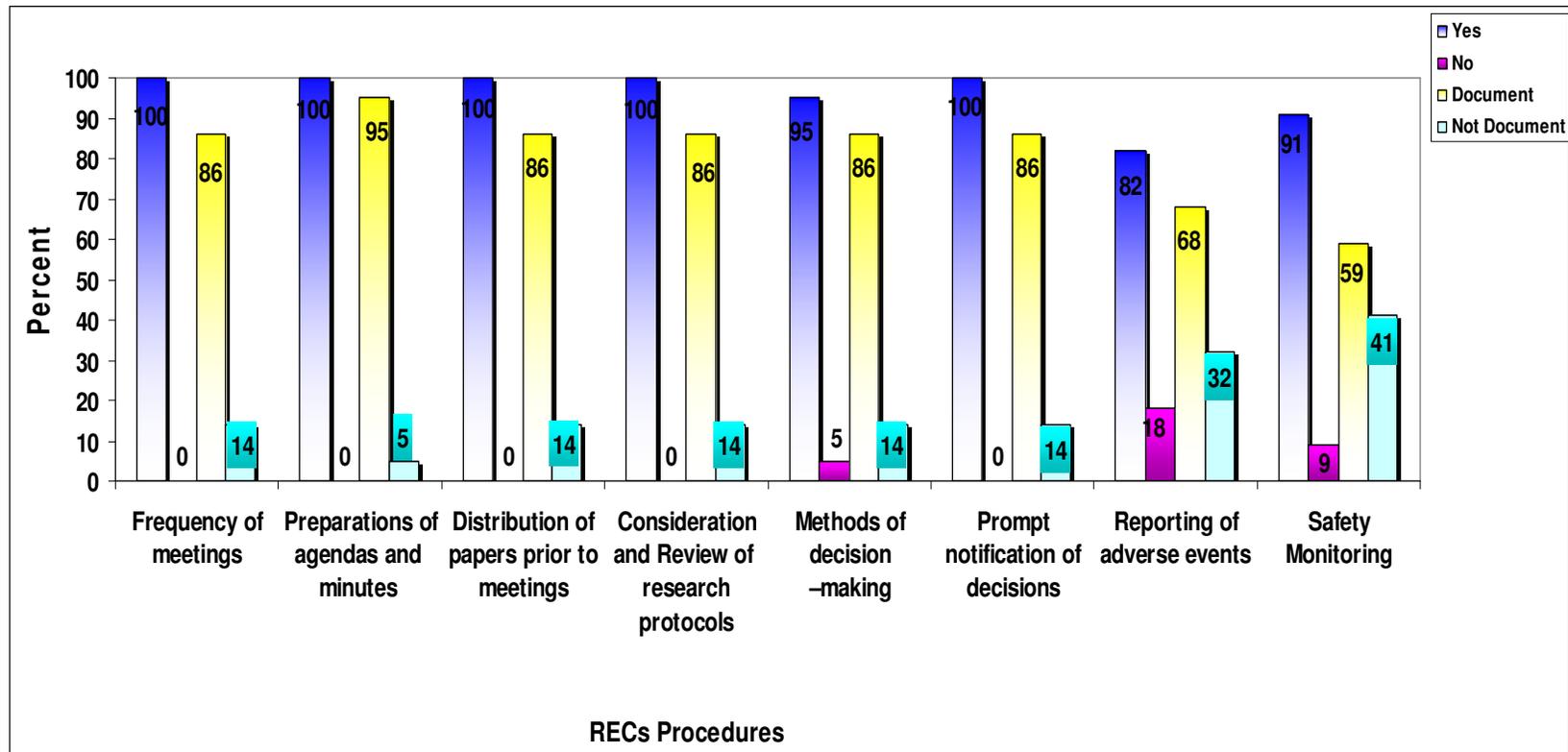


Figure 4. Percentage of RECs who implemented procedures according to DOH Guidelines

4.3 REC PROCEDURES

4.3.1 LEVELS OF REC COMPLIANCE TO DOH PROCEDURES

Figure 4, compares RECs reported to implement procedures according to DOH guidelines and those who documented the implementation of procedures. All 22 RECs (100%) reported to implement the first six DOH procedures (*frequency of meetings, preparations of agendas and minutes, consideration and review of research protocols and lastly, methods of decision-making*). At least 82% (18/22) of RECs reported to implement the remaining two procedures (Adverse events and safety monitoring). It is worth noting that all RECs are expected to implement 7 of 8 procedures except reporting adverse events which is implemented by level two REC (who also evaluate clinical trial research protocols) only. On the other hand, all RECs are expected to implement a system to actively monitor (safety monitoring) approved research.

Documentation of activities is regarded as an indicator to implement DOH activities. RECs who documented DOH procedures ranged from 59% (13/22) to 95% (21/22). A closer look at the data shows that, like reporting of activities, there are more RECs implementing the first six procedures compared to the last two. However, 68% (15/22) of RECs implemented reporting of adverse events. Of significant concern is that 41% (9/22) of all REC did not implement safety monitoring systems. Some REC particularly those who registered for level 1

reported that the reason for not implementing safety monitoring system is that they do not evaluate clinical trials.

Table 2. Number of RECs by Type which Implemented DOH Procedures

	Public Hosp.	Public Univ.	Private Univ.	Gov. Department	Gov. Statutory Agency	Private Profit Non-Profit	Private for-Profit
Frequency of meetings	2	6	5	1	2	1	2
Preparations of agendas and minutes	2	6	6	1	2	2	2
Distribution of papers prior to meetings	2	6	5	1	2	1	2
Consideration and Review of research protocols	2	6	5	1	2	1	2
Methods of decision –making	2	6	5	1	2	1	2
Prompt notification of decisions	2	6	5	1	2	1	2
Reporting of adverse events	2	4	5	0	1	1	2
Safety Monitoring	1	3	5	0	1	1	2

According to Table 2, RECs which implemented 6 of 8 procedures according to DOH guidelines ranged from 59% (13/22) to 95% (21/22). The six procedures include; frequency of meetings, preparations of agendas and minutes, consideration and review of research protocols and lastly, methods of decision-

making. RECs which implemented reporting of adverse events and safety monitoring ranged from 59% (13/22) to 68% (15/22).

As expected, 93% (13/14) of RECs operating from universities and government statutory agencies implemented 6 of 8 procedures according to DOH guidelines. Conversely, on average 67% (4/6) of RECs based at public hospitals, government department and private non-profit organizations implemented 6 of 8 procedures according to DOH guidelines. While 100% (2/2) private for-profit RECs implemented 6 of 8 procedures accordingly.

Related to the two remaining procedures (reporting adverse events and safety monitoring), it is important to note that the REC based at government department did implement the two procedures. Implementation of the two procedures by RECs based at universities and government statutory institutions ranges between 64% (9/14) and 71% (10/14).

4.3.2 COMMONALITIES AND DIFFERENCES AMONG RECs

It is expected that there are commonalities and differences between RECs. More closely, the research question anticipates less commonality in RECs based elsewhere except those operating from universities and government statutory agencies.

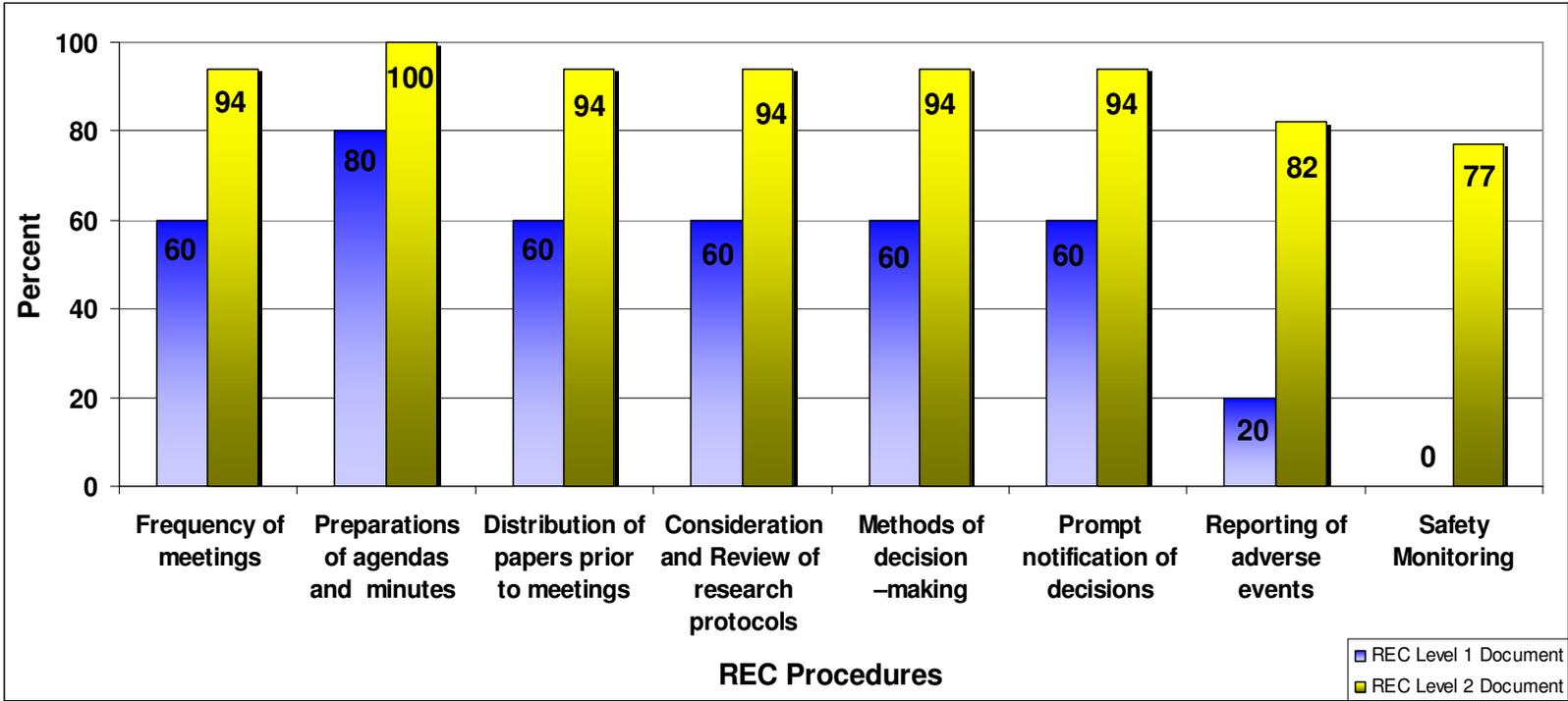


Figure 5 Percentage of RECs by level who Implemented DOH Guidelines Procedures

According to Figure 5, level 2 RECs implemented between 94% and 100% of procedures according to DOH guidelines, except for “reporting adverse events and monitoring safety at 82% and 77% respectively. While implementation of procedures according to DOH guidelines by level 1 RECs has a lower range of 60% to 80%. Implementation of the two procedures (reporting adverse events and safety monitoring) by level 1 RECs ranges between 0% to 20%.

4.3.3 OVERALL EXAMINATION PER TYPE OF COMPLIANCE

Regarding requirements for REC composition, 19/22 (86%) RECs registered with NHREC displayed a systematic compliance with the composition requirement of at least 09 members; while 3/22 (14%) complied in a non-systematic manner. The 6% differential between RECs’ men and women members shows a non compliance. Twenty-one (95%) RECs showed a systematic compliance related to having at least one member as a professional scientist or clinician; while 5% (1/22) exhibited non compliance.

Relating to lay persons, 82% (18/22) of RECs demonstrated a systematic compliance whereas 18% (4/22) showed non compliance. Seventeen (77%) RECs presented a systematic compliance regarding having a legal representative whilst 23% (5/22) displayed non compliance.

Related to requirements for REC procedures, 19/22 (86%) RECs displayed systematic compliance to six of the eight procedures (i.e *frequency of meetings*,

preparations of agendas and minutes, consideration and review of research protocols and lastly, methods of decision-making) while 3/22 (14%) displayed non compliance. Fifteen (68%) RECs and 13/22 (59%) demonstrated systematic compliance to the remaining two procedures respectively (i.e. adverse events and safety monitoring) whereas 32% (7/22) and 9/22 (41%) RECs exhibited non compliance.

CHAPTER V

DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

This section pools together in summary form the major findings from the study. The findings are used to generate discussions and conclusions. Finally, recommendations are made with regards to further research in the same direction as this study, as well as with regards to policy implications for the National Health Research Ethics Council and Department of Health.

5.2 Discussion

The findings are arranged according to the way research questions have been ordered in the study. The findings are encouraging in that they display a powerful structure of research ethics committees (RECs) registered with the National Health Research Ethics Council (NHREC) throughout the country. The majority (86%) of RECs demonstrate some level of compliance with DOH national guidelines.

5.2.1 Composition

The composition of RECs registered with NHREC display a certain lack of compliance with principles in the international ethic guidelines (CIOMS, 1991

and 2002), and DOH national guidelines which mention that RECs should be composed by members from different disciplines such as scientific professionals with training and experience in research methodologies, men and women, lay persons from the community being researched and legal representative (DOH, 2004) and (Valdez-Martinez, et al, 2005). The general non-systematic composition compliance by committees in SA was also highlighted by the 2007 Moodley and Myer, study and little has since changed.

For example, like in the 2005 Mexican study, Moodley and Myer 2007 study, the finding of this study is that RECs registered with NHREC in SA are male dominated (53%) with a 47% women representation. The marginal (6%) difference regarding gender of REC membership demonstrates non-systematic compliance with DOH national research ethics guidelines requirement for composition. The trend is not unique to South Africa, but is displayed by committees in different parts of the world. For instance, it was displayed by the Mexican local research ethics committees (LRECs) (Valdez-Martinez et al, 2005) and Japan ethics committees (EC) (Saito, 1992 and Akabayashi, et al, 2007); (Wegner, et al, 2002) and (Borovecki, et al, 2006).

Another example is that membership of ethics committees in the 2006 Croatian study had at least 5 members as regulated by the Law on the Health Protection. In SA 86% (19/22) of RECs have at least 09 members as requirement by DOH national research ethics guidelines, while 14% (3/22) of RECs did not comply with this minimum requirement. Elsewhere, according to Fischer 2006, US

oversight expects IRBs to be composed by at least 5 members. The observation that both in developed and less developed countries composition requirements seem to be the same except that the minimum numbers required for REC / IRB members in some developed countries is 5. While in some less developed countries is 9.

Nevertheless, the finding in this study regarding requirements for REC composition is that 19/22 (86%) of RECs registered with NHREC displayed a systematic compliance with the composition requirement of at least 09 members. Like the Moodley and Myer study, 2005 Mexican study, regarding lay persons, 82% (18/22) of RECs demonstrated a systematic compliance whereas 18% (4/22) showed non compliance. While Seventy seven percent of RECs had legal representative and 23% did not comply with this requirement. Both community and legal representatives (9% and 7% respectively) constituted less than 10% of REC members. However, community representatives did not come from the communities being research as per definition of the national guidelines on research ethics. Again some RECs did not have either a community or legal representative.

It is concerning that lay persons and community representation in SA RECs is low as indicated above. Some authors (Moodley and Myer, 2007) advocate that representation by both legal and lay persons should constitute at least 25% of the composition of RECs. This study echoes the same sentiments because at least the approach will ensure that RECs will be advised to respect the culture

of communities where research happens. It will also ensure that lay persons are not intimidated by professional scientist members and they (lay persons) fully participate in the discussions during REC meetings

5.2.2 REC procedures

It is again encouraging that 86% of RECs registered with NHREC in SA displayed a systematic compliance with six of the eight procedures (that is, *frequency of meetings, preparations of agendas and minutes, consideration and review of research protocols and lastly, methods of decision-making*) which is a similar trend at some parts of the world such as Mexico, Japan, Israel, and Croatia. For instance the 2005 Mexican study found that 70% of LRECs displayed systematic compliance with the procedures to allocate research projects to reviewers. While the Croatian and Israel studies found that there was evidence of discrepancies between practice and the Law on the Health Protection and Patients Right Act Regulations respectively.

In SA, most RECs who complied with DOH requirements related to procedures are based either at universities, government statutory agencies and private for-profit organizations that are all registered at level 2. The short coming for this category of RECs is that 5% (1/19) of RECs exhibited non compliance to implementation of procedures including reporting adverse events and monitoring safety of approved research. It is concerning that level 2 RECs

based at institutions where most of the workload to approve research proposals take place, did not implement important procedures which are intended to protect the safety of participants in research. It is worth noting that the fundamental REC function according to national and international research ethics principles is to protect the rights and well being of research participants.

In this case, 5% of RECs based at universities and government statutory institutions and private for-profit organizations failed to execute this function by not implementing a system to report adverse events and monitoring the safety of approved research studies. Level 2 RECs approve research including clinical trials which inherently carry higher risks than other types of health research. The NHREC should educate level 2 RECs about the significance of safety monitoring and encourage them to implement system.

While it is encouraging that on average 60% of level 1 RECs implemented procedures according to DOH guidelines, thereby displaying systematic compliance. It is worrying that none of these RECs implemented safety monitoring systems which constituted to non-compliance. In this case, safety monitoring relates to active and regular follow-up to approved research protocols. It could be argued that level 1 RECs approve research which has minimal risks. However, all levels and types of RECs are expected to comply with all national guideline requirements. In this case the NHREC should build or strengthen capacity of level 1 RECs given their human and financial resources constrains and that they (level 1 RECs) might be relatively new.

There is a 25% differential between RECs based at universities and government statutory agencies and those based at public hospitals, government department and private non-profit organizations. This finding adds to the need for NHREC and DOH to prioritise strengthening the capacity of level 1 RECs.

5.2.3 Commonalities and differences

Most (86%) RECs implemented composition and procedures according to DOH guidelines. This generally displayed a non-systematic compliance which is a common feature among RECs in SA and other parts of the world. Majority (12/22) of RECs are commonly based at universities and they are all registered at level 2.

Conversely, few (4/22) RECs are registered for level 1 and are based at government public hospitals and government departments. Unlike level 2 RECs, none level 1 RECs implemented procedures to monitor safety of approved research which violates protection of prospective research participants. This approach by level 1 RECs, is somewhat expected since they approve research protocols which have minimal risks. Implementation of DOH guidelines related procedures varied by REC levels. Similarly, implementation of DOH procedures varied by REC types. In particular RECs based at universities and government statutory agencies are homogenous. Secondly, implementation of procedures according to DOH guidelines is low at other types of RECs operating from

public hospitals, government department and private non-profit and private for-profit organizations.

5.3 Conclusions

This study has attempted to plug the research literature gap on Research Ethics Committees (RECs) registered with National Health Research Ethics Council (NHREC) and their compliance level with the South African (SA) 2004 national ethics guidelines in health research. The local existing literature was highlighted. Comparison and differences with the international literature, compositions and functions of RECs were drawn and discussed. Of most importance this study provided the baseline information on the current status of RECs in SA registered with the NHREC.

The conclusions drawn in this study are based on the secondary data analysis of 22 RECs registered with NHREC. The 22 RECs constitute 65% of 34 RECs known to the DOH. The study findings and conclusions are limited to RECs registered with NHREC during the period 2008 and 2009. Unregistered RECs were not considered because they are yet to complete the registration questionnaire developed to capture information relevant to this study.

Most RECs in SA registered with NHREC have a well organized and functional structure like elsewhere in the world such as in Mexico, Croatia and Japan. However, these RECs demonstrated a non-systematic compliance with composition and procedures of DOH national guidelines on research ethics. Fundamental differences exist related to REC levels and types. Most RECs

based at public hospitals, government department and private organizations experienced high variations. Disparities related to gender, profession identity, legal and lay representations are superficial and can be rectified within a short period of time by RECs.

Non compliance with reporting adverse events and monitoring safety of research studies at public hospitals and government department are related to registration as level 1 RECs which evaluates low risk research protocols. Whilst, non compliance with reporting adverse events and monitoring safety of research by RECs at universities and private RECs relates to high workload experienced. Effects of the legacy of the previous policy of apartheid still influence access to human and financial resources by REC types and levels.

5.4 Recommendations

The study showed that there was non systematic compliance and non compliance with DOH guidelines for both composition and procedures by RECs. Furthermore the study indicated surface diversities among RECs. The study recommends the following:

- Development of strategies by NHREC to increase REC compliance with DOH national research ethics guidelines is crucial.
- NHREC and DOH to invest in establishment of RECs particularly at government departments and public hospitals is important.

- NHREC and DOH to lead and support establishment of RECs.
- NHREC and DOH to invest in training and building capacity of level 1 RECs.
- DOH Policy maker to consider developing policy to improve the health research ethics area.
- DOH Research Directorate may consider using this study to complement its work, particularly the local and international literature; comparisons and difference among local RECs; and comparisons with internationally based RECs. Similarly researchers and RECs may draw the same benefits like the DOH research directorate.
- Future research studies should be designed such that levels 1 and 2 are handled slightly different because of their different characteristics.
- Policy measures to correct the previous effects of apartheid are still needed to increase access to research resources need by RECs.
- Future research studies in this area could focus on comparisons of registered RECs before and after the planned audit by NHREC like the 2005 Valdez-Martinez study.

REFERENCES

Akabayashi A, Slingsby B T, Nagao N, Sato H. (2007) An eight-year follow-up national study of medical school and general hospital ethics committees in Japan. **Journal of Medical Ethics**, 29: 8.

Ashcroft R (2005) Reforming research ethics committees: Latest proposals are a missed opportunity for a radical review. **British Medical Journal**, 331(7517) 587- 588.

Beecher H K. (1996) Ethics and clinical research. **New England Journal of Medicine**, 274: 1354-1360.

Benatar S. (2007).Research Ethics Committees in Africa: Building Capacity. **PLoS Medicine** 4(3): e135

Borovecki A, Have T, Oreskocic S. (2006). Ethics committees in Croatia in the healthcare institutions: the first study about their structure and functions, and reflections of the major issues and problems. **Health Ethic Council Forum**, 18: 49 – 60.

Brasel J B. (2005) Research Ethics Primer. **Journal of Surgical Research**, 128: 221-225.

Caniza M. (2006) Establishment of ethical oversight of human research in El Salvador: lessons learned. **The Lancet.**, 7: 1027-1033.

Central for Research Ethics Committees. United Kingdom, Organization (2010) **Centre of Research Ethical campaign.** [Online] Available at <http://www.corec.org.uk/new-ethics-committees.php> (04 February 2010)

Chima S. (2006) Regulation of Biomedical research in Africa. **British Medical Journal**, 332: 848-851.

Cho MK, Tobin SL, Greely HT, McCormickJ, Boyce A, Magnus D (2008) Strangers at the Benchside: Research Ethics Consultation. **American Journal of Bioethics**, 8(3): 4-13.

Cleaton-Jones P. (2000) Scientific misconduct in a breast-cancer chemotherapy trial: response of University of Witwatersrand. **Lancet** , 355: 1011.

Coleman C and Bouesseau M. (2008) How we know that research ethics committees are really working? The neglected role of outcomes assessment in research ethics review. **BMC Medical Ethics**, 9: 6.

Republic of South Africa, Organization, (1996), **Constitution of South Africa**, Number. 108. South Africa.

Council for International Organizations of Medical Sciences, Organization,
International **Guidelines for Ethical Review of Epidemiological Studies**.
Geneva.1991 Council for International Organizations of Medical Sciences

Council for International Organizations of Medical Sciences, Organization,
**International Ethical Guidelines for Biomedical Research Involving Human
Subjects**. Geneva. 2002. Council for International Organizations of Medical
Sciences.

Department of Health, Organization (1965). **Medicines and Related
Substances Act, 1965** (Act No. 101 of 1965). Pretoria: Department of Health.

Department of Health, Organization (2001) **Health Research Policy in South
African**. Pretoria: Department of Health.

Department of Health, Organization (2003) **National Health Act 2003, No. 61**.
Pretoria: Department of Health.

Department of Health, Organization (2004) **Ethics in Health Research:
Principles, Structures and Processes**. Pretoria: Department of Health.

Department of Health, Organization (2006) **Guidelines for Good Practice in
the Conduct of Clinical trials with Human Participants in South Africa**.
Pretoria: Department of Health.

Department of Health, Organization (2007) **Regulations Related to Establishment of National Health Research Ethics Council. No. R.134** (No. 29637). Pretoria: Department of Health.

Department of Health, Organization (2007) **Regulations related to Establishment of National Health Research Committee. No. R. 136** (No. 29637). Pretoria: Department of Health.

Department of Health, Organization (2007) **Regulations related to Human Subjects in Health Research. No. R. 135** (No. 29637). Pretoria: Department of Health.

Department of Health, London. Organization, (2001) **Research Governance Framework for Health and Social Care**. Department of Health, London.

Department of Health, London. (2001) **Research Governance Framework for Health and Social Care[online]** Available at http://www.dh.gov.uk/dr_consum_dh/groups/dh_digitalassets/dh_4014757.pdf (Accessed 04 February 2010).

Department of Health and Human Services, US. (2010) **Code of Federal Regulations title 45 Part 46 Protection of Human subjects**. [online] . Available at <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm> (Accessed 28 January 2010).

Department of Social Development, Organization, (2005) **Children's Act 2005**, Number. 38. [Online] Available at <http://ci.org.za/depts/i/plr/pdf/bills/childrens/Act38-2005pdf>.

Effa P, Massougbodji A, Ntoui F. (2007) Ethics committees in western and central Africa: concrete foundation. **World Bioethics**, 136 -142.

European Federation of Pharmaceutical Industries and Associations, Organization (1990), Brussels. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Steering Committee. **ICH Harmonised Tripartite Guideline for Good Clinical Practice (E6)**. 1996). [Online]. Available at www.ich.org (Accessed 28 January 2010)

Fletcher J C and Siegler M. (1996) What are goals of ethics consultation? A consensus statement. **Journal of Clinical Ethics**, 7: 122 -126.

Fischer B. (2006). A summary of Important Documents in the field of Research Ethics. **Schizophrenia Bulletin**, 32(1): 69-80.

Harris S. (1992) Japanese biological warfare research on humans: a case study of microbiology and ethics. **Annual New York Academic and Sciences**. 666: 21-52.

Horton R (2000) After Bezwoda. **Lancet**, 355: 942-943.

Hyder A. (2004) Ethical review of Health research: a perspective from developing country researchers. **Journal of Medical Ethics**, 30: 68-72.

Kaas N, Hyder A, Ajuwon A, Appiah-Poku J, Barsdorf N (2007). The structure and function of research ethics committees in Africa: A case study. **PLoS Medicine**;4(1): e3

Kass N, Adnan A, Ademola A, Appiah-Poku J, Barsdorf N, Elsayed D, Mokhachane M, Mupenda B, Ndebele P, Ndossi G, Sikayeto B, Tangwa G, Kirigia, J. and Wambebe, M. (2006) Status of national health research systems in ten countries of the WHO African Region. **BMC Health Services Research**, 6: 135.

Kaas N. (2004) Public Health Ethics: From Foundations and Frameworks to Justice and Global Public Health. **Journal Law, Medicine and Ethics**, 32: 232-242.

Kalima W, Wangwa C, Chilengi R, (2007) Towards an African-Driven Malaria Vaccine Development Programme: History and activities of the African Malaria Network Trust **AJTMH** 77: 282-288

Kessel A. S. (2003) Public Health Ethics: Teaching Survey and Critical Review. **Journal of Social Science and Medicine**, 56: 1439-1445.

Hatcher T. (2004) Environmental Ethics as an alternative for evaluation theory in for-profit business contexts. **Journal of Evaluation and Program Planning**, 27: 357-363.

Langlosi A. (2008) The UNESCO universal Declaration on Bioethics and Human Rights: Perspectives from Kenya and South Africa. **Health Care Analysis**, 16(1): 39-51.

Moodley K and Myer L (2007) Health Research Ethics Committees in South Africa 12 years into democracy. **BMC Medical Ethics**, 8: 1.

National Institute of Health, Organization, 1979. Regulations and Ethical guidelines: The Belmont Report. **Ethics Principles and Guidelines for the Protection of Human Subjects of Research**. Available at <http://ohsr.od.nih.gov/guidelines/belmont.html>.

National Institute of Health, Organization,(2004). **Guidelines for the Conduct of Research Involving Human Subjects**, [Online]. Available at [http://ohsr.od.nih.gov/guidelines/ Gray Booklet 82404.pdf](http://ohsr.od.nih.gov/guidelines/Gray%20Booklet%2082404.pdf) (Accessed 28 January 2010).

National Institute of Health. (2010) **Regulations and Ethical Guidelines: The Belmont Report. Ethical Principles and Guidelines for the Protection of Human Subjects of Research** [online]. Available at <http://ohsr.od.nih.gov/guidelines/Belmont.html> (Access date: 28 January 2010).

National Patients Safety Agency, Organization, (2008) **National Research Ethics Service** [Online]. Available at <http://www.nres.npsa.nhs.uk/aboutus/what-are-recs/> (Accessed 28 January 2010).

Noor A. (2009). Health Research Oversight in Africa. **Acta Tropica**, 112: 63-70.

Office of Human Research Protections, Organization, (2004) **Recent Compliance Oversight Determinations**. [Online]. Available at <http://www.hhs.gov/ohrp/compliance/findings.html> (Accessed 04 February 2010)

Rustam A. (2005) Research ethics committees in UK-the pressure is now on research and development departments. **Journal of the Royal Society of Medicine**, 98(10): 444-447.

Slack C, Strode A, Fleischer T, Gray G and Randchod (2007) Enrolling adolescents in HIV vaccine trials: reflections on legal complexities from South Africa. **BMC Medical Ethics**, 8: 5.

Saito T. (1992) Ethics Committees in Japanese Medical Schools. **Health Education Council Forum**, 4 : 281 – 287.

South Africa Health Info. Organization (2010). **What is meant by research ethics?** [online]. Available at <http://www.sahealthinfo.org/ethics/ethicsresearch.htm> (accessed 28 January 2010).

Straight M (2009). Clinical Regulation: Challenges to the institutional review board system. **Clinics in Dermatology**, 27: 375-383.

Strugo J (2007). **The impact of regulatory research structure on smaller ethics committees in South Africa**. A dissertation. Tshwane University of Technology, Pretoria.

Tindana P (2007). The Structure and Function of Research Ethics Committees in Africa: A Case Study. **PLoS Medicine**;4(1): e3.

United Nations, Organization, (1948). **Universal Declaration of Human Rights Adopted by United Nation General Assemble Resolution 217A (III) of 10 December 1948** [Online]. Available at <http://www.un.org/Oversight/rights.html> (Accessed 28 January 2010).

Unites States Department of Health and Human Services, Organization (2004)
Office for Human Research Protection fact sheet. [online] Available at
<http://www.hhs.gov/ohrp/about/ohrpfactsheet.htm>. (Accessed 28 January 2010).

Unites States Department of Health and Human Services, Organization (2004).
Review Human Health Services Grant Application. [online] Available at
<http://www.dhhs.gov/ohrp/humansubjects/guidance/aplrev.htm> (Accessed 04
February 2010).

Valdez-Martinez E, Garduno_Espinosa J, Martinez-Salgado H, Porter J D H.
(2004). Local research ethics committees of the Mexican Institute of social
Security: results of the national survey. **Public Health Journal**, 118: 329-336.

Valdez-Martinez E, Garduno_Espinosa J, Porter J D H. Understanding the
structure and practice of research ethics committees through research and
audit: a study of Mexico. **Public Health Journal** 74 (2005): 56-68.

Weaver G. R and Trvino L K. (2001). The role of human resources in
ethics/compliance management: A fairness perspective. **Journal of Human
Resource Management Review**, 11: 113-134.

Wegner N S, Golan O, Shalev C, Glick S. (2002) Hospital ethics committees in
Israel: structure, function and heterogeneity in the setting of statutory ethics
committees. **Journal of Medical Ethics**, 28: 177 – 182.

Weis R (2000) High-dose chemotherapy for high risk primary breast cancer: an on-site review of the Bezwoda study. **Lancet**, 355: 999-1003.

Whitworth J. A, Kokwaro g, Kinyanjui S, Snewin V, Tanner M, Walport M, Sewankambo. Strengthening capacity for health research in Africa 372 (2008) 1590-1593.

World Health Organization, Organization (2000), **Operational guidelines for Ethical Committees that review biomedical research**. Geneva. World Health Organization

World Medical Association, Organization, (1964) **Declaration of Helsinki**. [Online] Available at <http://www.wma.net/e/policy/b3.htm> (Accessed 28 January 2010)

World Medical Association, Organization, (2004). **Ethical Principles for Medical Research Involving Human Subjects**. [Online] Available at www.wma.net (Accessed 28 January 2010).

APPENDIX

1. University of Limpopo Medunsa Campus, Medunsa Research and Ethics Clearance Certificate.
2. Request for permission to use Department of Health – National Health Research Ethics Council Research dataset for registered RECs.
3. Permission from Department of Health to use National Health Research Ethics Council dataset