

**KNOWLEDGE AND COMPLIANCE WITH ETHICAL GUIDELINES IN CLINICAL
RESEARCH AMONG MEDICAL RESEARCHERS IN ENUGU STATE, NIGERIA**

by

DR F N Chukwuneke

**Student No: 28450940
ichiefn2002@yahoo.com**

**Submitted in partial fulfillment of the requirements for the degree of Master of
Public Health (Research Ethics), in the School of Health Systems and Public
Health, Faculty of Health Sciences, University of Pretoria, Republic of South
Africa.**

**SUPERVISOR: PROFESSOR MARIANA KRUGER
South African Research Ethics Training Initiative
(SARETI)**

June 2011

DECLARATION

This is to certify that this study is my original and independent work. The dissertation has never been presented to any examining body, nor has it been submitted elsewhere for publication. The finding and opinion expressed in this work are entirely mine and should not be taken as representing the views of the School of Health Systems and Public Health, Faculty of Health Sciences, University of Pretoria, Republic of South Africa.



Dr Felix N Chukwuneke: s 28450940

MPH (Health Research Ethics) Student, School of Health Systems and Public
Health, Faculty of Health Sciences, University of Pretoria, South Africa

TABLE OF CONTENTS

ACKNOWLEDGEMENT	4
ABSTRACT	5
CHAPTER 1 INTRODUCTION	7
CHAPTER 2 LITERATURE REVIEW	11
CHAPTER 3 SIGNIFICANCE OF THE STUDY	22
CHAPTER 4 AIM AND OBJECTIVES	23
4.1 Aim	23
4.2 Objectives	23
4.3 Primary endpoint	23
CHAPTER 5 METHODOLOGY	24
5.1 Study Setting	24
5.2 Study Design	25
5.3 Data Analysis	26
5.4 Ethical Considerations	26
CHAPTER 6 RESULTS	28
6.1 Knowledge and application of ethical guidelines and principles	28
6.2 Involvement of IRBs and compliance with ethical guidelines	34
CHAPTER 7 DISCUSSION	37
7.1 Involvement of IRBs and compliance with ethical guidelines	40
7.2 Limitations of the study	41
7.3 Conclusion	42
7.4 Recommendations.....	42
REFERENCES	49
APPENDIX 1	56
APPENDIX 2	57
APPENDIX 3	58

ACKNOWLEDGEMENT

I express my gratitude to the South African Research Ethics Training Initiative (SARETI) with funding from the Fogarty International Center/National Institutes of Health, USA, grant number 5 R25 TW00 1599-08 for fully sponsoring my training in health research ethics. I wish to register my sincere and heartfelt gratitude to my supervisor Professor Mariana Kruger for support, guidance and encouragement towards this study. My appreciations also go to the staff at the four tertiary health institutions visited in Enugu Nigeria for their cooperation during the research. I am very grateful to SARETI staff in Pretoria especially Dr Teresa Rossouw and Ms Faith Seme for their assistance during the ethical review of this proposal by the University of Pretoria Research Ethics Committee. In the same vein I would also like to express my thanks to Dr Oseloka Ekwueme of the Community Medicine Department, University of Nigeria Teaching Hospital Enugu for his assistance in the statistic analysis and Mrs. Carla Pettit SARETI administrator for her encouragement. I am also grateful to Professor Douglas Wassenaar, Nancy Kass and Adnan Hyder for their directions. To my lovely daughters Chisom and Chiamaka I say thank you for your support in ensuring to the conclusion of this work despite the odds.

ABSTRACT

Context: Knowledge of ethical guidelines among medical researchers will increase the likelihood that medical research is subjected to ethical standards that promote respect for all human beings and protect their health and rights

Aims/Objectives: The aim of this study was to assess researchers' knowledge of ethics guidelines and their perceptions regarding research and human subject protection and the functions of the ethics review committees in Enugu Nigeria.

Methods: This was a questionnaire-based descriptive study in which a total of 180 questionnaires were distributed, using a simple random sampling method to senior registrars and consultants of all specialties in Enugu State of the Federal Republic of Nigeria. These participants were either at the time doing research towards their dissertation as requirement for specialist qualifications or had done clinical research in the process of qualifying as specialists. Data collected were entered using Microsoft Excel package and exported to STATA for analysis and presented in simple frequency distribution tables and charts. We carried out Chi-square test of association between being a researcher and having adequate knowledge of ethical principles and guidelines.

Results: Of the 180 questionnaires distributed, 167 were returned anonymously, which is 93% response rate. Of the 167 respondents, 98 (58.6%) were males while 69 (41.4%) were females with a male-to-female ratio of 1.4: 1 Most respondents 130 (77.8%) were aware of the existing ethical guideline in biomedical research but only 96 (57.5%) had adequate knowledge of its principles and practice. Regarding application and compliance with ethical guideline, 114 (68%) agreed they always

comply with ethical guidelines by ensuring that their research proposal obtains ethics approval from Research Ethics Committee before commencement. Sixty-nine (41.3%) researchers conduct their research occasionally without research ethics committee for approval. The most common reason for this practice was the lack of an existing research ethics committee in the home institution (88.2%).

Conclusion: This study demonstrates that there is a need for research ethics training for researchers in Enugu State, Nigeria and that some of these researchers do not have adequate knowledge of research ethics guidelines. Of concern is the occurrence of research without ethics review, mostly due to absence of an ethics review committee in the home institution. This calls for an urgent need to launch an awareness campaign on health research ethics through education, training, seminars and institutionalizing research ethics committees in our tertiary institutions and hospitals as well as for the international agencies and health care organizations to collaborate with the Nigerian government in areas of legislation for strict compliance with ethical principles and practices amongst biomedical researchers in Nigeria.

CHAPTER 1

INTRODUCTION

Biomedical research with human research participants is based on a fundamental moral commitment to promote human health, advance the goal of science and protect human dignity and well-being. Advances in medicine have been made possible through health care or biomedical research as well as scientific experimentation on animal and human subjects [1]. Health research is therefore critical to understanding disease processes/health events and develops medicine. The ultimate goal of research is the improvement of health of the individual and of society at large. However, to be meaningful, research must protect human participants from harm and ensure accruable benefits, as well as respect for their dignity [2,3].

While research risks may be unavoidable, ethical misconduct in human research is reprehensible because of the danger it poses to human life [3]. Research with humans as experimental subjects especially in a vulnerable population may be subject to exploitation and abuse [4]. It is the professional duty of health care researchers to ensure that they are familiar with international and national research ethics guidelines and have undergone training in good clinical practice. This will maximise benefits and protect participants against harm. According to Emmanuel et al., ethical standards in research require that prospective research participants be fully informed of the nature, procedures, risks and benefits involved in a research and that their participation in the same be not coerced or forced [5]. The purpose of these guidelines therefore aims among other things, to minimise unethical practice in the conduct of research, to protect research subjects from undue harm and to ensure

that the desire for knowledge does not lead to “inhumane, unethical or inconsiderate treatment in experiments on human beings” [6].

In recent times, there has been a tremendous international collaboration in health research between the developed and developing countries due to the heavy disease burden, high poverty levels and paucity of health facilities and treatment options in developing countries [8]. As a developing country, Nigeria must therefore appreciate and establish a system that ensures that human participants in research are protected from potential exploitation, injury, and harm. This in turn will encourage future research participants thereby attracting foreign investment in research as well as deriving its benefits for the betterment of the people. Building capacity for ethical review of clinical research is the bedrock for any successful health research project [9]. The potential benefits of ethically-conducted trials, in the vast majority of studies, far outweigh the risks. A vibrant independent and funded IRB would discourage exploitative studies and misconduct by researchers. Since the international research enterprise is so important to the future of Nigeria and indeed Africa, a policy that would require that clinical research investigators and staff involved in health care and education obtain specific and standard training in the conduct of biomedical research would provide assurance that health researchers can competently conduct their work as required. There should be increased motivation and great effort in training IRBs and ethics committees in Nigeria in order to ensure that researchers in Nigeria are properly guided to maintain ethical standards while carrying out their research. The aim of this study was to assess researchers' knowledge of ethics guidelines and their perceptions regarding research and human participant protection and the functions of the ethics review committees in Enugu Nigeria.

In Nigeria, ethical principles on biomedical research with human participants came into serious focus following the enactment of ***National Code of Health Research Ethics*** (NCHRE) in 2005 [7]. Before then, many research involving human participants never followed proper ethical review because only very few institutions had research ethics committees with members who also had limited knowledge about research ethics principles and practices. Consequently, NCHRE was mandated to establish research ethics committees (RECs) in various Teaching Hospitals and Federal Medical Centers [7]. Accordingly, NCHRE was also established to regulate clinical research involving human participants based on the fundamental ethical guidelines regarding informed consent, respect for privacy and confidentiality, and risk/benefit assessment. The existence of viable and active ethical review committees and exposure and training of researchers and medical personnel in research ethics is no doubt a pre-requisite to ensuring that research is carried out in compliance with ethical standards [4]. It is also a veritable way for encouraging and increasing investment in research and a step towards ensuring that researchers comply with the research ethics guidelines and principles.

CHAPTER 2

LITERATURE REVIEW

Since antiquity, as demonstrated in the Hippocratic Oath, the key principles in health care are the principles of beneficence and non-maleficence (“Do no harm”) [10]. As medicine broadened its parameters to include research, and as wider processes of democratization changed the perception of the relationship between doctor and patient, the adequacy of the Hippocratic Oath was questioned [11]. For many, however, the oath still exemplifies the key virtues of a doctor in its emphasis on the obligations towards the wellbeing of the individual patient or research participant. Early attempts to articulate codes of ethics in medical research date as far back as 1803 when Thomas Percival presented *Medical Ethics or a Code of Institutes and Precepts, adapted to the Professional Conduct of Physicians and Surgeons* [12] and in 1931 which, the Weimar Republic in Germany passed a directive, which included a demand for the informed consent of research participants [9].

On the whole, the question of ethical regulation of medical science was only of peripheral concern until World War II. Following the experiments in Nazi concentration camps, several German doctors were convicted in Nuremberg for violations of human dignity, and informed consent was codified on the principle that individuals must never be sacrificed for the benefit of society [13]. During the Nuremberg War Crime Trials, the Nuremberg Code was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on concentration camp prisoners. This code became the prototype of many later codes [14] intended to assure that research involving human subjects would be carried out in an ethical manner. The codes consist of research ethics

guidelines, some general, others specific that guide the investigators or the reviewers of research in their work. The statement further consists of a distinction between research and practice, a discussion of the three basic ethical principles (autonomy, beneficence and justice), and remarks about the application of these principles [15].

The Nuremberg trial, however, did not have any major, practical influence on research ethics in the rest of the world [16] because, for example, the Tuskegee syphilitic experiment was conducted as late as the early 70s. Due to the development in the human rights movement, greater patient autonomy emerged in the US from the 1960s onwards. Chronologically, the various national policy changes in 1953, the 1954 Resolution on Human Experimentation, and the Jewish Chronic Disease Hospital case in 1963, lead to the World Medical Association's Declaration of Helsinki in 1964 [17].

The Declaration of Helsinki, issued by the World Medical Association in 1964, is the first comprehensive research ethics guideline and has influenced the formulation of international, regional and national legislation and codes of conduct. The Declaration, amended several times, most recently in 2002, is a comprehensive international statement of the ethics of research involving human subjects. It sets out ethical guidelines for physicians engaged in both clinical and non-clinical biomedical research [18].

Since the publication of the CIOMS 1993 Guidelines, several international organisations have issued ethical guidance on clinical trials. This has included, from the World Health Organisation, in 1995, Guidelines for Good Clinical Practice for Trials on Pharmaceutical Products; and from the International Conference on

Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), in 1996, Guideline on Good Clinical Practice, designed to ensure that data generated from clinical trials are mutually acceptable to regulatory authorities in the European Union, Japan and the United States of America [19]

In 2001 the Council of Ministers of the European Union adopted a Directive on clinical trials, which will be binding in law in the countries of the Union from 2004. The Council of Europe, with more than 40 member States, is developing a Protocol on Biomedical Research, which will be an additional protocol to the Council's 1997 Convention on Human Rights and Biomedicine, concerned with biomedical research involving human subjects. These documents are influenced by the Universal Declaration of Human Rights, which, was significantly influenced by the Nuremberg Code; the International Covenant on Civil and Political Rights; and the International Covenant on Economic, Social and Cultural Rights [19]. Since the Nuremberg experience, human rights law has expanded to include the protection of women (Convention on the Elimination of All Forms of Discrimination Against Women) and children (Convention on the Rights of the Child). These and other such international instruments endorse, in terms of human rights, the general ethical principles that underlie the CIOMS International Ethical Guidelines in biomedical research.

The Declaration also stressed the importance of institutional review boards (IRBs) and stipulated that researchers should not take ethical responsibility entirely upon themselves. Research ethics guidelines and practice have held that the individual holds the right not only to know of, but also to accept or decline, risks imposed on his/her body in the course of medical research [20]. Informed consent has thus gradually become a matter of key importance in medical research, sustained and

codified by the Food and Drugs Administration (FDA) and major funding bodies [20]. Subsequent cases where consent procedures were overruled only underscore its dominance in medical research ethics.

The western ethical standards have influenced the rest of the world, by granting the rights of the individual pivotal attention in medical research and initiating ethical debates to address ethical dilemmas in a pluralistic society like Africa. This reflects what has been described as the Western notion of individuality, which also influenced the Human Rights Declaration. Thus, medical research ethics has tended to take the protection of the individual as its main objective irrespective of the political or cultural context [20]. Interestingly, the emphasis on protection signifies an important development in what we might term the medical ethos. From the basic intention of beneficence, the introduction of research necessitated balancing of interests among various actors in a pluralistic society for present and future patients, researchers, and the subjects of research [21].

With the Tuskegee syphilis study in 1972, and the resulting Belmont Report, the idea of non-maleficence gained increasing importance, changing the understanding among many clinical researchers of what medical ethics is [11]. Most medical researchers are conscientious in protecting the rights of their research participants. Informed consent is integral to these aspirations, and it is now applied even in cases in which the initial right to assess risks imposed on the body of the individual is not necessarily at stake. In African countries, considering the cultural setting, informed consent may not be individually based but an issue of reaching consensus where family values take precedence over individual autonomy [22].

The pertinent issue therefore, has been the extent to which ethical principles are considered universal or as culturally relative – the universalist versus the pluralist view. The challenge to international research ethics is to apply universal ethical principles to biomedical research in a multi-cultural world with a multiplicity of health-care systems and considerable variation in standards of health care. The Guidelines take the position that research involving human participants must not violate any universally applicable ethical standards, but acknowledge that, in superficial aspects, the application of ethical principles, e.g., in relation to individual autonomy and informed consent, needs to take account of cultural values, while respecting absolutely the ethical standards [22].

The issue of human rights of the research participants, as well as of health professionals as researchers in a variety of socio-cultural contexts concerns largely, though not exclusively, two principles: respect for autonomy and protection of dependent or vulnerable persons and populations. In the preparation of the Guidelines the potential contribution in these respects of human rights instruments and norms was discussed, and the Guideline drafters have represented the views of commentators on safeguarding the corresponding rights of participants [23].

Debates on the ethical requirements for conducting medical research in developing countries have achieved considerable prominence in recent years [24]. To some extent this is the result of growth of interest in research in developing countries since the HIV/AIDS pandemic [25]. It also reflects renewed and encouraging interest in, and concern about, the nature of the relationship between researchers and participants. While researchers are generally privileged people many research participants are among the most vulnerable in our world, living under the worst

conditions of deprivation and exploitation [26]. Appreciation of concerns regarding research in developing countries requires some knowledge of the growing global disparities in wealth and health, and of the lifestyle and worldview of potential research participants [27]. Against this background, it is apparent that the ethical dilemmas faced in conducting biomedical research can only be addressed satisfactorily if research ethics is seen as intimately linked to health care, to human health globally and to the promotion of social and economic processes that could begin reversing widening global disparities in health care [24].

Despite the availability of ethical guidelines and regulations, violations of the rights of research participants continue to occur in both higher and lower income countries [26-29]. In Nigeria, as is often the case in other developing countries, exploitation and manipulation of human participants in clinical research is possible because of high level of poverty and ignorance [30]. It has been suggested also that African research participants are more susceptible than their counterparts in developed countries due to limited access to basic health care [16,31], and inadequate local regulation of biomedical research [32].

In Africa, public awareness of abuses to human research participants has remained problematic. In recent time ethical guidelines in clinical research with human participants has come into focus with several research ethics controversies in Africa including the Pfizer drug trials of *Trovan* in Nigeria and *Tenofovir* in Cameroon that have again highlighted the need for African professionals to have sophistication in research ethics in order to be able to participate in the debates locally [32]. This is important considering the fact that medical research involving human participants has increased greatly in many developing countries during the recent decade, which

has been motivated by the need to address the high burden of serious health problems facing most African countries.

Although the ethics declarations themselves are not binding legal documents, they arguably represent customary law – law based on an established pattern of behaviour that can be objectively verified within a specific field. The Declaration of Helsinki is a respected document of long standing and esteemed pedigree that is cited in numerous international and national legal instruments, giving it force of law in certain jurisdictions and under certain well-established principles, such as voluntary participation and informed consent [33]. It is signed by all member-state medical associations. It is also subject to intermittent revisions approved by the General Assembly of the World Medical Association (WMA), and therein lies its vulnerability: the WMA is a non-governmental association and is subject only to private law while the rights of participants in clinical trials is increasingly being viewed through the prism of international human rights law [33].

Declarations, by their very nature, are non-binding instruments that guide the conduct of research, but may hold mandatory rules within single institutions, not inter-state. Some argue that research ethics have become too regulated [34]. The ethical conduct of research specific to developing countries has been the subject of recent discussions with issues such as the relevance of the research to the health needs of the community and the country, avoidance of exploitation, and assurance that the informed consent process is sensitive to the local context, yet also representative of genuine, independent choice [32, 35, 36]. Developed countries have legislation or legal case law that determine the required standard for ethical guideline in clinical research involving human participation and ensure that they are

guided by such regulation while carrying out biomedical research [13]. In Nigeria and most of the developing countries these research ethics guidelines are not often complied with as could be cited in the case of the Pfizer drug trials of *Trovan* in Nigeria and *Tenofovir* in Cameroon [32, 37].

Ideally, specific legislation should exist to protect trial participants. This should include provisions relating to the conditions under which research may be conducted on vulnerable groups, informed consent, confidentiality and privacy related to research participation or diagnosis/treatment, compensation for trial-related injuries and protection stigma. In South Africa, for example, research participants have the right to participate in research only if they have given informed consent, as set out in the South African Constitution [38], and participants are protected from some social harm such as unfair discrimination against applicants/employees based on disease status, as set out in the Employment Equity Act of 1998.

Other countries such as Sri Lanka though, a developing country with a population of 19 million, has strengths in health and education [39] and the tradition of biomedicine, both western and eastern, is firmly established. Sri Lanka has a long history of scientific research with the establishment of the Medical Research Institute (MRI) in 1901 [40]. Influential international research collaborations have been reported [41-43] and leading funding agencies, including the Wellcome Trust (UK), National Institutes of Health (USA) and the World Bank have funded research in Sri Lanka. In spite of the volume of research, bioethics is at an early stage of development in Sri Lanka [44]. There were no formal training courses for clinical researchers except for some limited teaching in the six medical faculties from which the majority of research emanates [34]. This was the case some years ago but due

to the training programme through the NIH/FIC grants, research ethics have improved in Sri Lanka.

In Nigeria, the code of conduct in biomedical research with human participants was enacted in 2005 named *National Code of Health Research Ethics* (NCHRE) [7]. This was established by office of the presidency with reference to chapter 1V article 34 of the Nigeria Constitution which deals with the fundamental right of Nigerian citizens. NCHRE was empowered to regulate clinical research involving human participants based on the fundamental ethical guidelines for obtaining informed consent, respect for privacy and confidentiality, and risk/benefit assessment. The code also extended its terms of reference to include recognizing the fact that research participants are essential to the conduct of research which enables researchers to make progress and discoveries in the fields of medicine and health. This code applies to all health research involving human participants, conducted, supported or otherwise subject to regulation by any institution in Nigeria. But with the vast population of Nigeria more often it becomes very difficult to monitor the implementation of and compliance with these ethical principles and practices as presented in the National Research Ethics Code.

In Nigeria there is limited access to research ethics training [46]. Reports suggest that medical graduates in the United States who received ethics training while at medical school revealed that they could better understand ethical issues in clinical practice and would encourage continuation and expansion of ethics training in medical schools [46]. This can also be done in Nigeria, with the significant difference that social norms, cultural practices and local moral values and practices are enmeshed into the ethics training programme. This in turn will ensure that

researchers in Nigeria have adequate knowledge of research ethics principles to carry out their work in accordance with ethical standards that are in line with the protection of research participants.

CHAPTER 3

SIGNIFICANCE OF THE STUDY

In Nigeria, as often the case with most African countries, research may be hampered by chains of reaction of events *viz*: lack of good infrastructure for effective collection of data especially in most rural areas, erratic power supply, lack of adequate manpower, poverty, ignorance and financial limitations. Consequently, most researchers may face difficulties in carrying out their research. This may result in inadequate information about some procedures or treatment being given to the research participants as their refusal may stall the progress of the research. On the other hand, most researchers do not have adequate knowledge of ethical guidelines in clinical research because of limited access to training in research ethics. Ademola and Kass [46] in their study observed that training and continuing education sensitise scientists to the ethical issues in biomedical research which has been shown in some settings to be effective in providing scientists with skills for dealing with the ethical dilemmas they encounter in their own research. Knowledge of ethical guidelines among medical researchers will no doubt increase the likelihood that medical research in our environment is subjected to ethical standards that promote respect for all human beings and protect their health and rights [47]. Therefore, there is an urgent need not only for an awareness campaign but also strict legislation on compliance with ethical guidelines in medical research among researchers in Nigeria and other developing countries.

CHAPTER 4

AIM AND OBJECTIVES

4.1 Aim

The aim of this study is to address researchers' knowledge of ethics guidelines and their perceptions regarding research and human participant protection and the functions of the ethics review committees in Enugu, Nigeria.

4.2 Objectives

- ❖ To assess the knowledge of ethical guidelines in medical research among researchers in Enugu, Nigeria.
- ❖ To determine to what extent medical researchers in Enugu, Nigeria involve research ethics committees for ethical clearance in biomedical research.

4.3 Primary endpoint

To plan research ethics training workshops and improve compliance with ethical guidelines in biomedical research among researchers in Enugu, Nigeria.

CHAPTER 5

METHODOLOGY

5.1 Study Setting

The study was carried out in Enugu State in the eastern part of the Federal Republic of Nigeria among medical researchers. Nigeria is the most populous black nation worldwide [48]. Enugu state is made up of about 6 million people out of the estimated 40 million Ibo speaking population in the eastern part of Nigeria [49]. The state was created on August 27, 1991 among the 36 states of the Federal Republic of Nigeria with the city of Enugu as its capital. It derives its name from the capital city which was established in 1912 as small coal mining town by the British, but later grew to become the capital of the former Eastern Region of Nigeria. The immediate fortunes of the state appear to be tied up, among other things, with the rehabilitation of the coal industry, and citizens of the state take delight in being associated with the pseudonym of "the coal city state". Because of its socio-economic development relative to other states of Nigeria, Enugu state can boast of many tertiary and specialist hospitals where biomedical researches involving human participants are routinely carried out [49]. These tertiary and specialist health centres receive referrals from the lower levels of health care and have the capacity to train medical students and resident doctors in all fields of medical and health endeavour. Consequently, they are expected to carry out clinical research. However, limited knowledge and poor access to health research ethics as well as no-availability of research ethics committees in these centres are serious impediments to ensuring that researchers are guided by the research ethics principles while carrying out their research work.

There are four tertiary academic hospitals in Enugu state with capacity to train medical students as well as resident doctors in various areas of specialties with research work going on routinely. These academic hospitals include University of Nigeria Teaching Hospital, Enugu State University Teaching Hospital, Federal Neuropsychiatric Hospital and National Orthopaedic Hospital. These hospitals functions as referral centres for about 40 million people living in the eastern state of Nigeria.

5.2 Study Design

This is a descriptive study in which a semi-structured questionnaire was randomly administered to medical researchers in Enugu state of Nigeria. The questionnaire design is adapted from a template from the HIV/AIDS Vaccine Ethics Group (AAVP) questionnaire [50], School of Psychology, University of KwaZulu-Natal [Appendix 1]. A total of 180 questionnaires were distributed using a simple random sampling method to senior registrars and consultants of all specialties in Enugu state of the Federal Republic of Nigeria. These groups of people were either at the time doing their research dissertation towards qualifications as specialist or had done clinical research in the process of qualifying as specialists. The questionnaire was in three parts in order to address specific research questions relating to knowledge of ethical guidelines, as well as its application and compliance with standard research guidelines in biomedical research, and involvement of local ethics committees (IRBs) in research approval. No indentifying information of the participants or institutional affiliation was recorded to protect the confidentiality of the individual and the affiliated institution. The completed questionnaires were returned anonymously through the post in a self-addressed envelope to the principal investigator.

5.3 Data Analysis

There was no identifiable marker on the questionnaire and the collected data was entered into a computer with password protection only accessible to the principal investigator and thereafter, analysed in collaboration with the Department of Biostatistics College of Medicine University of Nigeria Teaching Hospital Enugu. Data from the questionnaire was double-entered using Microsoft Excel package and exported to STATA for analysis and presented in simple frequency distribution tables and charts. We carried out Chi-square test of association between being a researcher and having adequate knowledge of ethical principles and practice. The level of significance was set at 0.05 where $P < 0.05$ is considered significant and $P > 0.05$ non significant.

5.4 Ethical Considerations

Approval was sought and obtained from the University of Pretoria Faculty of Health Sciences Ethics Review Committee and the University of Nigeria Teaching Hospital Health Research Ethics Committee prior to commencement of the study. The participants' consent was sought and the purpose of the research fully explained in a participant information leaflet attached to the questionnaire. The goals of the study and procedures were described to the participants on the first page of the questionnaire. Those who filled and returned the questionnaire were considered to have given consent. The study did not pose any risk since that data was collected anonymously.

CHAPTER 6

RESULTS

Out of the 180 questionnaires distributed, 167 were returned anonymously resulting in a 93% response rate. Of the 167 respondents, 58.6% were males and 41.4% were females giving a male-to-female ratio of 1.4: 1. The age of the respondents ranged between 27 and 65 years with a mean age of 44 ± 3.5 years. More than half (53.4%) were surgeons and the rest (46.6%) were physicians. Physicians here refers to pediatricians, internal medicine clinicians, cardiologists, neurologists and dermatologists while surgeons include general surgeons, orthopaedic surgeons, paediatric surgeons, urologist, ENT surgeons, obstetrics & gynaecologists, dental surgeons, cardiothoracic surgeons and ophthalmologists.

6.1 Knowledge and application of ethical guidelines and principle

Most respondents 130 (77.8%) were aware of existing ethical guidelines in biomedical research but only 96 (57.5%) have adequate knowledge of its principles and practice. Participants had adequate knowledge and understanding of the ethical principles regarding informed consent (63.7%), voluntariness (55.7%), confidentiality (57.7%), justice regarding fair subject selection (51.5%), beneficence illustrated by concept of anticipated research benefit (49.1%) and risk reduction (66.9%) as shown in Table 1.

Table 1. Responses rate on adequate knowledge of ethical principles based on informed consent, voluntariness and confidentiality; fair subject selection; anticipated benefit and risk reduction.

Benchmark (n=167)	Response rate (%) on scale 1 to 3*		
	1	2	3
Informed Consent	63.7	23.3	13
Voluntariness	55.7	32.4	11.9
Confidentiality	57.7	30.7	11.6
Fair Subject Selection	51.5	25.6	22.9
Anticipated Benefit	49.1	37.7	13.2
Risk Reduction	66.9	28	5.1
Mean Values	57.5	29.6	12.9

*Keys: Adequate knowledge: 1; Not enough knowledge: 2; Don't Know: 3

Most respondents are familiar with ethical guidelines such as Declaration of Helsinki (77.3%) and the Council for International Organisations of Medical Sciences (CIOMS) guidelines (72.5%), but not with other international guidelines such as the Nuremberg Code (7.8%) and the Belmont Report (4.8%). Table 2 shows the Chi-square test of association between being a researcher and having knowledge of ethical guidelines and principles.

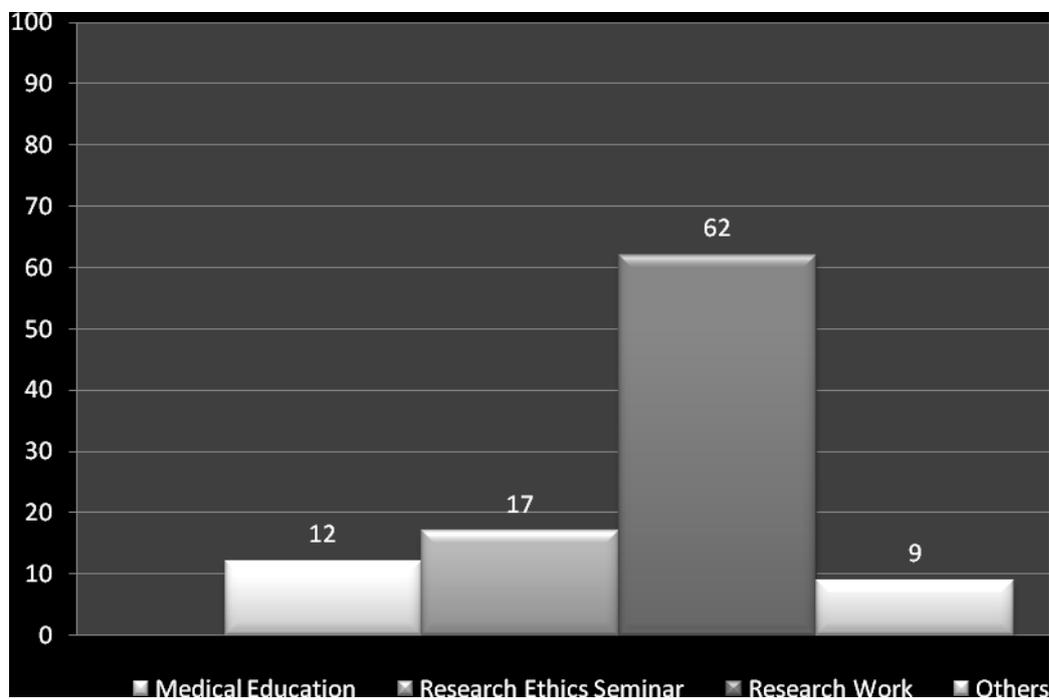
Table 2: Association between being a researcher and having knowledge of ethical principles characterised by socio-demographic variables, using chi-square.

Socio-demographic variables	Yes	No	χ^2	P-value
Gender				
Male (n= 98)	59 (60.2%)	39 (39.8%)	17.31	0.000*
Females (n=69)	38 (54.6%)	31 (45.4%)	1.42	0.233*
Specialty				
Surgeons (n = 89)	64 (72.3%)	25 (27.7%)	34.18	0.000*
Physicians (n=78)	32 (42.7%)	46 (57.3%)	5.03	0.025*
Years in Practice				
5 – 15 years (n= 93)	57 (61.4%)	36 (38.6%)	9.48	0.002*
16 – 25 years (n=74)	39 (53.6%)	33 (46.4%)	0.97	0.324*
Total (n=167)	96 (57.5%)	71 (42.5%)	7.49	0.006*

Years in practice also seem to have significant effect on the respondents' knowledge of ethical guidelines as those within 5–15 years in practice have adequate knowledge, which was statistically significant ($p = 0.002$) in comparison to those than those with working experience from 16–25 years ($p = 0.324$) [Table 1]. This is probably explained by the recent awareness on health research ethics globally and NHREC directive on institutional requirement for ethics clearance before any biomedical research using human participants in Nigeria may be conducted. With regards to clinical specialties, surgeons ($p = 0.000^*$) and physicians ($p = 0.025$) have

adequate knowledge of research ethics guidelines. Of the 130 (77.8%) respondents that were aware of existing ethical guidelines, 12% had the information from medical schools, research ethics seminars (17%), research work (62%) and others (9%) as shown in Figure 1.

Figure 1: Shows the rate percentage comparison of how Respondents acquired information on existing research ethics guidelines.



Many saw certain aspects of research as not important for ethical considerations such as giving incentive to research participants and the interpretation of clinical studies [Table 3].

Table 3: Aspects of research considered important for ethical Considerations?

Very important = 1; Important = 2; Not so important = 3; Not important = 4

Research Aspects	1	2	3	4
Research design.	124	43	-	-
The use of placebo controlled trials.	145	22	-	-
Community participation in clinical trials	156	11	-	-
The interpretation of clinical studies.	46	72	39	10
Fair subject selection.	86	61	12	8
HIV vaccine research.	161	6	-	-
Assessment of anticipated benefits.	102	63	1	
Appropriate risk reduction interventions.	147	20	-	-
Provision post trial benefits.	135	29	3	-
Retention of women in clinical trials	89	57	19	2
Incentives for research participants.	29	54	63	21
Understanding of informed consent.	88	79	-	-
Cultural sensitivity for informed consent.	75	56	21	15
Privacy and confidentiality.	126	41	-	-

The majority (74.3%) of the respondents considered research design as very important in research while the use of placebo control trials was also a very important ethical issue for them (86.8%). Regarding community participation in clinical trials, most of the respondents (93.4%) were of the opinion that community participation is essential and should be addressed before research is conducted.

Forty-nine (29.3%) of the respondents do not find interpretation of clinical studies as an important ethical issue, while 46 (27.5%) were of the opinion that it is a very important ethical issue to be considered. Surprisingly, 51.5% found fair selection of research participants not important versus 48.5% who found it important. Many of the respondents (96.4%) found HIV vaccine research had very important ethical issues that should be of concern to researchers and ethical committees approving research protocols.

Risk-benefit assessments were also considered very important ethical issues amongst many respondents with 102 (61.1%) regarding risks and 147 (88%) regarding benefits. Post-trial benefit was also very important for 135 (80.8%) of the respondents. Understanding of informed consent (52.7%) and cultural sensitivity for informed consent (44.9%) was not viewed as very problematic for research ethics. The majority of the respondents 138 (82.6%) also do not see provision of incentives for research participants as an important ethical issue to be considered, while 26 (17.4%) disagreed. One hundred and twenty-six (75.4%) respondents considered privacy and confidentiality as very important ethical issues in conducting research with human participants, or important for 41 (24.6%).

Most respondents were of the opinion that some studies such as descriptive (68.2%) and qualitative researches (73.1%) do not require ethical approval because they pose minimal risks to the participants.

Regarding application and compliance with ethical guidelines, 114 (68%) agreed they always comply with ethical guidelines while carrying out their research by ensuring that their research work obtains ethical approval from a research ethics committee before commencement. Sixty-nine (41.3%) researchers carry out

research work occasionally without involvement of research ethics committees for approval and the most common reason (88.2%) was the lack of a research ethics committee in the home Institution. Other reasons include research considered as minimal risk to the participants such as questionnaire-based research and post-data collection analysis. Notwithstanding, 54 (32.3%) think that strictly following standard ethical guidelines and principles in our environment will be an impediment to successful completion of their research project on time because of difficulty in getting participants' consent and unnecessary delay in getting ethical approval from research ethics committees.

6.2 Involvement of IRBs and compliance with ethical guidelines

There was still a lack of ethics committees reported by 62 (37%) respondents in their health institution. However, the requirement for ethical approval on their research work such as dissertations and during the process of publishing an article prompt most of them to get ethical approval from another centre with a functioning research ethics committee. Thirty-eight (23%) of the respondents are not aware of any regulation that governs ethical review of biomedical research in their institution while some are not familiar with the working principles of the research ethics committees in their health institutions and often abandon their research proposal when ethical approval was denied. Twenty-five (15%) send their proposal to another research ethics committee for consideration. According to the majority of the respondents 134 (80.2%) the most common reasons given for rejection of their protocol is when the research poses a considerable risk to the participants. Notwithstanding, almost all the respondents 155 (93%) were of the opinion that research ethics committees should ensure strict compliance with ethical guidelines before approving any

research proposal. Regarding challenges for research ethics committees in Nigeria, respondents include lack of adequate knowledge (79.1%) amongst research ethics committee members as a serious challenge (Table 4). One hundred and twenty-three (73.7%) respondents were of the opinion that conflict of interest among REC members is a serious challenge in ensuring that researchers comply with ethical guidelines while (23.3%) expressed a different opinion. Only few (25.1%) agreed that pressure from sponsors poses challenges to RECs while 49.1% cited lack of transparency of REC members. Not many (37.7%) reported that preferential treatment in the review process is a challenge to ensuring that proper review of research protocols is carried out which in turn ensures that researchers comply with ethical guidelines. The response rate of 79.1% for lack of adequate knowledge amongst research ethics committee members and 73.7% on conflict of interest amongst the ethics committees underscores the need to have proper training of the research ethics committee members in our environment. Interestingly, many of the respondents (40.7%) did not agree that preferential treatment in the review process is a challenge to RECs ensuring that researchers comply with ethical guidelines.

Table 4: Responses to question on the challenges RECs in Nigeria are facing to ensure that researchers comply with ethical guidelines

Response	Response rate (%) on scale 1 to 3*		
	1	2	3
Conflict of interest among REC members	73.7	23.3	3
Pressure from Sponsor	25.1	47.4	27.5
Preferential treatment in the review process	37.7	40.7	21.6
Lack of adequate Research Ethics Knowledge	79.1	15.6	5.3

Lack of Transparency of REC members	49.1	37.7	13.2
-------------------------------------	------	------	------

*Key: YES: 1; NO: 2; Don't Know: 3

Most of the respondents 162 (97.1%) think that invitation of researchers to attend a session during discussion of their proposal will be beneficial to improving ethical knowledge and compliance with ethical standards in biomedical research in Nigeria. Overall, there is a desire to comply with ethical guidelines while carrying out their research amongst most of the respondents as 155 (93%) think the RECs should ensure strict compliance with ethical guidelines at all times.

This result demonstrates that there is a need for research ethics training for researchers in Enugu, Nigeria and that some of these researchers do not have adequate knowledge of research ethics guidelines. Most respondents 130 (77.8%) were aware of existing ethical guidelines in biomedical research but only 96 (57.5%) had adequate knowledge of its principles and practice. Some researchers carry out research without ethical approval because of limited access and number of research ethics committees reviewing research protocols in the various tertiary health institutions in Enugu State. Sixty-nine (41.3%) researchers carry out research work occasionally without involvement of research ethics committees for approval and the most common reason (88.2%) was the lack of a research ethics committee in the home Institution.

CHAPTER 7

DISCUSSION

Bioethics generally, is new to most African countries including Nigeria so challenges to health research ethics cannot be underestimated [46]. Gradually awareness is been created in Nigeria about the need to ensure that researchers carry out their research in compliance with proper ethical guidelines [7]. In this line, several organizations have been promoting Bioethics: West African Bioethics Initiative (WAB), Nigerian Bioethics Initiative (NIBIN) and Association for Good Clinical Practice in Nigeria (AGCPN). The South African Research Ethics Training Initiative (SARETI) under Fogarty International Center (NIH/FIC) grant has been training many Nigerians in health research ethics who are empowered with enough health research ethics knowledge to impart on others (web.up.ac.za/sitefiles/File/healthsciences/SARETI/)

Also WAB ([://www.westafricanbioethics.net](http://www.westafricanbioethics.net)) has an M.Sc Bioethics programme at the University of Ibadan which has also benefited from a Fogarty International Center (NIH/FIC) grant. Others have also benefited from an EDCTP funded “Strengthening the Capacity of Research Ethics Committees in Africa” (CABREC) project. AGCPN ([://www.agcpn.org](http://www.agcpn.org)) promotes Bioethics, GCP and Responsible Conduct of Research in Nigeria and has a versatile online training programme powered by the Collaborative Institutional Training Initiative (CITI); a global training programme based at the University of Miami. Prompted by these efforts, Nigeria set up a National Health Research Ethics Committee (NHREC) which is a regulatory authority charged with regulating the ethical review process of health research ethics committees. This role includes establishment/enforcement of norms and standards

for conducting clinical trials and research on humans and animals among other statutory roles [51]. NHREC has commenced regulatory functions but has some hurdles; the legal instrument empowering it is still a Bill before the legislative house. However, NHREC is operating fully under a presidential fiat with the hope that institutions will establish research ethics committees that will be functional in their locality to guide and regulate researchers while carrying out their research.

This is because of the need to have ethical approval from the institution as a prerequisite for conducting research as recently directed by NHREC to all the tertiary health institutions in Nigeria where research is being conducted [52]. In Nigeria, health research and clinical ethics over the years have been neglected and hardly included in the educational curriculum for medical students [37]. Most often researchers carry out research without following or understanding the ethical principles involved in biomedical research because they do not have the knowledge. This study shows there is a need to inculcate research ethics training in our educational curriculum to ensure that biomedical personnel become exposed to research ethics principles early enough in their career. This will no doubt assist in ensuring that research in our environment is carried out according to standard ethical guidelines. The Council for International Organisation for Medical Sciences (ICOMS) report 2002 stated that one of the strategies for addressing this situation is initial and continuing education in the ethics and science of biomedical and behavioural research for investigators, members of Institutional Review Boards (IRBs), and sponsors of research [53]. It is therefore problematic that of the 130 respondents that were aware of existing research ethics guideline, only 12% had the information on from medical school, while the majority acquired this information during their research endeavours (62%), which emphasizes the need for increasing and

sustaining research ethics training at the primary health care level through curriculum development in our various medical schools.

According to Ademola et al. [46], training has three roles to play in ensuring the protection, safety, and integrity of study participants. First, formal and educational updates in research ethics can help increase professionals' knowledge and sensitivity to new and emerging ethical concerns in the conduct of research. For example, training and continuing education sensitize scientists to the ethical issues arising from rapid advances in medicine and biotechnology, such as research into genome, stem cells, multi-country field trials and experimentations involving vulnerable human populations [54]. Second, training has been shown in some settings to be effective in providing scientists with skills for dealing with the ethical dilemmas they encounter in their own research. In a training programme for American surgical residents, Pollock and colleagues [55] found that trainees in research ethics were better able than non-trainees to deal with problems relating to how to proceed if they lacked a sufficient quantity of a reagent critical for experimental data replication, and if they had problems with discordant or outlier experimental data. Trainees were prepared to seek third party input for resolving a dilemma involving their own work [56]. A study by Brown and Kalichman [56] among graduate students in experimental sciences also showed that training resulted in improved reports of knowing what to do if faced with an ethical dilemma. Finally, training in research ethics affords scientists, especially those from developing countries, the opportunity to contribute to ever-increasing international debates on ethical issues [53], many of which are likely to take place in developing countries.

Although the number of formal and online training programmes in research ethics has increased recently due largely to the efforts of many regional and international organizations, many professionals in African countries still have limited access to formal training in research ethics [46]. At the same time, more and more African scientists are involved in research, as greater numbers of clinical trials are being carried out in developing countries, such as Nigeria [58]. Even partially correcting the 10/90 gap – that 90 percent of global research is targeted at diseases comprising only 10 per cent of the global burden of disease – will contribute to more health research being conducted in developing countries [58]. This situation emphasizes the need to urgently develop the capacity of professionals in developing countries who have the skills to provide quality ethical oversight on these studies. Training professionals in health research ethics will ensure that studies conducted in developing countries respond to local health conditions, protect the rights and integrity of study participants, develop local capacity, and improve existing infrastructure. There is no doubt however, that there is an increase in research ethics awareness across the world through the help of several world health bodies training researchers, scientists and health policy makers in Africa such as Fogarty International Center/National Institutes of Health (NIH) which some countries have benefited from especially under the guidance of the South African Research Ethics Training Initiative (SARETI). This further explained the result of this study which shows that medical researchers with less than 15 years working experience have more knowledge of research ethics principles and practice which was statistically significant ($p = 0.002$) when compared with those with more than 15 years working experience ($p = 0.324$).

7.1 Involvement of IRBs and Compliance with Ethical Guidelines

Some researchers do not comply with research ethics principles and guidelines because of many reasons which include: inadequate knowledge of research ethics principles; lack of functioning research ethics committees, and environmental factors such as participants' attitude to cooperate with researchers especially in an environment where ignorance and illiteracy is high. Although capacity development in research ethics for researchers, members of IRBs, and sponsors of research may not entirely be a guarantee of safety for research participants, it is an important component of the interventions that can contribute to that goal [46]. The presence of RECs in our various tertiary health institutions will ensure that every research is subjected to review by the ethics committee before the commencement of such research. Sixty-two (37%) respondents that do not have functioning research ethics committees in their health institution effectively means that researchers will be conducting research without ethical approval because of the need to publish articles for promotion. Thirty-eight (23%) of the respondents are not aware of any regulation that governs ethical review of biomedical research in their institution while some are not familiar with the working principles of the research ethics committees in their health institutions.

Most research ethics committees in Nigeria are not functioning in a proper manner because of inadequate knowledge and inexperience of the ethics committee members. In a situation where one or two members are knowledgeable while others are not, there is a tendency that protocols will be given to non-members to assist in reviewing the protocols without any formal exposure to research ethics principles. More often these groups of people are more concerned about the grammatical and

syntax nature of the protocol they are reviewing and do not consider the ethical aspect of the protocol.

The dearth of research ethics committees in our various tertiary health institutions also poses a serious impediment to carrying out research in conformity with the laid down ethical principles. The most common reason (88.2%) the respondents gave for carrying out research occasionally was non-availability of research ethics committee in the parent institution. This apparently makes some researchers conduct their research without ethical approval; especially with respect to research they considered to be of minimal risk and felt did not require ethical clearance before commencement. Although RECs have existed in various tertiary health institutions in Nigeria as early as the 1980s, they have been very rudimentary. They were made prominent by the revitalization of the National Health Research Ethics Committee (NHREC) with the introduction of the National Code for Health Research Ethics in 2007 to ensure good ethical principles of research, optimizing benefits while minimizing its potential harm and undue exploitation of research participants in Nigeria [7]. The National code spells out the roles and responsibilities of the Nigerian NHREC with terms of references to ensure that health institutions set up RECs to review and approve research proposals from health researchers in line with protecting human rights and research participants. Notwithstanding, currently in Nigeria, of the existing 53 RECs in our tertiary health institutions where research is being conducted routinely only 13 were accredited by NHREC, thus emphasizing the need to ensure strict compliance by the NHREC. As observed in this study, Patricia Marshal [61] in 2001 while conducting a US-sponsored research on ethical and policy issues involved in clinical trials in developing countries also highlighted the same problems confronting researchers and research ethics committees in Nigeria.

Onyemelukwe [62] was of the opinion that while establishing the Code and setting up the NHREC by Nigerian government may not necessarily dispose of all unethical practices in research, these steps at least convey concern by the Nigerian government for the safety of research participants and, to some degree, close the existing vacuum in this area. Most importantly, ethics review has now become mandatory for all health research in Nigeria.

In addition, biomedical research in Africa would benefit greatly from regulations backed by law that provide guidance on forming viable and active local ethics committees, shaping informed consent, regulations for distributive justice such as post-trial benefits and procedures of setting relevant standards of care for injuries incurred during sponsored research due to negligence or unethical conduct by researchers and funding agencies [63]. Therefore, the successful establishment of RECs in various institutions in Nigeria by the individual institution under the supervision of NHREC and willingness to assist in training research ethicists to ensure the smooth running of the local REC will augur well for improved health research ethics capacity building initiatives in Nigeria. This in turn will ensure that biomedical research in Nigeria is conducted with standard ethical guidelines that are devoid of exploitation of research participants.

7.2 Limitations of the Study

This study was a self-administered questionnaire unanimously completed that was randomly distributed to biomedical researchers in Enugu. Their responses might not have aptly reflected the views of the others. The sensitivity of the questionnaire being a kind of self-appraisal on issue of ethics may create the tendency to give

inaccurate information by some respondents. The study therefore may not be sufficient enough to reflect the accurate situation regarding researchers' practice in biomedical research in Enugu applying research ethics principles while carrying out their studies. This is a quantitative study and as such may not ascertain the real situation regarding individual researcher's attitude and knowledge of research ethics principles and practices. We are therefore of the opinion that further qualitative assessment through in-depth interviews amongst biomedical researchers in Enugu will further give a clue on the conduct of researchers regarding application of research ethics principles.

7.3 Conclusion

This study demonstrates that there is a need for research ethics training for researchers in Enugu, Nigeria and that some of these researchers do not have adequate knowledge of research ethics guidelines. Most respondents 130 (77.8%) were aware of existing ethical guidelines in biomedical research but only 96 (57.5%) had adequate knowledge of its principles and practice. Some researchers carry out research without ethical approval because of limited access and dearth of research ethics committees reviewing research protocols in the various tertiary health institutions in Enugu. Sixty-nine (41.3%) researchers carry out research work occasionally without involvement of research ethics committees for approval and the most common reason (88.2%) was the lack of a research ethics committee in the home Institution. There is lack of research ethics training exposure in our medical schools as only 12% out of 130 respondents with knowledge of existing research ethics guideline had the information while in medical school compared to 62% that

had the information in the process of conducting research involving human participants.

7.4 Recommendations

There is a need to inculcate research ethics training in Nigerian educational curriculum to ensure that biomedical personnel become exposed to research ethics guideline early enough in their career.

There is an urgent need to launch an awareness campaign on health research ethics through education, training, seminars and institutionalizing research ethics committees in our tertiary institutions and hospitals as well as for the international agencies and health care organizations to collaborate with the Nigerian government in areas of legislation for strict compliance with ethical principles and practices amongst biomedical researchers in Nigeria.

REFERENCES

1. Hemeren G. Epidemiology and ethics experts. In: *Nordic Journal of Psychiatry* 1996; 50 (36): 5-14.
2. Council for International Organisation of Medical Sciences. Ethical guidelines for biomedical research involving human subjects. Geneva: Council for International Organisation of Medical Sciences; 1993.
3. London A.J. Justice and the human development approach to international research. *Hastings Center Report*. 2005;35(1):24-37.
4. Ogulana C. The Requirement of Informed Consent in Research Ethics: Procedure for Implementing a Crucial Ethical Norm in African Communal Culture. *European Journal of Scientific Research* 2010; Vol.44 (No.2): pp.204-219.
5. Emanuel E. J, Wendler D, Killen J, Grady C. What makes clinical research in developing countries ethical? *Infect Dis*. 2004; 189(5): 930-7.
6. McNeill P. M. Experimentation on human beings. In: Helga, H and Singer, P (eds.), *A Companion to Bioethics*. Oxford: Blackwell Publishers Ltd: 1998.
7. National Code of Health Research Ethics: Federal Ministry of Health Abuja, Nigeria; 2007: [://www.nhrec.net](http://www.nhrec.net) .
8. Amdur RJ, Bankert EA. Institutional review board: Member handbook. Massachusetts: Jones and Bartlett Publishers; 2007.
9. Kiriga JM, Wambebe C, Bab-Mousa A. Status of national research bioethics committees in the WHO African region. *BMC Medical Ethics*. 2005;6.

10. Collier PF. Oath and Law of Hippocrates. Harvard Classics 1910; Volume 38: [://nktiuro.tripod.com/hippocra.htm](http://nktiuro.tripod.com/hippocra.htm) .
11. Hoeyer K, Dahlager L, Lynöe N. Conflicting notions of research ethics The mutually challenging traditions of social scientists and medical researchers. *Social Science & Medicine* 61; 2005: 1741–1749.
12. Lynöe N. Mellan Cowboyetik och Scoutmoral. Medicinsk Forskningsetik i Praxin [Between cowboy ethics and scout morality. Medical research ethics in practice]. Stockholm: Liber: 1999.
13. Nuffield Council on Bioethics :The ethics of research related to healthcare in developing countries. London: Nuffield Council on Bioethics; 2002.
14. Human Participant Protection Education for Research Team: National Institutes of Health. U.S. Department of Health and Human Resources; Nov. 2002.
15. Beauchamp TL, Childress JF. Principles of Biomedical Ethics. Oxford University Press (5th Edtn) Washington DC. 2001; p: 322.
16. Rothman DJ. Strangers at the bedside. A history of how law and bioethics transformed medical decision making. New York: Basic Books: 1991.
17. Brody B. A historical introduction to the requirement of obtaining informed consent from research participants. In L. Doyal, & J. Tobias (Eds.), Informed consent in medical research (pp. 7–14). London: BMJ Books.
18. WMA 2000. World Medical Association. Recommendations guiding physicians in biomedical research involving human subjects (Declaration of Helsinki) 5th revision, Edinburgh. [.wma.net/e/policy/17-c_e.html](http://wma.net/e/policy/17-c_e.html). Accessed 22 July 2007.
19. Council for International Organisations of Medical Sciences (CIOMS): International Ethical Guidelines for Biomedical Research Involving Human Subjects. Geneva, Switzerland: CIOMS; 2002.

20. Benatar SR. Reflections and recommendations on research ethics in developing countries. *Social Science & Medicine* 2002, 54:1131-114.
21. Zulfiqar AB. Ethics in international health research: a perspective from the developing world. *Bull World Health Organ* 2002, 80:114-120.
22. Onuoha C. Bioethics across borders: An African perspective [PhD Thesis]. Uppsala University; 2007.
23. Research Triangle Institute: Road map for success in international research: strategies for protecting human research subjects globally. Report of workshop 2005.
24. Benatar SR. Global disparities in health and human rights: A critical commentary. *American Journal of Public Health* 1998; 88: 295–300.
25. Benatar SR, Singer. Avoiding exploitation in clinical research. *Cambridge Quarterly in Healthcare Ethics* 2000; 9: 562–565.
26. Angell M. The ethics of clinical research in the third world. *New England Journal of Medicine* 1997; 337: 847–849.
27. Sponholz G. Teaching scientific integrity and research ethics. *Forensic Science International* 2000, 113(1–3):511-154.
28. Jeffers BR. Continuing education in research ethics for the clinical nurse. *The Journal of Continuing Education in Nursing* 2002, 33(6):265-269.
29. Rosenstein DL, Miller FG, Rubinow DR :A curriculum for teaching psychiatric research bioethics. *Biological Psychiatry* 2001, 50(10):802-808.
30. Irabor DO, Omonzejele P. Local Attitudes, Moral Obligation, Customary Obedience and Other Cultural Practices Their Influence on The Process of Gaining Informed Consent for Surgery in a Tertiary Institution in a Developing Country. *Developing World Bioethics* ISSN 1471-8731 (print) 2007; 1471-8847 (online).

31. Shapiro HT, Meslin EM. Ethical issues in the design and conduct of clinical trials in developing countries. *N Engl J Med* 2001, 345:139-142.
32. Chima SC. Regulation of biomedical research in Africa. *British Medical Journal* 2006, 332:848-851.
33. Simpson B: Ethics regulation and the new reproductive technologies in Sri Lanka: perspectives of ethics committee members. *Ceylon Med J* 2001, 46(2):54-57.
34. Kasturiarachchi N, Lie R, Seeberg J. Health Ethics in Six SEAR countries. WHO-SEARO 1999, 1:76-84.
35. Shapiro HT, Meslin EM. Ethical issues in the design and conduct of clinical trials in developing countries. *N Engl J Med* 2001, 345:139-142.
36. Susan SK et al. Attitudes, understanding, and concerns regarding medical research amongst Egyptians: A qualitative pilot study. *BMC Medical Ethics* 2007, 8:9.
37. Anya I, Raine R. Strengthening clinical and research ethics in Nigeria—an agenda for change *The Lancet* 2008; Volume 372 (9649): 1594 – 1597.
38. Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants, in South Africa, Department of Health, Pretoria; 2000.
39. World Health Organisation: World Health Report. Geneva. 2000.
40. Uragoda CG: History of Medicine in Sri Lanka. Colombo: Sri Lanka Medical Association; 1987.
41. Weerasooriya MV, Gunewardena NK, Itoh M, Qiu XG, Kimura E: Prevalence and intensity of *Wuchereria Bancrofti* antigenaemia in Sri Lanka by Og4C3 ELISA. Using filter paper absorbed whole blood. *Trans R Soc Trop Med Hyg* 2002; 96:41-45.

42. Ahluwalia N, De Silva A, Athukorale S, Weaver V, Molls R: Ferritine concentration in dried serum spots from capillary and venous blood in children in Sri Lanka; a validation study. *Am J Clin Nutr* 2002, 75:289-94.
43. Sumathipala A et al. Ethics Review Committee approval and informed consent: an analysis of biomedical publications originating from Sri Lanka. *BMC Medical Ethics* 2008; 9: 3doi:10.1186/1472-6939-9-3.
44. Simpson B: Ethics regulation and the new reproductive technologies in Sri Lanka: perspectives of ethics committee members. *Ceylon Med J* 2001; 46(2):54-57.
45. Cha SS, Ross JS, Lurie P, Sacajiu G MD. Description of a Research-Based Health Activism Curriculum for Medical Students. *Journal of General Internal Medicine* 2006; Vol. 21 (12): 1326-1328.
46. Ademola A, Nancy K. Outcome of a research ethics training workshop among clinicians and scientists in a Nigerian university. *BMC Medical Ethics* 2008, 9:1.
47. Cohn F, Manetta A. A teachable moment: research ethic revisited. *American Journal of Obstetric and Gynecology* 2003, 188:2.
48. Enugu state of Nigeria 2006: <http://www.onlinenigeria.com/links/enuguadv.asp>
49. Enugu Nigeria 2008: <://www.ngex.com/nigeria/places/states/enugu.htm>.
50. Ethics Law and Human Rights Working Group: African AIDS Vaccine Programme. Defining and strengthening priority areas in terms of ethics, law, human rights and HIV Vaccine research. University of KwaZulu-Natal, Scottsville, Pietermaritzburg 3209.
51. Clement A et al. Developing Ethical Oversight of Research in Developing Countries: Case Study of Nigeria. *Ethics of Public Health Research*. Social Science Academy of Nigeria: April 2008.

52. National Health Research and Ethics Committee. The National code of health research ethics. Abuja: Federal Ministry of Health, Nigeria; 2007 [updated 2007; cited 2010 25/07]; Available from: [://www.nhrec.net/nhrec/NCHRE.pdf](http://www.nhrec.net/nhrec/NCHRE.pdf).
53. Daar AS, Singer PA. Human capital is key to research ethics. [[://www.scidev.net/dossiers/index.cfm](http://www.scidev.net/dossiers/index.cfm)] webcite 2002.
54. Council for International Organisation for Medical Sciences International Ethics Guidelines for Biomedical Research Involving Human Subjects. Geneva, Switzerland; 2002.
55. Pollock RE, Curley SA, Lotzova E: Ethics of research training for NIH T32 surgical investigators. *Journal of Surgical Research* 1995, 247-251.
56. London L, McCarty G: Teaching medical students on the ethical dimensions of human rights: meeting the challenge in South Africa. *Journal of Medical Ethics* 1998, 24(4):257.
57. Brown S, Kalichman MW: Effects of training in responsible conduct of research: a survey of graduate students in experimental sciences. *Science and Engineering Ethics* 1998, 4:487-498.
58. Kilama WL. Equipping Africa's researchers for global collaboration. [[://www.scidev.net/dossier/index.cfm](http://www.scidev.net/dossier/index.cfm)] 2003.
59. Falusi A, Olupade O, Olupade C. Establishments of a standing Ethics/Institutional Review Board in a Nigerian University: A BLUEPRINT FOR DEVELOPING COUNTRIES: 2007.
60. Obono O, Ajuwon A, Arowojolu A, Ogundipe G, Yakubu J, Falusi A. Ethics in Research (2nd Ed.) Ibadan, Nigeria: Corporate Graphics.2006.
61. Marshal P. The relevance of culture in informed consent on US-funded international health research in ethical and policy issues in international research in

- 11 Clinical Trials in Developing Countries, Commissioned Paper and Staff Analysis; NABC 2001 [://heinonline.org/HOL](http://heinonline.org/HOL) accessed 2011. .
62. Onyemelukwe C. Regulation Research Involving Humans in Nigeria: Some Recent Improvement. *Health Law Review*; 2008;16:4.
63. Sylvester C, Chima A. (2006). Global medicine: Regulation of biomedical research in Africa, *British Medical Journal* 2006; 7545: 848-851.

APPENDIX 1
Participant information leaflet and Questionnaire

A Questionnaire Survey on Attitude and Knowledge of Ethical guidelines in clinical research among medical researchers in eastern Nigeria.

Dear Sir/Madam

Please, I would like to invite you to participate in the above named questionnaire-based study. The study is part of my training program at the University of Pretoria towards a Master degree in Public Health, Health Research Ethics Track which has been approved by the Research Ethics Committees of the University of Pretoria and the University of Nigeria Teaching Hospital Enugu.

The study is primarily aimed at determining the knowledge and compliance with ethical guidelines, as well as having their research protocols ethically reviewed in clinical research among medical researchers in eastern Nigeria. You are being asked to be part of this study because you live in Enugu State-eastern Nigeria and you are a registrar or specialist involved in biomedical research.

It is sponsored by South African Research Ethics Training Initiatives (SARETI) through Fogarty International Centre. The questionnaire design is a template from HIV AIDS Vaccine Ethics Group, (AAVP) questionnaire, School of Psychology, University of KwaZulu-Natal, used in determining the knowledge and compliance with ethical guidelines, as well as having their research protocols ethically reviewed in clinical research among medical researchers in Nigeria. The questionnaire should take less than 30 minutes to complete.

In the questionnaire, demographic data such as sex, academic background and involvement in biomedical research will be asked. There will be no name or any identifiable marker required. No one but the investigator will have access to the completed questionnaires which will be stored in locked cabinets.

The completed questionnaires will be return anonymously through the post in a self addressed envelop bearing the name of the principal investigator. If the results of this study are published, your identity as well as your affiliated institution will remain unknown. If you decide to complete the questionnaire it is assumed you have given your consent to participate. It is therefore up to you to decide whether to complete this questionnaire. You also have the right to skip any question you find uncomfortable to answer

Please complete the form and return to Dr FN Chukwuneke at:
Address: Dept. of Oral & Maxillofacial Surgery,
University of Nigeria Teaching Hospital Enugu Nigeria
PMB 1130 Enugu
Tel: 042314946; 07064531609. E-mail: [@yahoo.com](mailto: @yahoo.com)

A Demographic Data

Gender	
--------	--

Age:			
Specialty:			
Position:			
No. of yrs in practice			
Institution Affiliation:			
Religion:			
<p>Please tick the appropriate answer (1=yes; 2= no Are you involved in biomedical research? (1) Yes (2) No</p>			
How many articles or dissertations have you authored or co-authored or at present working on? Articles----- Dissertation :_____			
B	Knowledge of Ethical Guidelines and Principle		
1a	Are you aware of existing ethical guidelines in biomedical research?	(1) Yes	(2) No
1b	If yes, how did you get the knowledge? 1) During the medical training 2) From research ethics seminars/workshop 3) Through research work activities 4) Others (specify)		

	11	Please indicate whether the following aspects of research are/might be important for ethical consideration?	
		Tick the appropriate answer in this order: very important=1; Important=2; Not so important= 3; Not important=4	
	2a	Research design.	
	2b	The use of placebo controlled trials.	
	2c	Community participation in clinical trials	
	2d	The interpretation of clinical studies.	
	2e	Determination of appropriate subject selection.	
	2f	Determination of potential risks of research such as HIV vaccine research.	
	2g	Assessment of anticipated benefits.	
	2h	Provision of appropriate risk reduction interventions.	
	2i	Provision post trial benefits.	
	2j	Enrolment and retention of women in clinical trials	
	2k	Incentives for research participants.	
	2l	Understanding of informed consent.	
	2m	Assessment of cultural sensitivity for informed consent.	
	2o	Privacy and confidentiality.	
	2p	Determinations to run Clinical Trials phases (I, II, III) in a country or community	
	2q	Risk/benefits ratio of the proposed research.	
	2r	Monitoring and oversight.	
	2s	Respect for the research participants	
	<i>Please Choose one by a tick</i>		
3a	Do you think you have been applying ethical principles in all your research work where human participants are involved		
3b	If your answer is no, which research areas do you consider not necessary for application of these principles? 1) Clinical trials 2) Qualitative research 3) Descriptive studies 4) Case reports 5) Analytic studies Others (specify)		

4a	Which of the following international bodies on ethical guidelines and practice are you familiar with? 1) Council for International Organisations of Medical Sciences (CIOM) 2) World Medical Association Declaration of Helsinki 3) Nuremberg Code by United Nations 4) Belmont report 5) Nuffield 6) other (specify)			
4b	How did you get the knowledge of these international bodies on ethical guideline and practice? 1) At medical school 2) At residency training programme 3) As a qualified specialist 4) Other (specify)			
C	Applications and Compliance with Ethical Guidelines			
5	Please mark the appropriate answer (1=yes, 2=no, 3=don't know (DK)): In your institution, is it possible to conduct biomedical research without any ethics approval?	(1) Yes	(2) No	(3) DK
6a	Do you know if there is any regulation that governs ethical review of biomedical research in your institution?	(1) Yes	(2) No	(3) DK
6b	If yes, how often do you comply with the regulation during research 1) Always 2) Occasionally 3) Never			
7a	Is there any research you have done in the past which you did not consider application of Ethical guidelines and principles necessary?	(1) Yes	(2) No	(3) DK
7b	If yes, reasons? 1) Research considered minimal risk to the participants 2) Questionnaire based research 3) Post data collection and analysis 4) Others (specify)			
8a	Do you think applying the standard ethical guideline and practice to protect human participants will in one way or the other be an impediment to Successful completion of your research project?	(1) Yes	(2) No	(3) DK

8b	If yes, in what way? 1) Difficulty in getting participants 2) Unnecessary delay in the research process 3) Research may become cumbersome 4) Others (specify)			
9	What do you consider as an impediment to ensuring the protection of research participants in our environment, Nigeria?			
9a	1) Lack of research ethics awareness	(1) Yes	(2) No	(3) DK
9b	2) Non compliance with research ethics principles	(1) Yes	(2) No	(3) DK
9c	3) Limited number of Research ethics committees	(1) Yes	(2) No	(3) DK
9d	4) No regulation on research ethics guidelines	(1) Yes	(2) No	(3) DK
9e	Other (specify)			
D	Involvement of Research Ethics Committee for protocols approval			
10	<i>Please mark the appropriate answer (1=yes, 2=no</i> Is there an existing research ethics review board in the institution you are presently working and carrying out research?	1) Yes	(2) No	
11	Are you familiar with the workings of Research Ethics Committees (RECs) or Institutional Review Boards (IRBs)?	(1) Yes	(2) No	
12a	If there is no REC in your working place have you been carrying out research without ethical approval?	(1) Yes	(2) No	
12b	If your answer is no, how do you get your research protocol approved? 1) Send to any available REC for approval 2) Never mind getting approval 3) Others (specify)			
13	If you have REC in your centre, do you send your protocol for approval before embarking on your research work? 1. never 2. Occasionally 3. always 4. other (specify)			

14a	How many proposals have you submitted to the REC in your centre? (1) 0 –5 (2) 6-10 (3) 11 – 15 (4) 16 – and more			
14b	How many of these proposals have been approved? 1) all of them 2) some of them 3) Don't know			
15	If and when you send a protocol and it is rejected what do you do? 1) Go ahead with the research 2) Send the protocol to another Research ethics committee 3) Abandon such protocol			
16	What are the reasons often given for rejection of your protocol? 1) Research has substantial risk to the participants 2) Incomplete submission of a proposal (e.g. missing of Information leaflet; Informed consent form) 3) Not well developed proposal 4) Duplication of other ongoing or completed research			
17	Are you satisfied when your research protocol is rejected if such research may constitute a serious harm to the participants in an environment with limited options of standard of Care such as ours? 1) Always 2) Occasionally 3) Never			
18	Do you think REC should ensure strict compliance with the ethical guidelines at all times?	(1) Yes	(2) No	
19	<i>Please mark the appropriate answer (1=yes, 2=no, 3=don't know (DK)):</i> What challenges do you think your REC is facing to ensure that researchers in your institution comply with ethical guidelines?			
	1) Conflict of interest among REC members	(1) Yes	(2) No	(3) DK
	2) Pressure from sponsors	(1) Yes	(2) No	(3) DK
	3) Preferential treatment of applicants in the review process	(1) Yes	(2) No	(3) DK
	4) Lack of members with adequate research ethics knowledge	(1) Yes	(2) No	(3) DK

	5) Lack of transparency of REC members	(1) Yes	(2) No	(3) DK
	6) Other (please specify)			
20	Do you think invitation of Researchers to attend a session during discussion of their proposal would be beneficial?	(1) Yes	(2) No	(3) DK

APPENDIX 2
Ethical Clearance Certificate
University of Nigeria Teaching Hospital

UNIVERSITY OF NIGERIA TEACHING HOSPITAL
ITUKU-OZALLA, P.M.B. 01129, ENUGU, NIGERIA,

TEL: 042-252022, 252573, 252172, 252134, Fax: 042-252665
 E-mail: cdunth@infoweb.abs.net

Prof. O. O. MBONU, MB (Lond.), FRCS(c), FWACS
 Chairman, U.N.T.H. Management Board

Barr. (Mrs.) M. U. OKONKWO, LL.B. (HONS) BL, NFA, MNSM, PMY, FCAI
 Director of Administration/Secretary
 U.N.T.H. Management Board



Dr. A. U. MBAH, MD (LOND), FMCP, FRCR, (KSA)
 Chief Medical Director

Dr. C. C. AMAH, MBBS, FWACS, FCS, MNM, MWPR
 Chairman, Medical Advisory Committee

Our Ref..... UNTH/CSA.329/Vol.6

Date..... 5th January, 2010

NHREC/05/01/2008B
ETHICAL CLEARANCE CERTIFICATE

TOPIC ATTITUDE, KNOWLEDGE AND COMPLIANCE WITH ETHICAL
GUIDELINES IN CLINICAL RESEARCH AMONG MEDICAL
RESEARCHERS IN NIGERIA.

BY DR. F. N. CHUKWUNEKE

FOR RESEARCH PURPOSE

This research project on the above topic was reviewed and approved by the University of Nigeria Hospital Research Ethics Committee.

This certificate is valid for one year from date of issue.


Prof. R.F. Umeh
 Chairman, Health Research Ethics Committee.

Date: 07/01/10

APPENDIX 3
Ethical Clearance Certificate
University of Pretoria, Faculty of Health Sciences

The Research Ethics Committee, Faculty Health Sciences, University of Pretoria complies with ICH-GCP guidelines and has US Federal wide Assurance.

* **FWA** 00002567, Approved dd 22 May 2002 and Expires 13 Jan 2012.

* **IRB** 0000 2235 IORG0001762 Approved dd Jan 2006 and Expires 13 Aug 2011.



UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Health Sciences Research Ethics Committee
 Fakulteit Gesondheidswetenskappe Navorsingsetiekkomitee

DATE: 3/05/2010

PROTOCOL NO.	65/2010
PROTOCOL TITLE	Attitude, Knowledge and Compliance with Ethical guidelines in clinical research among medical researchers in Nigeria
INVESTIGATOR	Principal Investigator: Dr F N Chukwuneke
SUBINVESTIGATOR	None
SUPERVISOR	Prof Mariana Kruger
DEPARTMENT	Dept: Phone: E-Mail: @yahoo.com
STUDY DEGREE	MPH
SPONSOR	SARETI
CONTACT DEATAILS	Representative: Dr Theresa Rossouw Phone: 012 3541319 Fax: 012 354 1367 E-Mail: rossouw@up.ac.za Mobile: 0828942224
VAT NO.	Not Applicable
SPONSORS POSTAL ADDRESS	University of Pretoria, Faculty of Health Sciences, HW Snyman Building level 2-15 , Box 667, Pretoria 0001 South Africa
ORDER / CONTRACT NUMBER	Not Applicable
MEETING DATE	21/04/2010

The **Protocol and Informed Consent Document** were approved on **21/04/2010** by a properly constituted meeting of the Ethics Committee subject to the following conditions:

1. The approval is valid for 2 years **period**, and
2. The approval is conditional on the receipt of 6 monthly written Progress Reports, and
3. The approval is conditional on the research being conducted as stipulated by the details of the documents submitted to and approved by the Committee. In the event that a need arises to change who the investigators are, the methods or any other aspect, such changes must be submitted as an Amendment for approval by the Committee.

