

TANZANIA NATIONAL HEALTH RESEARCH .FORUM

**GUIDELINES OF ETHICS FOR HEALTH
RESEARCH IN TANZANIA**

**Prepared by the National Health Research
Ethics Committee**

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TABLE OF CONTENTS

DEDICATION

This work is dedicated to all persons and animals that have been involved and will continue to be involved in health research either as human subjects or as experimental animals in the search for new knowledge for the better care of mankind.

FOREWORD

Guidelines on Ethics for Health Research in Tanzania (Second Edition, 2009)

FOREWORD

Once again, Professor Yohana Mashalla is to be congratulated for the commendable work that he has done in revising and upgrading this very important document relating to health research, the Guidelines on Ethics for Health Research in Tanzania. Among the most useful additions to the First (and very popular) Version of 2001 is the inclusion of sections on i) a wide range of important Definitions of Health Research Terminologies, ii) Socio-cultural Factors in Health Research, and iii) the increasing number of categories of Vulnerable People in the community, with a timely caution on undue reliance on research protocols emanating from developed countries for 'exclusive' use in developing countries.

May I also take this opportunity to extend our appreciation to other members of the TANHER Forum Ethics Editorial Task Force, Dr Andrew Kitua and Dr Godwin Ndossi, and others, for their valuable inputs that have helped to enrich this document, since it was first published in 2001.

As with the first version of the Ethical Guidelines, I have no hesitation in warmly recommending this Second Version to all its users, ranging from health researchers themselves to health trainees and practitioners and also to health policy makers and administrators at all levels.

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PREFACE

This is the first publication of guidelines on research ethics by the National Health Research Ethics Committee. It aims at providing health researcher in Tanzania with guidelines that will assist them to carry out health research in accordance with accepted ethical standards and norms.

Health research has in recent years become a subject of great interest and attracts funding from both local as well as international collaborators. There is a growing trend for health research in developing counties to rely on protocols that have been developed elsewhere. Researchers in these countries have sometimes engaged themselves in researches over which they have no control, and the utilization of which have no relevance to their own countries. Such reseats have triggered concern in the sense of physical or psychological harm. With increasing categories of vulnerable people in the community e.g. pregnant women, street children, prisoners, orphans and detainees, refuges, PLWA and AIDS patient, the need for guidelines on health research has become even more pressing.

In preparing these Guidelines, special attention was given to socio-cultural factors that are pertinent to Tanzania. At the same time the Editorial Board wisely decided not to re-invent the wheel. Therefore, cross-reference was made to a number of excellent reports; Special gratitude is given to the Royal College of Physicians of London, the BMA, CMA, MAT CIOMS, WMA, the SAMRC and the Code of Federal Regulations ICH Guidelines whose publications formed the basis for these guidelines. It is anticipated that the guidelines will find a place in research and training institutions, as well as the hospitals, in Tanzania. The process of establishing useful ethical guidelines is dynamic and requires more inputs so that it can continuously be tailored to fit the needs of a dynamic environment. In this edition, the scope and descriptions have been expanded to make the document much more reader friendly.

It is now my privilege to thank all members of the National Health Research Ethics Committee, as well as member of the special Forum Editorial Task Force for their dedication and hard work. Without their commitment, this exercise would not have been possible.

A very special word of thanks goes to members of the Editorial Board, the National Institute for Medical Research, Tanzania Food and Nutrition Centre and the Tanzania Commission for Science and Technology for their continued support. I sincerely also wish to thank those whose thoughts have in one way or another enriched this document, many thanks to all of you. Finally, my sincere appreciation are directed to EDCTP for providing financial support which enabled the revision of the previous national guidelines into the current state.

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ACRONYMS

AIDS	Acquired Immune Deficiency Syndrome
BMA	British Medical Association
CIOMS	Council for International Organizations of Medical Sciences
CMA	Commonwealth Medical Association
COHRED	Council on Health Research for Development
COSTECH	Commission for Science and Technology
EDCTP	European and Developing Countries Clinical Trial Programme
FRCS	Fellow of the Royal College of Surgeons
GMC	General Medical Council
HIV	Human Immunodeficiency Virus
HRUTF	Health Research Users Trust Fund
ICRIA	Institutional Committee for Research Involving Animals
IREC	Institutional Research Ethics Committee
MAT	Medical Association of Tanzania
MB ChB	Bachelor of Medicine and Bachelor of Surgery
MD	Doctor of Medicine
MRCC	Medical Research Coordinating Committee
NHRCC	National Health Research Coordinating
NHREC	National Health Research Ethics Committee
NIMR	National Institute of Medical Research
PhD	Doctor of Philosophy
PLWA	People Living with AIDS
RCT	Randomized Controlled Trials
SAMRC	South African Medical Research Council
TANHER	Forum Tanzania National Health Research Forum
TDR	Special Programme for Research and Training in Tropical Diseases
TFNC	Tanzania Food and Nutrition Centre
WMA	World Medical Assembly

DEFINITIONS

The primary objective of this section is to introduce readers, researchers and the general populations to the meaning of the terms as well as providing a common understanding for easy communication and reference. In this document, unless stated otherwise:

(i) Adverse event

Is an untoward medical occurrence in a participant in a clinical trial administered a pharmaceutical product and that does not necessarily have a causal relationship with the treatment. An Adverse event can therefore be any unfavourable and unintended sign, symptom or disease temporarily associated with the use of a pharmaceutical product, whether or not related to the pharmaceutical product.

(ii) Applicable regulatory requirement(s)

Applicable regulatory requirement(s) is any law(s) and regulation(s) addressing the conduct of clinical trials of investigational products of the jurisdiction where trial is conducted.

(iii) Biomedical Research

Biomedical research may be defined as activities involving subjects undertaken with the prime objectives of testing a hypothesis and permitting conclusion to be drawn for the purpose of contributing to medical knowledge. The spectrum of biomedical research is such that on one end it consists of studies of analysis of identifiable or non-identifiable data without any subject/ patient contact, or change in medication. On the other end of spectrum, there are studies that involve changing a patient from a proven treatment to a different regime but the benefit and risks of which are not fully known. Biomedical research may either be “Therapeutic” or “Non-therapeutic” in nature.

(iv) Children

Children means persons who have not attained the legal age for consent to treatments or procedures involved in clinical trials, under the applicable law of the jurisdiction in which the clinical trial will not be conducted.

(v) Clinical trial

Clinical trial means any investigation in human subjects intended to discover or verify the clinical, pharmacological, and/or other pharmaco-dynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the primary objective of ascertaining its safety and/or efficacy. In most cases the terms clinical trial and clinical study are used interchangeably.

(vi) Closed system

Closed system means an environment in which system access is controlled by persons who are responsible for the content of electronic documents that are on the system.

(vii) Confidentiality

Confidentiality is the prevention of disclosure, to other than authorized individuals, of a sponsor's proprietary information or of a subject's identity.

(viii) Digital signature

Digital signature means an electronic signature based upon cryptographic method of originator authentication, computed by using a set of rules and a set of parameters such that the identity of the signer and the integrity of the data can be verified.

(ix) Data Safety and Monitoring Board

Data Safety and Monitoring Board is an independent Board or Committee that may be established by the sponsor to assess at intervals the progress of implementation of

a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a clinical trial.

(x) *Electronic document/record*

An electronic document/record means any combination of text, graphic, data, audio, pictorial or other information representation in digital form that is created, modified, archived, retrieved or distributed by a computer systems.

(xi) *Electronic signature*

An electronic signature means a computer data compilation of any symbol or series of symbols executed, adopted or authorized by an individual to be the legally binding equivalent of the individual's handwritten signature.

(xii) *Flawed research*

Flawed research is defined as an imperfect research that contains mistakes either in the design, planning implementation, interpretation or dissemination of the research results.

(xiii) *Foetus*

Foetus means the product of conception from implantation until delivery. A nonviable foetus means a neonate after delivery that although living, is NOT viable. A viable neonate however, means, a foetus after delivery being able to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beats and respiration.

(xiv) *Guardian*

Guardian means an individual who is authorized under applicable local law to consent on behalf of a child to general medical care when general medical care includes participation in research. It also means an individual authorized to consent on behalf of a child to participate in a clinical trial or research.

(xv) Hand written signature

Hand written signature means the scripted name or legal mark of an individual hand written by that individual and executed or adopted with the present intention to authenticate writing in a permanent form. The act of signing with a writing or marking instrument, such as a pen or stylus is preserved. The scripted name or legal mark, while conventionally applied to paper, may also be applied to other devices that capture the name or mark.

(xvi) Healthy volunteers

“Healthy volunteers” are defined as individuals who do not suffer from any significant illness relevant to the proposed study. Individuals who are temporarily “healthy” but they are only on a remission from a relapsing condition cannot be considered healthy volunteers for a study related to that condition.

(xvii) Human subject

A human subject is an individual who is or becomes a participant in research, either as a recipient of the test product or as a control. A subject may either be a healthy human or a patient.

(xviii) Informed consent

Is a process by which an individual voluntarily confirms his or her willingness to participate in particular trial, after having been informed of all aspects of the research that are relevant to the individual’s decision to participate. Informed consent is documented by means of a written, signed and dated consent form.

(xix) Innovative Treatment

Is a procedure where for specific reasons pertinent to a specific patient, the clinician digresses from what is accepted as normal practice. The primary objective of innovative treatment is to provide alternative treatment to the patient.

The responsibility for deciding and employing, innovative treatment lies entirely on the clinician. When the digression is small and designed merely to deal either the

particular circumstances of an individual patient, it is wise to consider an extension of the treatment. However, when a major digression is being considered for regular use, while it has not been approved for medical practice, the innovation should become subject of formal research so that its true worth can be evaluated. In the eyes of many people, therefore, innovative treatment straddles the gap between research and medical practice.

(xx) Institution

An institution means any public or private entity or agency or medical, dental or non-medical or dental facility where clinical trials or health research are conducted.

(xxi) Institutional Ethics Review Committee

An Institutional Ethics Review Committee means a board or other group formally designated by an institution to review biomedical research involving humans as subjects, to approve the initiation of and conduct periodic review of such research. In these guidelines, the term carries the same meaning as Institutional Review Board.

(xxii) Investigator/researcher

The investigator/researcher means an individual who actually conducts an investigation i.e. under whose immediate direction the test product is administered or dispensed to, or used involving, a subject, or in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

(xxiii) Legally acceptable Representative

A legally acceptable representative is an individual or juridical or other body authorized under applicable law(s) to consent on behalf of a prospective subject, to the subject's participation in a clinical trial or any other health research.

(xxiv) Medical practice

Medical practice means the practice of physicians in the course for diagnosis, prescription of, and administration treatment of patients or non-sick individuals in clinics and bedside.

(xxv) Minimal risk

Minimal risk mean that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or investigations.

(xxvi) Monitoring

Monitoring is the process of overseeing the progress of implementation of a clinical trial or health research and of ensuring that it is conducted, recorded and reported in accordance with the approved protocol/proposal, standard operating procedures (SOPs), and the applicable regulatory requirement(s).

(xxvii) Multi-centre trial

Is a clinical trial or any other health research conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator and institutions.

(xxviii) Neonate

A neonate means a newborn.

(xxix) Non-therapeutic research

Is defined as activities or treatment whose prime objective is to extend knowledge about a particular condition in such a manner that the benefits are for the future. It may either involve healthy volunteers or patient and is carried out with the purpose of testing a hypothesis and contributing to the knowledge.

(xxx) Open system

An open system means an environment in which system access is not controlled by persons who are responsible for the content of electronic documents/records that are not on the system.

(xxxi) Patients

“Patient” in the research context is defined as individuals with a known illness and has been recruited in the research study because of any of the following:

- Have sought medical attention,
- Have a known illness or disability of interest to the research,
- Form a control group of subject suffering from an illness which is not of interest to the proposed study.

(xxxii) Permission

Permission in the context of the guidelines means the agreement of parent(s) or guardian to the participation of their child in clinical trial.

(xxxiii) Pregnancy

Pregnancy encompasses the period of time from implantation until delivery. A woman shall be considered to be pregnant if she exhibits any pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

(xxxiv) Prisoner

Prisoner means any individual involuntarily confined or detained in a penal institution. The term is intended to include individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial or sentence.

(xxxv) Protocol

A protocol is a document that describes the summary (abstract), background, rationale, objective(s), design, methodology, statistical considerations, and organization of a clinical trial or health research. Occasionally the terms protocol and proposal are used interchangeably.

(xxxvi) Protocol/proposal amendment

Protocol/proposal amendment is a written description of a change or changes made to or formal clarification of the original protocol or proposal(s).

(xxxvii) Randomization

Randomization is a process of assigning trial/research subjects to treatment or control groups by using an element of chance to determine the assignment in order to reduce bias.

(xxxviii) Sponsor

Sponsor means a person who initiates a clinical trial, but who does not actually conduct the investigation, i.e. the test product is administered or dispensed to or used involving, a subject under the immediate direction of another individual.

(xxxix) Standard Operating Procedures (SOPs)

Standard Operating Procedures are detailed, written instructions aimed at achieving uniformity in the performance of a specific function.

(xl) Student

A student is defined as a pupil or any person admitted to a primary or secondary school, tertiary institution, college or university for the purpose of acquiring primary, secondary, technical or university education in Tanzania or any other institution to which a researcher has direct or indirect control.

(xli) Test product

A test product means any drug (including a biological product for human use), medical device for human use, human food additive, colour additive, electronic product, or any other product subject to TFDA Act.

(xlii) *Therapeutic research*

The world Medical association first published its Code of Ethics on Human experimentation the Helsinki Declaration in 1964 and modified it in 1975. *The Ethical Code states that; "In the field of biomedical research a fundamental distinction must be recognized between medical researches in which the aim is essentially diagnosis or therapeutic for a patient, and medical research, the essential object of which is purely, scientific and without implying direct diagnostic or therapeutic value to the person subjected to the research".* Therefore, therapeutic research means research intended to benefit a subject by establishing diagnosis and treatment.

(xliii) *Vulnerable subjects*

Vulnerable subjects in health research are individuals whose capacity and willingness to volunteer in a clinical trial or health research may be unduly influenced by the expectation(s), whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in the case of refusal to participate (e.g. student, military, subordinate staff, persons with incurable diseases, unemployed, patients in emergency situations, refugees, minors, impoverished persons and those incapable of giving consent).

(xliv) *Well-being*

The well-being of the trial subjects means the physical and mental integrity of the subjects participating in a clinical trial.

INTRODUCTION

Research or experimentation connotes a set of activities undertaken to test a particular hypothesis with the intention of drawing conclusions about a given unknown situation. Medical research specifically refers to the scientific investigations carried out for the purpose of contributing to medical knowledge. It is the means by which 'scientists discover new knowledge that may lead to the prevention or treatment or even elimination of certain categories of disease and disability' (CIOMS, 1993).

Confusion sometimes arises from the wide range of procedures covered under the term 'medical research'. In defining medical research, a distinction has to be made between research that consist of analysis of identifiable or non-identifiable data without any patient contact or change of medication, and research that involves changing a patient from one regimen of known benefits (efficacy) to one the benefit and risks of which are not fully known. With increasing diversity in the health profession and involvement of social scientists in health related studies, the term 'Health Research' is now increasingly becoming more acceptable than "medical" or "biomedical research"

The history of human experimentation is ancient and for centuries, society's attitude to medical research had been very positive. In the 18th century, convicted prisoners of Newgate jail volunteered for medical experimentation in exchange for their freedom. In recent years people living with HIV/AIDS (PLWA), women, homosexuals, cigarette smokers and other groups have sought to be included in medical studies mostly in anticipation of finding relief of suffering, prolongation of life, getting cured from their disease conditions and/ or, in a few cases, simply to contribute to the advancement of medical knowledge.

However, this positive attitude changed following the Second World War, when it became clear that Nazi research physicians committed atrocities in the concentration

camps in the name of medical research. This raised serious world concern and led to the formulation of the first international code of ethics, the Nuremberg Code, for research involving human subjects. Subsequently two other guidelines namely, the Declaration of Helsinki (Declaration) and the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Guidelines) have been formulated and implemented worldwide. The Declaration was formulated by the World Medical Assembly (WMA) while the Guidelines were formulated by the Council for International Organizations of Medical Sciences (CIOMS). The CIOMS guidelines specifically related to the application of the Declaration, particularly in developing countries. In addition, many countries including developing countries have formulated country specific guidelines on ethics of biomedical research taking into account the country's, unique socio-cultural, political, economic, religious and moral factors.

Another development in the formulation of guidelines was the publication of a report in London in 1986 by the Royal College of Physicians on Research on Healthy Volunteers. The publication defined "healthy volunteers" and also described the risks associated with biomedical research and the possible safeguards for the volunteers, sponsors and Research Ethics Committee. Further development was made in 1990 when the London Royal College of Physicians published guidelines on Research Involving Patients. Development of such guidelines was pivotal to the future understanding of this importance of maintaining ethical standards in research involving human subject. The fundamental principle in all of the guidelines is the value placed on human life and the protection of the rights and welfare of all human subjects who participate in scientific experimentation.

Apart from medical students and nurses, the vast majority of health research or human experimentation are carried out in lay people who, as is the case in many developing countries are poor, illiterate and lack awareness of both civil and consumer rights. Moreover, the doctor-patient or researcher-subject relationship is still skewed in favour of the former. In Tanzania, the attitudes about the relation are

changing and research subjects and patients rightly expect both information and support. The fact that this is not easy for either side is well described by Faulder ⁷.

“Doctors do not like to confess about their own doubts and worries; indeed they regard such revelations as a sign of weakness, a threat to the patient’s morale and a major offence against the canon of trust in the patient-doctor relationship. But who has established this canon of trust? And why is it that trust is almost uniquely in terms of patient’s confidence in the doctors? Seldom do we hear about doctors trusting their patient. Trust between two people, if it is to mean anything must be reciprocal”

The sentiment expressed above underscore the importance of mutual between the health professionals and patients or research subjects who in many cases, will not accept to participate in research if they feel suspicious about consent. Veracity is therefore, an essential element especially in the complex undertaking involving human experimentation. The problems associated with telling truth include that of undermining the subject’s morale and confidence, or introducing difficult decision at a vulnerable time. On the other hand, evidence suggests that uniformed subjects may also be alarmed, anxious and subject to considerable stress, balance between these two opposing feelings is crucial in cultivating trust between researcher and the human subject.

Tanzania has a number of training and research institutions that carry out research on a variety of national health research priority areas. Due to the phenomenon of globalization and given the pace at which medical science and technology is changing, health researchers are constantly exposed to new ethical dilemmas, and in some cases, those dilemmas are in direct conflict with their professional ethics. It is the opinion of the National Health Research Forum that researchers of today in Tanzania need to be thoroughly grounded and guided in the health related components of human rights and ethics for them to be able to analyze the complex issues raised by the political, socio-economic and cultural changes in society. The

purpose of the National Health Research Ethic Guidelines is to provide guidance to researchers and other stakeholders on how to balance between the rights of individuals and the need of the society within the context of health research.

CHAPTER ONE

1.1 RATIONALE FOR HEALTH RESEARCH GUIDELINES

As earlier stated, Tanzania is one of the poor countries in the world still fighting poverty, illiteracy and diseases. Unlike in the developed world, the Tanzania people still have communicable diseases contributing significantly to the burden of diseases. Currently, unlike in the past, there is an increasing trend of non-communicable diseases. The prevalence of diabetes, cardiovascular accidents, hypertension, occupational diseases etc are more than a decade ago. Care must therefore be taken to ensure that such vulnerability is not exploited.

The need for research involving human subjects has for years been beyond argument. This is because researches on human subjects provide knowledge on the physiology and psychology of disease pattern. In addition, there are situations where there is no evidence of studies and results from experimental animals, the drugs need to be tested in human subjects to determine efficacy and safety.

Research in healthy volunteers has advantages in that physiological variations are likely to be minimal and the response more uniform. However, research in the patients must be carried out in the best interest of the patient although the individual patient may not benefit from the research. The society on the other hand may in the future benefit from the research results.

It is now generally accepted that it is unethical to use healthy individuals on a trial of a drugs with known side effects within therapeutic closed. However, in trials involving drugs with known side effects, it is better that the drug is tried first in patients suffering from a known illness, who are more likely to benefit from the trial.

In addition, since WMA prescribed guidelines on Biomedical Research; there has always been good concern for flawed research involving human subjects because flawed researches have continued to be reported even in recent years. Therefore,

there is a need for any country to put in place guidelines and regulations that will safeguard the interests of research participants during research.

The need for achieving good standards has prompted many countries to develop guidelines and regulation for safeguarding the interests of research participants. This stems from the fact that the apprehension of patient and societies about biomedical research is justified. Therefore, society and professionals must concentrate on building an ethical framework that will permit research activities to progress, but at the same time, maintain public confidence that individual autonomy is respected.

1.2 Machinery for approving and monitoring health research

A pre-requisite to achieving good standards is by ensuring that there is a well functioning and efficient system of regulating and monitoring the conduct of research, and reporting, is in place at all levels.

1.2.1 Research Ethics Committees

Worldwide, National, Institutional or Local Research Ethics Committees exist and have the responsibilities of monitoring the research conduct and approving health research proposals for ethical clearance. In Tanzania, most institutions that engage in health research have established Institutional Research Ethics Committee (IRECs). The IRECS are appointed by Appointing Authorities in the institutions and the sizes of the committees vary significantly. A sizable committee consisting of up to twelve members would be most appropriate. The WHO Guideline, (2000) stipulates that a minimum should be five members. Unfortunately, most IRECS are challenged by a number of problems making them unable to function according to their terms of reference. The problems facing IRECS range from lack of funds, training, competence, independence to practice, clear job description and the more serious lack of legal backing. In 1983, the BMA drew up guidelines on what was to be considered in ideal composition of Local Research Ethics Committees. There was general agreement that committees should have:

- (i) Gender balance so that both men and women are well represented;
- (ii) Senior as well as junior members of the profession;
- (iii) Representative from the nursing profession;
- (iv) A Pharmacologist;
- (v) A Pharmacist or Pathologist;
- (vi) A Lay member to represent the views of the community in general; and
- (vii) A Chairman who is appointed from among committee members or in some cases appointed from among researchers in the institutions and holding the post for duration determined by the institution.

Subsequent studies in England have shown that most IRECs were dominated by doctors, while women and lay members of the society were under-represented. The general view should be that IRECs should have a separate panel of experts who could be co-opted when required to obviate the imbalances.

1.2.2 Institutional Ethics Research Committees (IRECs)

In 1991, the London Royal College of Physicians described the Guidelines on the Practice of Ethics Committees in Medical Research Involving Human Subjects. The primary objectives of the IRECs are to ensure that:

- (i) Ethical standards in research are maintained;
- (ii) Research subjects and research workers are protected from harm and any form of exploitation;
- (iii) The rights and autonomy of research subjects are preserved;
- (iv) The public is reassured that the research is being conducted in an acceptable manner and in the best interests of the community.

1.2.3 Function of IRECs

All research involving human subject must be subjected to IRECs for peer review. In reviewing the protocols, consideration should always be given to the following:

- (i) Scientific quality of the protocol should be critically assessed. The proposed study should be designed with a view of obtaining what is considered to be the problem for study by involving as few as possible people who will be exposed to minimal risks as much as possible. It should be borne in mind that a poorly designed study, which might not yield scientifically desirable results, is unethical;
- (ii) The objectives of the proposed study should be directed at advancing biomedical knowledge and in line with the prevailing community interests;
- (iii) Competence of the investigator in terms of qualification, knowledge and experience in the area of the proposed study. Similarly, the competence in handling proposed research equipment and procedures and in ensuring that research subjects are protected from harm;
- (iv) For all research proposals, there is adequate literature review on the proposed subject and that risks have been studied and measures for preventing risks have been clearly defined. A thorough literature review is essential to avoid duplication of what may have been studied already;
- (v) Determine whether efforts have been made to ensure that prospective research subjects will adequately be provided with information on the aims, the methods, benefits and risks they are likely to be subjected to by agreeing to participate in the study;
- (vi) Assess whether the procedure for seeking consent from prospective research subjects are adequately detailed and non-ambiguous. Also determine whether appropriate safeguard have been made to ensure that the rights of the participating subjects would not be abused;
- (vii) Assess the proposed provisions for storage and handling of data and how subject-identifiable information will be used. Appropriate measures should be proposed to ensure confidentiality of all data generated in the course of the research;

- (viii) Investigate research fraud and take appropriate or recommended to relevant authorities for immediate action where scientific fraud has been suspected or proved;
- (ix) Offer Class Approvals to investigators who conduct multiple projects, which pose no, risks e.g. some projects in epidemiology or training. This will reduce repetitive submissions from the same researchers;

For effective operations, IRECs should hold meeting as frequently as possible as a strategy to facilitate fast ethical clearance and minimize complaints of delays; the Chairman may be given powers to approve minor matters on behalf of the Committee, but ensure that the papers are made available to the rest of the members of IREC at the next meeting; and The committees should have powers to co-opt professional or lay members for particular or specific signed where necessary.

1.2.4 Criteria for IREC approval of research

In order to approve research covered by these guidelines, the IREC shall determine all of the following requirements are satisfied:

- (i) Risks to subjects are minimized:
 - (a) By using procedures that are consistent with sound research design and which do not unnecessarily expose subjects to risk; and
 - (b) Whenever appropriate, by using procedures already being used on the subjects for diagnostic or treatment purposes.
- (ii) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result. In evaluating risks and benefits, IREC should consider only those risks and benefits that may result from the research. The IREC should not consider possible long range effects of applying knowledge gained in the research as among those research risks that fall within the purview of its responsibility.
- (iii) Selection of subjects is equitable. In making this assessment IREC should take into account the purposes of the research and the setting in which the research

will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations.

- (iv) Informed consent will be sought from each subject or the subject's legally authorized representative.
- (v) Informed consent will be appropriately documented.
- (vi) Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of the subjects.
- (vii) Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality.
- (viii) When some or all of the subjects such as children, pregnant women, prisoners, handicapped or mentally disabled persons, or economically or educationally disadvantaged persons are likely to be vulnerable to coercion

1.2.5 The Roles of Health Research Ethics Committees

- (i) The national and institutional ethical committee have the duty to ensure that the dignity, rights, safety and well being of all actual and potential research participants are safeguarded during the process of conducting research. These roles are in accordance with the operational guidelines of ethics committees that review biomedical research, developed by the World Health Organization (TDR/PRD/Ethics/2000.1).
- (ii) The committees must be composed of competent individuals in reviewing research work that must always be independent of any political, religious, or financial pressures while reviewing the relevant proposals. If at any time a member of the committee should have any conflict of interest in a particular proposal including authorship, then such a member should not participate in reviewing the particular proposals but should be replaced by any other person with similar competence but who has no such conflict of interest.
- (iii) It shall be the responsibility of every member of the committee to sign a form declaring no conflict of interest before reviewing any proposal.

- (iv) The health research committees should be multidisciplinary and multi-sectoral in composition, and taking into consideration gender representation. It must perform its duties of reviewing proposals in the interest of actual and potential research participants and concerned communities. In performing their work, the committees have to pay due attention to the requirements of the relevant regulatory agencies and applicable laws of Tanzania.

1.2.6 Safeguards for children in clinical investigations

Research Ethics Committee at all levels shall in addition to other responsibilities and guidelines contained in this document review critically clinical investigations involving children and approve only those clinical investigations that satisfy the conditions described below:

(i) Clinical investigations not involving greater than minimal risks

IREC may approve any clinical investigation involving children only as subjects in which no greater than minimal risk to children is presented; and only if IREC finds and documents that adequate provisions have been provided for soliciting the assent of children and the permission of their parents.

(ii) Clinical investigations involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects

Any clinical investigation in which no more than minimal risk to children is presented by an intervention procedure that holds out the potential of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, may involve children as subjects only if IREC finds and documents that:

- (a) The risk is justified by the anticipated benefits to the subject;
- (b) The relation of the anticipated benefit to the risk is at least as favourable to the subjects as presented by available alternative approaches; and

- (c) Adequate provisions are made for soliciting the assent of their children and permission of their parents or guardians.

(iii) Clinical investigations involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalisable knowledge about subjects' disorder or condition

Any clinical investigation in which more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is not likely to contribute to the well-being of the subject, may involve children as subjects only if IREC finds and documents that:

- (a) The risk represents a minor increase over minimal risk;
- (b) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations;
- (c) The intervention or procedure is likely to yield generalisable knowledge about the subject's disorder or condition that is of vital importance for the understanding or amelioration of the subject's disorder or condition; and
- (d) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

(iv) Clinical investigations not otherwise approved that present an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children

If an IREC or NHREC does not believe that a clinical investigation involving children only as subjects does not meet the requirement in *(i)*, *(ii)* and *(iii)* above, the clinical investigation may be approved ONLY if:

- (a) The IREC or NHREC finds and documents that the clinical investigation presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children; and

- (b) The TFDA after consultation with experts in pertinent disciplines, and following opportunity for public review and comment, determines either:
- That the clinical investigation in fact, satisfies the conditions under this section; or
 - That the following conditions are met:
 - (i) The clinical investigation presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children;
 - (ii) The clinical investigation will be conducted in accordance with sound ethical principles; and
 - (iii) Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.
- (v) **Requirements for permission by parents or guardians and for assent by children**

In addition to the determinations required under this section, IREC or NHREC:

- (a) Must determine that adequate provisions are made for soliciting the assent of the children when in the judgement of the IREC the children are capable of providing assent;
- (b) In determining whether children are capable of providing assent, the IREC or NHREC must take into account the ages, maturity and the psychological state of the children involved. This judgement may be made for all children to be involved in clinical investigations under a particular protocol or for each children, as the Ethics Committee deems appropriate;
- (c) The assent of children is not a necessary condition for proceeding with the clinical investigation if IREC determines:
 - (i) That the capacity of some or all the children is so limited that they cannot reasonably be consulted;
 - (ii) That the intervention or procedure involved in the clinical investigation holds prospect of direct benefit that is important to the

health or well-being of the children and is available only in the context of the clinical investigation.

- (d) Even when it is established that the subjects are capable of assenting, IREC or NHREC may still waive the assent requirement if it finds and documents that:
 - (i) The clinical investigation involves no more than minimal risk to the subjects;
 - (ii) The waiver will not adversely affect the rights and welfare of the subjects;
 - (iii) The clinical investigation could not particularly be carried out without the waiver; and
- (e) Whenever appropriate, the subjects will be provided with additional pertinent information after participation;
- (f) In addition to the determinations required under this section, the IREC or NHREC must determine that the permission of each child's parents or guardian is granted; and
- (g) Where parental permission is to be obtained, IREC or NHREC may find that the permission of one parent is sufficient if consistent with the Laws of the country;
- (h) Where the clinical investigation requires obtaining parental permission, both parents must give their permission unless one parent is deceased, unknown, incompetent or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child;
- (i) Permission by parents or guardians must be documents in accordance with and to the extent described under Chapter 3 (3.5); and
- (j) When IREC or NHREC determines that assent is required, it must also determine whether and how assent must be documented.

1.2.7 Electronic records and electronic signatures

1.2.7.1 General consideration

Advances in science and technology have made life easier and transmission, storage and retrieval of records is now much more efficient. It is common practice now for Institutional Research Ethics Committee to receive electronic documents which contain electronic signatures. Therefore, there is a need to provide guidelines on the use of electronic documents and electronic signatures. This section therefore, describes the criteria under which IRECs will consider electronic records, electronic signatures, and handwritten signatures executed to electronic documents to be trustworthy, reliable and generally equivalent to paper records and handwritten signatures executed on paper. This section applies to records in electronic form that are created, modified, maintained, archived or transmitted under any record requirement set forth by IRECs or NHREC.

Where electronic signatures and their associated electronic records meet the requirement of this section, IREC or NHREC will consider the electronic signatures to be equivalent to full handwritten signatures, initials, and other general signings as required by IREC/NHREC.

Implementation of the guidelines on electronic records and signature will depend on how advanced are the receiving units at the respective IRECs and NHREC. As a general rule, for records submitted to the Committee, researchers and persons at the receiving units may use electronic record in lieu of paper records or electronic signatures in lieu of traditional handwritten signatures, in whole or part, provided that:

- (i) The requirements of this section are met;
- (ii) The document or parts of the document to be submitted have been identified by IREC/NHREC as being the type of submission the committee accepts in electronic form;
- (iii) Documents submitted to receiving units at IREC or NHREC not meeting the above condition shall not be considered as official if they are submitted in an electronic form.

1.2.7.2 Controls for electronic documents

There are two forms of controls for electronic documents (records); i.e. controls for closed systems and controls for open systems. The definition of each term has been provided under definitions.

(a) Controls for closed systems

Staff of IREC and NHREC who will be using closed systems to create, modify, maintain, or transmit electronic documents shall be required to employ procedures and controls designed to ensure the authenticity, integrity, and when appropriate, the confidentiality of electronic document, and to ensure that the signer cannot be repudiate the signed document as not genuine. Such procedure and controls shall include the following:

- (i) Validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered documents;
- (ii) The ability to generate accurate and complete copies of documents in both human readable and electronic form suitable for inspection, review, and copying by IREC/NHREC;
- (iii) Protection of documents to enable their accurate and ready retrieval throughout the document retention period;
- (iv) Limiting systems access to authorized persons only;
- (v) Use of operational system checks to enforce permitted sequencing or steps and events as appropriate;
- (vi) Use of authority checks to ensure that only authorized persons can use the system, electronically sign documents, access the operation or computer system input or output device, alter a record or perform the operation at hand;
- (vii) Determination that persons who develop, maintain or use electronic records and/or electronic signature systems have the education, training and experience to perform assigned tasks; and

- (viii) Use of appropriate controls over systems documentation including:
 - Adequate controls over the distribution of, access to, and use of documentation for system operation and maintenance;
 - Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation.

(b) Controls for open systems

Persons who use open systems to create, modify, maintain or transmit electronic documents shall apply similar to those for closed systems to ensure authenticity, integrity, and confidentiality from the point of creation to the point of receipt. In addition, additional guidelines such as ensuring document encryption and use of appropriate digital signature standards to ensure record authenticity, integrity and confidentiality.

1.2.7.3 Electronic signature manifestation

(a) General requirements

- (i) Signed electronic documents shall contain information associated with the signing that clearly indicates all of the following:
 - (a) The printed name of the signer;
 - (b) The date and time when the signature was executed; and
 - (c) The meaning (such as review, approval, responsibility or authorship) associated with the signature.
- (ii) The items identified under (i) of this section shall be subject to the same controls as for electronic documents and shall be included as part of human readable form of the electronic record.

(b) Electronic signature/document linking

Electronic signatures and handwritten signatures executed to electronic documents shall be linked to their respective electronic documents to ensure that the signatures

cannot be excised, copied, or otherwise transferred to falsify an electronic document by ordinary means.

1.2.7.4 Electronic signature general requirements

- (i) Each electronic signature shall be unique to one individual and shall not be reused, by or reassigned to anyone else;
- (ii) Before an IREC/NHRC establishes, assigns certifies, or otherwise sanctions an individual's electronic signature, the Committee shall verify the identity of the individual;
- (iii) Persons using electronic signatures shall, prior to or at the time of such use, certify to IREC/NHREC that the electronic signatures are intended to be the legally binding equivalent of traditional handwritten signatures; provided that:
 - (a) The certification shall be submitted in a paper form signed with a traditional handwritten signature;
 - (b) Persons using electronic signatures shall, upon IREC/NHREC request, provide additional certification or testimony that a specific electronic signature is the legally binding equivalent of the signer's handwritten signature.

1.2.7.5 National Health Research Ethics Committee (NHREC)

Upon realizing the level of vulnerability of its communities, Tanzania felt the need to have a system of ensuring that health research is coordinated and conducted in a more transparent way and observing ethical and human rights standards that will protect the community. The TANHER Forum was also established in 1991 to among other things, address matters related to ethics of research in the country. The National Health Research Ethics Committee was formed as an arm of the Forum.

1.2.7.6 Composition of National health Research Ethics Committee

The National Health Research Ethics Committee is an advisory body to TANHER Forum, and its composition shall include:

- (i) The Chairman
- (ii) The Secretary
- (iii) Representatives from health research institutions, religious group, the legal profession, and a lay member.
- (iv) The Chairman and Secretary of the TANHER Forum as Ex-Officials.

1.2.7.7 Functions of the NHREC

For practical purposes, NHREC shall have the following functions:

- (i) Prepare and revise national guidelines on health research in Tanzania;
- (ii) To grant accreditation to other ethics committees, which conform to satisfactory standards of evaluation and supervision of health research;
- (iii) To monitor and coordinate activities of other accredited research ethics committees which conduct or supervise research that is funded by NIMR HRUTF and TANHER forum;
- (iv) To advise national and international research collaborators on matters related to the ethics of health research in Tanzania;
- (v) To participate in national and international discussions on the ethics of health research; and
- (vi) To enhance health research ethics, standards and discussion on the health researchers issues in Tanzania.

CHAPTER TWO

2.1 PRINCIPLES OF HEALTH RESEARCH

It is essential that health research is conducted in order to develop new knowledge for the better care of mankind. However, as earlier stated, health research may be associated with risks and the possibility of exploitation of the individual subjects or the community in which the study is to be carried out. Poverty, ill health, lack of resources and certain in communities increase the likelihood of exploitation especially in developing countries where community expectations on research are high. Therefore, in the field of health research selection of research subjects must take into account whether the study is carried out among healthy subjects, patients, children, women etc. Where relevant, the research protocol must describe the social contexts of a proposed research population, e.g. country or community that create conditions for possible exploitation or increased vulnerability among potential research subjects, and strategies that will be taken to overcome these conditions and protect the dignity, safety and welfare of the participants.

Further fundamental distinction must be recognized between health research the primary aim of which is diagnostic or therapeutic for the patient, and that which is purely scientific. The distinction is important and influences the approach and the conduct of the research.

The WMA has recognized the need to establish standards to guide research involving human subject and recommended that, the guidelines to researchers involved in health research should from time to time be reviewed. Furthermore, WMA cautions that researchers in health research are not relieved from criminal, civil and ethical responsibilities under the laws of their respective countries.

2.2 The basic principles of health research

While health research may be significantly influenced by the law of the country, institution, multinational and international agencies, there are fundamental principles that cut across any health research. These include:

Health research must be scientifically sound and should at all times conform to scientific principles and evidence based scientific knowledge. In order to conduct a research in a scientifically acceptable manners research protocol should have the following provisions:

- (i) Be scientifically appropriate;
- (ii) The outcomes of the research should benefit the population from which the research participants are drawn;
- (iii) Have justification for the selected population; and
- (iv) Address particular needs of the proposed research population.
- (v) Health research must be supported by a well thought out protocol detailing the experimental procedures, which, before implementation, must have been submitted to qualified independent reviewers for consideration, comments and guidance;
- (vi) The quality of researchers in health research must be qualified and competent to carry out the proposed study. At no time should health research be left in the hands of incompetent persons. While, in recent years, a multi-disciplinary approach to health research has been given emphasis, in dealing with patients, attention must be directed at ensuring that health research involving patients rests in the hands of qualified and competent personnel;
- (vii) The risk-benefit of the proposed study must be considered, and be established that the benefits of the research findings outweighs the associated risks, The research must:
 - (a) Establish safeguards for the protection of research subjects from potential harm.
 - (b) Be carefully monitored and whenever there are observable risks to research subjects, researchers should immediately discontinue such experiments.

- (viii) The privacy and integrity of research subjects must always be observed, and at all times, precaution must be taken to preserve and respect the privacy of individual research subjects;
- (ix) The right to information entails that research subjects must be provided with the necessary information related to the study in which they are going to participate. The information must include reason for the study, procedures, techniques, advantages, disadvantages and the right for research subjects to decline participation or discontinue from the study without consequences. The right to information is essential and fundamental in establishing trust between researchers and research subjects;
- (x) Accuracy of the results must be maintained, and should reflect what was done and what was observed. Fictitious and fabricated results should not be accepted for publication under any circumstances;
- (xi) Matters related to handling of research outputs must be clearly detailed. The communities where the study was carried out have the right to information on the research outputs. This must be prepared, repackaged and given in a simple language that the community understands;
- (xii) Capacity building must be given emphasis so that the research must bring and leave behind improvement in the way of life in terms of capacity buildings;
- (xiii) What happens after the research has come to an end is becoming a major subject for discussion and there should be clear plans on what will happen when the study comes to an end; and
- (xiv) As health research may carry physical, mental, and/ or psychological risks, health research protocols must therefore, detail the ethical issues and the strategies to counter or minimize effects.

2.1 Conclusion

These basic principles of health research must be followed because they are fundamental in advancing health sciences, knowledge and search for new cures and

care of humankind. Researchers are being directed to familiarize themselves with these principles and apply them. Adherence to the principles will minimize the duration of processing research protocols by either NREC or IRECs. Further details on the basic principles of health research are provided in the Helsinki Declarations (Appendix One)

CHAPTER THREE

3 CONSENT

3.1 Background

There is sufficient evidence that many forms of health research carry the risks of causing physical as well as psychological to the participating subjects or the society where it is being carried. To ensure that research participants are well protected, the Nuremberg Code of Ethics stressed that all subjects involved in the research should have a legal capacity to consent and researchers should ensure that:

- (i) Each healthy volunteer or patient participating in the research must have provided valid consent;
- (ii) Consent if freely given after the individual participant in the research must have received as full an explanation, as the research thinks appropriate;
- (iii) The subject may decline to participate without giving any reasons or incurring displeasure or penalty;
- (iv) Due regard should be given to the individual needs of the patients or participating research subjects;
- (v) Patients or healthy individual participating in the research must be well informed about the potential risks and benefits of the procedure(s), and why it is proposed and the significance in terms of advancing knowledge and the researcher's own sake in proposing the procedures;
- (vi) Where options are provided, the participating subjects in the research must be told about the alternatives; and when a clinical trial is being proposed, they need to know about the advantages and disadvantages of conventional regimes as well as options in the trial;
- (vii) Research subjects should be told that they are free to withdraw from the study at any stage without conditions; and
- (viii) The information obtained should be treated confidentially.

3.2 General requirements for informed consent

Consent is an important component of research involving human subject and in accordance with these Guidelines, no investigator shall involve a human subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such informed consent only under the circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in a language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or representative is made to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents the liability for negligence.

Care however, must also be observed in obtaining consent in societies where elders and community leaders have final say in matters related to the family, clan or tribe. It is not uncommon for women to rely on their husbands for consent. Researchers must ensure that in such circumstances, consent is given in the best interest of the participating subject.

3.3 Types of consent

Consent may be explicit or implicit. In practice however, implicit is more common than explicit consent e.g. in the process of measuring blood pressure or venepuncture, the researcher assumes that consent has been given by the subject extending the forearm. Consent may be given either orally or it may be written down. In biomedical research it is common practice to have a written down consent popularly referred to as informed consent. Written consent however, is not in any

way superior to verbally given consent especially in circumstances where illiteracy rates are high.

The consent form was originally introduced to protect surgeons from allegations of assault by patients who came to regret the surgical interventions, which, had been carried out upon them. This is still seen by some researchers as the function of the consent form. With regards to the consent form an eminent judge has said: "There seem to be some confusion in the minds of some as to the purpose of seeking consent from a patient. It has two purposes, the one clinical and the other legal. The clinical purposes stem from the fact that in many instances the cooperation of the patient and the patient's faith or at least confidence in the efficiency of treatment is a major factor contributing to the treatment's success. Failure to obtain such consent will not only deprive the patient and medical staff of this advantage, but will usually make it more difficult to administer the treatment. The legal purpose is quite different. It is to provide those concerned in the treatment with a defence to a criminal charge of assault or better or civil claim for damage for trespass to the person. For written consent to be valid:

- (i) The consent form should be simple but carrying the necessary and relevant message on the proposed study;
- (ii) Participating subjects should realize that they are taking part in the research willingly;
- (iii) The consent form must be submitted to an Ethical Clearance Committee for approval before it can be used.

3.4. Elements of informed consent

For all practical purposes, and in seeking informed consent, the following information shall be provided to each participating subject:

- (i) A statement that the trial involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a

- description of the procedures to be followed, and identification of any procedures which are experimental;
- (ii) A description of any reasonably foreseeable risks or discomforts to the subject;
 - (iii) A description of any benefits to the subject or others which may reasonably be expected from the research;
 - (iv) A disclosure of appropriate alternative procedures or courses of treatment, if any that might be advantageous to the subject;
 - (v) A statement describing the extent, if any, to which confidentiality of records identifying subjects will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records;
 - (vi) For research involving more than minimal risks, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if any injury occurs and, if so, what they consist of, or where further information may be obtained;
 - (vii) A description of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;
 - (viii) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled;
 - (ix) When appropriate one or more of the following elements of information shall also be provided to each subject:
 - (a) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or foetus, if the subject is or may become pregnant) which are currently unforeseeable;
 - (b) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
 - (c) Any additional costs to the subjects that may result from participation in the research;

- (d) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
- (e) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and
- (f) The approximate number of subjects involved in the research.

3.5. Documentation of informed consent

Informed consent shall for practical purposes be documented by the use of a written consent form approved by the IREC and signed and dated by the subject or subject's legally authorized representative at the time of consent. A copy shall be given to the person signing the form. The consent may be either of the following:

- (i) A written consent document that embodies the elements of informed consent described under 3.4. This form may be read to the subject or subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed;
- (ii) A short form written consent document stating that the elements of the informed consent have been presented orally to the subject or subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also the IREC shall approve a written summary of what is said to signed by the subject or subject's representative;
- (iii) However, the representative shall sign both the short form and a copy of the summary, and the person actually obtaining the consent shall sign a copy of the summary; and
- (iv) A copy of the summary shall be given to the subject or the representative in addition to a copy of the short form.

3.6. Witnessed consent

Witnessed consent is an alternative to written consent. It is useful for individuals who have intellectual or cultural difficult to understand or in speech, capable to

consent. In that case, a third party which may be a technician, doctor, nurse or any other persons may sign the document stating that at the time the investigator was explaining the methods and the purposes of the study to the research candidate, the witness was present, and that witness's option was given freely and with understanding.

3.7. Consent from vulnerable groups in the society

There are circumstances where prospective candidates are unable to freely consent to research procedures for one reason or another. They include children, mentally handicapped, prisoners, detainees, refugees, severely ill or unconscious patients and the elderly. Research that can be carried out on subjects who can consent should not be carried out on individuals who have no capacity to understand, or freedom to refuse is limited. It has always been argued that it is unethical to include in a study individuals whose capacity to consent is limited. However, there are those who have argued that excluding the entire groups of such people from a study on the basis of limited capacity to consent is unethical, discriminatory, and it means there is failure in the system to seek measure to improve their conditions. It is however, generally accepted that carrying out research in groups of people with limited capacity to consent is not unethical as long as it is governed by strict safeguards including:

- (i) Critical review by IRECs or NREC;
- (ii) The research should not be contrary to the interests of the subject;
- (iii) The research should not pose risks to the subjects or pose minimal risk;
- (iv) The research must be impossible to carry out in subjects with capacity to consent; and
- (v) Must be designed to have maximum benefits to other in the same category as the subject.

3.8. Consent for research involving minors

The British Paediatrics Association draws attention to the fact that many children are vulnerable, easily bewildered and frightened and unable to express their needs. In

law, parents or guardians cannot consent to any treatment or procedures, which are contrary to the child's interests. This has been expressed as guidance that; "Those acting for the child can only legally give their consent provided that the intervention is for the benefit of the child. If they are responsible for allowing the child to be subject to any risk (other than one so insignificant as to be negligible) which is not for the benefit of the child, it could be said that they were acting illegally". A research worker must therefore be able to recognize when a child is very upset by a procedure and accept that as genuine dissent from their being involved. However, as part of the society, researches in children have to be carried out. Researches involving minor must fulfil the following:

- (i) Must have identifiable benefit to minors in the same category;
- (ii) The procedures should have first been tested on consenting adults before they are carried out in children;
- (iii) The child may consent independently; and
- (iv) Where the child understanding is thought to be doubtful it may be a matter of good practice to seek the child's permission to explain the research proposals to parents, and if the minor objects, the objection should be given weight.

3.9. Consent involving the mentally disordered persons

The mentally disordered persons have been defined as including the mentally ill, mentally handicapped, demented and the unconscious. In these categories or persons, some will never have the capacity, to some will have it at times and not others and some will lose it irrevocably. However, many people with a mental disorder are able to consent as long as adequate time is taken to explain the procedures. Nonetheless, care should be taken not to exert undue pressure to any of the following categories:

3.9.1. *Consent for research on mentally ill persons*

- (i) Apart from patients suffering from severe conditions such as dementia, most patients will be able to give consent to therapeutic trials; and

- (ii) Non-therapeutic trial should not be carried out on mentally ill persons;

3.9.2. Consent for research on demented and unconscious patients

It is very unlikely that there is any justification in carrying out research on this category of patients. However;

- (i) Research may be carried out only if it not contrary to the interests of the patient. If it carries minimal risk as to be said to be negligible,
- (ii) May be potentially of benefit to the category of such patients, and;
- (iii) Should have been scrutinized and satisfied the Research Ethics Committee.

3.9.3. Consent for research involving people with learning disabilities

Research involving this category of patients may only be approved where;

- (i) The research is not contrary to the interests of people with learning disabilities;
- (ii) It exposes them to no risk or minimal risk as to be said to be negligible; and
- (iii) The research may potentially benefit others in the same category.

3.10 Consent for research in the elderly

The elderly constitute a special group of people in the community who are great consumers of pharmaceutical products and a number of drugs are targeting elderly people. In many societies, the numbers of elderly people is growing and studies in elderly people are therefore important if we are to understand the drug interaction in the elderly people whose physiology may have changed with age. It should however, be borne in mind that the elderly are more prone to exploitation because of their dependence on others or institutions in which they are living. While most elderly people may be considered to have capacity to consent, it is important that:

- (i) When considering inclusion of elderly patients in the research, special care must be exercised when involving elderly who have stayed long in the hospital or residential homes because of their vulnerability to suggestions and dependence to others;

- (ii) Research with potential benefits to individual and others in the same category should be discussed in the presence of an independent but caring observer (e.g. a senior nurse). The observer should be satisfied that the researcher explained the aims, procedures, benefit and risks if any to the patient and that the elderly person understood the intended research activities and agreed.

3.11 Protections for pregnant women, human foetuses and neonates

3.11.1 Research in pregnant women or foetuses

Pregnant women or foetuses may be involved in research if all of the following conditions are met:

- (i) Research among pregnant women should only be carried out if the pregnancy forms an essential part of the proposed research;
- (ii) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provided data for assessing potential risks to the pregnant women and foetuses;
- (iii) The risk to the foetus is caused primarily by interventions or procedures that holdout the prospect of direct benefit for the woman or the foetus; or, if there is no such prospect of benefit, the risk to the foetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
- (iv) Any risk is the least possible for achieving the objectives of the research;
- (v) If the research holds out the prospect of direct benefit to the pregnant woman, and the foetus, or no prospect of benefit for the woman nor foetus is not greater than minimal and the purpose of the research is development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of subpart (a) of this section, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;

- (vi) Each individual providing consent under paragraphs (iv) and (v) of this section is fully informed regarding the reasonably foreseeable impact of the research on the foetus or neonate;
- (vii) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- (viii) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- (ix) Individuals engaged in the research will have part in determining the viability of a neonate.

3.11.2 Research involving neonates

(a) General considerations

In research involving neonates, attention should be directed at ensuring distinction between neonates of uncertain viability from nonviable neonates. Generally, neonates of uncertain viability and nonviable neonates may be involved in research only if all of the following conditions are fulfilled:

- (i) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
- (ii) Each individual providing consent under paragraph (a)(2) or (b)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate;
- (iii) Individuals engaged in the research will have no part determining the viability of a neonate;
- (iv) The requirements of paragraphs of (b) or (c) of this section have been met as applicable.

(b) Neonates of uncertain viability

Until such time that it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following conditions have been fully met:

1. *The IREC or NHREC determines that:*
 - (i) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective; or
 - (ii) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research.

2. *Legally informed consent*

Legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective consent of either parent's legally authorized representative is obtained, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

(c) *Nonviable neonates*

After delivery, nonviable neonates may not be involved in research covered under this subpart unless the following additional conditions have been fulfilled:

- (i) Vital functions of the neonate will not be artificially maintained;
- (ii) The research will not terminate the heart beat or respiration of the neonate;
- (iii) There will be no added risk to the neonate resulting from the research;
- (iv) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means;
- (v) Legally effective informed consent of both parents of the neonates is obtained.

(d) *Viable neonates*

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accordance with the requirements of subparts of this section.

3.11.3 Research involving after delivery, the placenta, the dead foetus or foetal material

Often researchers have shown interests to research on the placenta, dead foetus and foetal materials. As a general rule:

- (i) Research involving after delivery, the placenta, dead foetus, macerated foetal material, or cells, tissues, or organs excised from a dead foetus, shall be conducted only in accordance with national laws and regulations regarding such activities;
- (ii) If information associated with materials described in the paragraph (i) of this section is recorded for research purpose in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this section are applicable.

3.12 Consent for research in prisoners and people in detention

Imprisonment or detention deprives individuals of their rights and autonomy. A detained person is less likely to give a free consent and may be restricted in terms of privacy. Prisoners and people living in detention are vulnerable in the sense that they are vulnerable to suggestions especially where hope for freedom has been advanced. It is however, not unethical to carry out research on prisoners or detained people as long as:

- (i) The research output would benefit the individual or others people in the same category, and
- (ii) The consent to participate in the research will be given without undue pressure, coercion including any impression that their participation in the research will result in a reduction in the sentence.

3.13 Consent of students in research

The student community has been involved in a number of research studies and their participation has been central in a number of researches involving healthy

volunteers. However, it should be born in the mind that students are a vulnerable group especially where the training institution is carrying out the research. It is however, not unethical to conduct research on students as long as:

- (i) The tutor involving in the tuition of the student should not be recruitment and other negotiations on the terms and research conditions;
- (ii) The informed consent should clearly state that the students might, wish at any stage of the research to withdraw from the study without any undue consequences;
- (iii) An impression should not be created that acceptance to participate in the study will benefit the student in the passing of their examinations;
- (iv) An impression should not be created that non-acceptance will result in discrimination and consequences on the studies; and
- (v) There should not be any form of coercion, pressure or financial inducement other than that proposed as fees for participants.

Similar considerations might be taken where research is being considered to involve junior staff in the department from which the Principal Investigators belong. Over enthusiasm aimed at impressing the senior member and fear for not participating might have significant influence on the consent of the junior staff. Junior staff may be included in the study as long as there is no any form of coercion pressure of inducement other than that proposed for all participants in the research.

3.14 Consent of Community

Ethical issue regarding consent of community are described in detail in Section 6.2 of Chapter Six.

3.15 Research without the consent of the patient

It is generally accepted that under no circumstances research should be conducted without the consent of the prospective research subject or any authorized person on his/her behalf; and IRECs or the NRECs should be consulted well in advance and should scrutinize such proposals.

3.16 Exceptions from general requirements

Though rare and efforts should be made to ensure that informed consent is obtained, there are few exceptions from the general requirements. The obtaining of informed consent shall be deemed feasible unless, before use of the test product, both the investigator and practicing physician who is not otherwise participating in the clinical trial certify in writing the following:

- (i) The human subject is confronted by a life-threatening situation necessitating the use of the test product;
- (ii) Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from the subject;
- (iii) Time is not sufficient to obtain consent from the subject's legal representative;
- (iv) There is no available alternative approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject;
- (v) If immediate use of the test product is, in the opinion of the investigator, required to preserve the life of the subject, and time is not sufficient to obtain the independent determination in paragraph (i) above in advance of using the test product, the determinations of the clinical investigator shall be made and, within five (5) working days after the use of the test product, be reviewed and evaluated in writing by an independent practicing physician who is not participating in the clinical trial; and
- (vi) The documentations required under paragraphs (i) and (ii) above shall be submitted to the Institutional Review Committee within five (5) working days after the use of the test product.

3.17 Exception from informed consent requirements for emergence research

Generally, there are rare cases where exception from informed consent requirements may be considered by an Institutional Review Committee for approval e.g. under emergency. In this case IREC may approve a clinical trial without requiring that informed consent of research subjects to be obtained provided that:

- (i) The human subjects are in a life threatening situation, and available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled trial, is necessary to determine the safety and effectiveness of the particular interventions;

- (ii) Obtaining informed consent is not feasible because of the following:
 - (a) The subject will not be able to give informed consent as a result of the medical condition;
 - (b) The intervention under investigation must be administered before consent from the subjects' legally authorized representative is feasible; and
 - (c) There is no reasonable way to identify prospectively the individual likely to become eligible for participation in the clinical trial;

- (iii) Participation in the trial holds prospects of direct benefits to the subject because:
 - (a) The subjects are facing a life threatening situation that necessitate intervention;
 - (b) Appropriate animal and other pre-clinical studies have been conducted, and the information derived from the studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects,
 - (c) The risks associated with the trial are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of a standard therapy, if any, and what is known about the risks and benefits of the proposed intervention.

- (iv) The clinical trial could not reasonably be carried out without the waiver;

- (v) The proposed trial activity plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for consent within the prescribed window rather than proceeding without consent;
- (vi) The IREC has reviewed and approved informed consent procedures. The procedures and informed consent documents are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible; and
- (vii) The IREC has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical trial.

3.18 The duration of consent

There has been concern in research circles on the length of time for which the given consent can still be considered valid. In practice, this is not at question since consent is an evolving matter and not a once and for all decision. The given consent is clearly only valid until such time as the person who had given consent expresses a change of mind. Therefore, researchers should take necessary precaution not to act on information on consent that cannot revoke and be confirmed.

3.19 Conclusion

Some countries or communities often described as “developing” have been perceived as inappropriate participants for some phases of clinical trials researches due to perceived increased level of vulnerability to exploitation or harm. It is therefore more useful to identify the particular aspect of the selected study community that create conditions for exploitation or increase vulnerability for the selected population group. Some factors to be considered include:

- (a) Governmental, institutional or social stigmatization or discrimination.
- (b) Social and legal marginalization of population segments.

- (c) Limited availability, accessibility and suitability of health care.
- (d) Limited ability of individual or group in the community to understand the research process.
- (e) Limited ability of individuals to be able to give freely their informed consent in the light of prevailing class, gender and other social and legal factors.
- (f) Lack of meaningful IRECs and review committees.

CHAPTER FOUR

4 CONFIDENTIALITY

4.1. Introduction

Privacy is a basic right which permits individuals to decide the manners, and extent to which information concerning them should be shared with others. Confidentiality is a central issue in the doctor-patient and researcher-research subject relationship and is based on trust. Information obtained in the researcher/research subject relationship must be regarded as strictly confidential. Any breach of confidentiality threatens that relationship.

However, there are occasions when public interest may be seen to override the privacy of an individual, but in such circumstances, the facts must be subject to close scrutiny as to whether there is genuine ground for disclosure. Arriving at a decision may be a dilemma as in the following examples:

- (i) In a study, a researcher discovers that a male research subject is sero-positive for HIV, but the sero-status of his partner who is not a research subjects is not known. The ethical dilemma includes whether the researcher should disclose the information to the partner.
- (ii) In a study among prison workers, a researcher discovers that a fellow physician, as an employee of the prison participates in cruel and inhuman practices. Ethical issues to be considered are whether the researcher should disclose this information to the Medical Licensing Authority or keep the information confidential. In either way, there are ethical implications to the profession as well as to the community.
- (iii) There are concerns that high level care provided during research might constitute undue incentives and inducement for communities to participate in subsequent studies.

- (iv) In a study among school children, the researcher discovers that a school child is on drugs. The child however, pleads that the information should not be disclosed to teachers and parents.

In all these cases, a decision has to be made in the best interest of the research subjects and society. In general, in order to safeguard confidentiality:

- (a) Identify of research subjects should be confidential.
- (b) The investigator must take all necessary precautions to ensure that information collected is handled and kept confidentially.
- (c) Investigators must be aware of the consequences that might result from the disclosure of information without the consent of the individual or any other person legally capable of consenting on that individual's behalf.

4.2. Confidentiality and medical records

Confidentiality with regard to the use of medical records is a controversial issue. Some have argued that it would be impractical to demand that research obtain individual consent from the patient. It has in some cases been proposed that each time a patient is attending a clinical trial? for the first time, he/ she should sign a form saying he/ she is willing or unwilling to allow information pertaining to their condition to be used in research. As a matter of principle:

- (i) Where the medical record is given in a form that does not able individuals to be identified, no breach of confidentiality will arise.
- (ii) Where the disclosure would enable one or more individuals to be identified, the person concerned or those who may legally give permission on their behalf must be made aware.
- (iii) Where the person or persons concerned have been identified, they should be made aware that they are at liberty at any stage, to withhold their consent to disclosure.
- (iv) In the case where a researcher requires information from records of patients attending a particular physician, it is the responsibility of the attending

physician to provide the required information without divulging the identity of his patients.

- (v) Any research, which will involve access to personal records, should have the approval of IREC.
- (vi) Information derived from medical records should be stored securely, and if possible, encoded so that the identity of the subjects is unidentifiable.

CHAPTER FIVE

5. ETHICAL ISSUE REGARDING RANDOMIZED CONTROLLED TRIALS

5.1 Introduction

Sir Austin Bradord Hill introduced Randomized Control Trials (RCTs) into medical research in 1946, in the trial of streptomycin in the treatment of tuberculosis. The pre-requisite for randomizing is embodied in the maxim “only randomize if uncertain principle”. Alternatively, the doctor may be described as being in “equipoise”. There is an ethical imperative to ascertain that the treatments doctors give are effective. Therefore:

- (i) Randomization is only ethical if there is substantial uncertainty about the best treatment for the patient;
- (ii) If the doctor considers that one of the treatments in the study is appropriate or inappropriate for the patient, then randomization would be unethical;
- (iii) To be “equipoise”, the doctor should be indifferent to the choice of treatment because he/she has no knowledge to indicate that one drug option is better than the other;
- (iv) Once there is unequivocal evidence of superiority of one drug over the other, it is unethical to deprive a patient of that treatment;
- (v) Randomized Controlled Trials are ethical when the trial subjects are provided with adequate information, counselling and support at all stages of the trial;
- (vi) At any stage of the trial subjects must have the option to withdraw and should be supported if that is their choice; and
- (vii) Where the product is known to have adverse effects, the proposal should carry provisions to indicate how such effects will be detected and minimized in the event they occur in a research subject.

5.2 Double-blind controlled trials

One major problem inherent with controlled trials is the introduction of bias by the doctor or researchers. Randomization therefore can be accompanied with “double-blind” procedures. This eliminates the subjective preferences of the doctor or researchers by keeping the assignee treatment secret to both the investigators and trial subjects. The current designs for double-blind trials have been refined such that the possibility of unintentional bias affecting the outcomes has been considerably reduced.

5.3 Ethical issues related to controlled trials

Practical problems may arise if the doctor considers that the appropriate drug for the patient is the new drug only available in a trial since randomizations would deprive the patient of the product. Problems might also arise if at the end of the trial a product may be beneficial but is no longer available or not licensed for general use. In such circumstances:

- (i) An investigator who has proved beyond reasonable doubt that one treatment is superior to the other is ethically unable to carry out controlled trials;
- (ii) Withholding a product that has shown to be beneficial for a time or given period should only be done after scrutiny and approval of the proposal by the IRECs or other relevant authorities;
- (iii) The proposal should indicate well in advance any provisions for continued supply of products at the end of the trials. In exceptional cases where the product has not been licensed, treatment can be provided on a “named patient” basis or by means of a doctor’s exemption certificate from the Medical Control Agency; and
- (iv) Where benefits have been observed in the trial sufficient to be of general use, the trial must be stopped and arrangements be made for those not on the product to be provided with the drug.

5.4 Consent in randomized controlled trials

Consent in randomized controlled trials has been a subject of discussion on whether consent may be given before or after randomization. As general guideline:

- (i) The allocation of the treatment should be conducted after the patient has consented to participate in the study. This is a precaution because knowledge of the treatment that will be given to a particular group might influence the research outcomes; and
- (ii) Any randomization of the treatment without the research patient consenting is unethical. Exceptional cases are where there is an argument for not telling the patient the truth, and must be subject of IRECs.
- (iii) Randomization before seeking consent should be discouraged because of the coercion and over emphasized advantages for research subjects participating in the study.

5.6 Phases of vaccine and drug development

5.6.1. Vaccine development

- (i) Phase I, refers to the first introduction of a candidate vaccine into a human population for initial determination of its safety and biological effects, including immunogenicity. This phase may include studies of dose and route of administration, and usually shall involve fewer than 100 volunteers;
- (ii) Phase II refers to the initial trials examining effectiveness in limited number of volunteers (usually between 200 and 500). The focus of this phase is immunogenicity; and
- (iii) Phase III, trials are intended for a more completed assessment of safety and effectiveness in the prevention of diseases, involving a larger number of volunteers in a multi-centre adequately controlled study.

5.6.2 Drug development

There are defined phases which must be followed in the development of any drug for use on humans. The specific phases include the following:

- (i) **Phase I** refers to the first introduction of a drug into humans. Normal volunteer subjects are usually studied to determine levels of drugs at which toxicity is observed. Such studies are followed by dose-ranging studies in patients for safety and, in some cases, early evidence of effectiveness.
- (ii) **Phase II** investigation consists of controlled clinical trials designed to demonstrate effectiveness and relative safety. Normally, these are performed on a limited number of closely monitored patients.
- (iii) **Phase III** trials are performed after a reasonable probability of effectiveness of a drug has been established and are intended to gather additional evidence of effectiveness for specific indications and more precise definition of drug-related adverse effects. This phase includes both controlled and uncontrolled studies.
- (iv) **Phase IV** trials are conducted after the national drug registration authority has approved a drug for distribution or marketing. These trials may include research designed to explore a pharmacological effect, to establish the incidence of adverse reactions, or to determine the effects of long-term administration of a drug in a populations not studied adequately in the pre-marketing phases (such as children or elderly) or to establish a new clinical indication for a drug. Such research is to be distinguished from marketing research, sales promotion studies, and routine post-marketing surveillance for adverse drug reactions in that these categories ordinarily need be reviewed by ethical committee.

In general practice and in accordance with these Guidelines, Phase I drug trials, and Phase I as well as Phase II vaccine trials shall be conducted according to the Articles of the Declaration of Helsinki that refer to non-clinical research. However, some exception can be justified. For example, it is customary and ethically justifiable to conduct Phase I studies of highly toxic chemotherapies of cancer in patients with cancer, rather than in normal volunteers as prescribed in the Declaration of Helsinki,

Article III 2. Similarly, it may be ethically justifiable to involve HIV-seropositive individuals as subjects in Phase II trials of candidate vaccines.

Phase II and **Phase III** drug trial shall in accordance with these Guidelines be conducted according to the Articles of the Declaration of Helsinki that refer to “Medical Research Combined with Professional Care (clinical research)”. However, the Declaration does not provide for controlled trials. Rather, it assures the freedom of the physician “to use a new diagnostic and therapeutic measure, if in his or her judgement it offers hope for saving life, re-establishing health or alleviating suffering” (Article II.1). Also in regard to Phase II and Phase III drug trials there are customary and ethically justified exceptions to the requirements of the Declaration of Helsinki. A placebo given to a control group, for example, cannot be justified by its “potential diagnostic or therapeutic value for the patient”, as Article II.6 of the Declaration of Helsinki prescribes.

Many other interventions and procedures characteristic of late-phase development have no possible diagnostic or therapeutic value of the patients and thus must be justified in other groups; usually such justification consist of a reasonable expectation that they carry little or nor risk and that they will contribute materially to the achievement of the goals of the research.

Phase III trials of vaccines do not use “a new diagnostic and therapeutic measure” that offers “hope of saving life, re-establishing health or alleviating suffering” (clinical researcher). Yet administration of the vaccine is intended to be a benefit to the subject rather than “the purely scientific application of medical research carried out on a human being” (non-clinical biomedical research). Thus Phase III vaccine trials do not conform to either of the categories defined in the Declaration of Helsinki.

5.7 Clinical trial protocol/proposal and protocol amendment

Institutional and the National Research Ethics Committees are currently receiving several clinical trials protocols/proposals for evaluation. Therefore there is a need for clear guidelines to be given to enable IREC and the NHREC to ensure standards for clinical trials is enhanced. The contents of a clinical trial should generally include items described below. However, site specific information may be provided on separate proposal pages or addressed in a separate agreement. IREC and the NHREC should scrutinize clinical trial protocols/proposals for the following:

5.7.1 General information

- (i) Proposal title, identification number and date. Any amendments should also bear the amendment number(s) and dates;
- (ii) Name and address of the sponsor and monitor (if other than the sponsor);
- (iii) Name and title of the person(s) authorized to sign the proposal and proposal amendment(s) for the sponsor;
- (iv) Name, title, address, telephone and fax contacts, and email address of the sponsor's medical expert(s) for the trial;
- (v) Name, and title of the investigator(s) who is(are) responsible for conducting the trial, and the physical address, telephone and fax contacts and email address;
- (vi) Name, title, address and telephone and fax contacts of the qualified physician(s) who is(are) responsible for all trial sites related to medical decisions, if other than the investigator;
- (vii) Name(s) and addresses) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the trial.

5.7.2 Background information

- (i) Name and description of the investigational product(s);
- (ii) A summary of findings from non-clinical studies that potentially have clinical significance and from clinical trials that is relevant to the trial;
- (iv) Abstract of known and potential risks and benefits if any to human subjects;

- (v) Description of and justification for the route of administration, dosage, dosage regimes and treatment period(s);
- (vi) A statement that the trial will be conducted in compliance with the proposal and applicable regulatory requirements;
- (vii) A description of the population to be studied;
- (viii) Reference to literature and data that are relevant to the trial and that provide background for the trial.

5.7.3 Trial objectives

A clinical trial proposal should contain a detailed description of the objectives and the purpose of the trial.

5.7.4 Trial design

A scientifically sound design of the proposal is a pre-requisite for scientific integrity and credibility of the data from any clinical trial. Therefore a description of a clinical trial design should include the following:

- (i) A specific statement of the measurable primary endpoints and the secondary endpoints;
- (ii) A brief description of the design of the trial to be conducted (e.g. double blind, placebo controlled, parallel design) and a schematic presentation of the trial design showing stages;
- (iii) A brief description of strategies for minimizing bias due to randomization and blinding;
- (iv) A description of the trial treatment(s), dosages and dosage regimes including dosage form, packaging, and labelling of the trial drug(s);
- (v) Projected duration of participation, the sequence and duration of trial periods including follow-up if any;
- (vi) A full description of criteria for discontinuation of participants from the trial as well as end of the trial;
- (vii) Maintenance of trial treatment randomization, codes and procedures for breaking the code; and

- (viii) Accountability procedures for the trial product(s) including the placebo(s) and comparator(s) if any.

5.7.5 Selection and withdrawal of research participants

Any clinical trial proposal submitted for ethical review, IREC should scrutinize the proposal for the following:

- (i) A full description of the inclusion criteria;
- (ii) A full description of the exclusion criteria;
- (iii) A description of the withdraw criteria i.e. terminating trial product, and procedures specifying:
 - (i) When and how to withdraw subjects from the trial;
 - (ii) Type and timing of the data to be collected for withdrawn subjects;
 - (iii) Whether and how subjects will be replaced, if needed;
 - (iv) How withdrawn subjects will be followed-up.

5.7.6 Treatment of research participants on clinical trial

IREC/NHREC are required to scrutinize all clinical trial proposals for procedures for treatment of research participants, medication(s) permitted including rescue medication as well as procedures for monitoring compliance to treatment(s).

5.7.7 Assessment of efficacy

All clinical trial proposals must be scrutinized by IREC/NHREC for a description of assessment of efficacy, specifying:

- (i) Specification of the efficacy measurable indicators; and
- (ii) Methods and timing for assessing, recording and analyzing efficacy parameters.

5.7.8 Assessment of safety

It shall be the responsibility of IREC/NHREC to establish in all clinical trial proposals assessment of safety, specifying:

- (ii) Specification of the safety measurable indicators;
- (iii) Methods and timing for assessing, recording and analyzing safety parameters;
- (iv) Procedures for eliciting reports of and for recording and reporting adverse event and inter-current illnesses;
- (v) The type and duration of the follow-up of subjects after adverse events have occurred.

5.7.9 Statistical analysis

All clinical trial proposals must provide a description on statistical analysis specifying:

- (i) A description of the statistical methods to be employed, including timing of any planned interim analysis;
- (ii) The number of subjects planned to be enrolled;
- (iii) For multi-centre studies, the proposal should specify the number of enrolled subjects projected for each trial site;
- (iv) Sample size, reason for the choice of sample size including reflections on calculations of, the power of the trial and clinical justification should clearly be specified;
- (v) The level of significance to be used;
- (vi) Criteria for the termination of the trial;
- (vii) Procedures for accounting for missing, unused and spurious data;
- (viii) Procedures for reporting any deviation(s) from the original plan and justification for deviation in the proposal and or report;
- (ix) The selection of subjects to be included in the analyses e.g. all randomized subjects, all dosed subjects, all eligible subjects, evaluate-able subjects.

5.7.10 Ethical issues

IREC/NHREC should scrutinize all submitted clinical trial proposals for adequate description of ethical issues and how they will be addressed during implementation of the trial.

5.7.11 Publication policy

Publications of research results have raised concerns among researchers in the developing countries. Weakness in signed contracts, supervision and lack of intellectual property rights are among reasons for researchers in developing countries feeling of being marginalized. It shall be the responsibility of IREC/NHREC to ensure that all submitted clinical trial proposals provide a description of how publication of research results will be addressed equitably.

5.7.12 Financing and insurance

Financing and insurance issues must be clearly described in all clinical trial proposals and it shall be the responsibility of IRECs/NHREC to determine the adequacy of the financing and insurance framework in line with institutional and laws of Tanzania.

5.7.13 Direct access to source data and documents

It shall be the responsibility of the IREC/NHREC to ensure that all clinical trial proposal contain a description to the effect that the sponsor specifies in the proposal or other written contract/agreement that the researcher(s) and or the responsible institution(s) shall permit trial-related monitoring, audits, IREC/NHREC review, and regulatory inspection(s) by providing direct access to source data and documents.

5.8 Investigator's Brochure

The Investigator's Brochure (IB) is a compilation of the clinical and non-clinical information in the investigational product(s) that are relevant to the study of the trial product in human subjects. The Investigator's Brochure serves the purpose of providing IRECs, NHREC, researchers and other stakeholders in the trial with information to empower them to understand the rationale for, and their compliance with many key features of the proposal, including doses, dose frequency or intervals, routes of administration and safety monitoring procedures. Generally, the

sponsor is responsible for ensuring that an up-to date Investigator's Brochure is made available to researchers who are responsible for providing the up-to-date IB to the responsible IREC or NHREC. It shall be the responsibility of the IREC or NHRE to ensure that Investigator's Brochure:

- (i) Contains information presented in a concise, simple, objective, balanced and non-promotional;
- (ii) Contains a title page specifying the sponsor's name, identity of each research product, chemical or approved generic name, trade name(s) and the release date;
- (iii) Confidentiality statement instructing researchers to treat the Investigator's Brochure as a confidential document;
- (iv) A brief introduction statement that contains the chemical name, all active ingredients in the trial product, pharmacological class, the rationale for carrying out the trial, anticipated prophylactic, therapeutic, or diagnostic indications and approach to be followed in evaluating the trial product;
- (vi) A description of the trial product substance(s), and the relevant physical, chemical and pharmaceutical properties of the trial product;
- (vii) IRECs and NHREC should scrutinize Investigator's Brochure for all relevant non-clinical pharmacology, toxicology, pharmacokinetic and metabolism summarized. The summary should provide information on the methodology used, the results, and a discussion of the relevance of the findings to the investigated trial product and the possible unfavourable and unintended effects in humans;
- (viii) A thorough discussion of the known effects of the trial product(s) in human subjects should be provided including information on pharmacokinetics, metabolism pharmaco-dynamics, dose response, safety, efficacy and other pharmacological activities related to the trial product(s);
- (ix) A description on marketing experience including countries where the trial product has been marketed or approved. All significant information arising from the marketed use should be summarized in the Investigator's Brochure.

5.9 Data Safety Monitoring Committee (Board)

For all clinical trial proposals it shall be the responsibility of IREC or NHREC to establish that there is full description of establishment of a Data Safety Monitoring Committee or Board (DSMB) to periodically assess the progress of implementation of a clinical trial, the safety data and the efficacy endpoints, and to recommend to the sponsor and IREC or NHREC whether to continue, modify or terminate a trial. In assessing the DSMB, the IREC or NHREC shall ascertain the following:

- (i) Composition of the Committee/Board;
- (ii) Qualification and competence of members of the Board;
- (iii) Experience in assessing clinical trial;
- (iv) Affiliation of members;
- (v) Terms of reference to members; and
- (vi) Reporting framework.

CHAPTER SIX

6. ETHICAL ISSUES REGARDING EPIDEMIOLOGICAL STUDIES

6.1 Definition

Epidemiology is the study of geographical trends and determinants of health-related conditions or events in a given populations of study. Studies of epidemiology have in the recent years contributed significantly to the understanding of physiological processes, behavioural and physical changes that have influence on the health of communities. Epidemiological studies have also enhanced understanding of the burden of diseases in difference communities, efficacy and effectiveness of proposed intervention strategies and formulation of policy on resource deployment, storage and allocation.

6.2 Observational epidemiological studies

Observational epidemiological studies include cross-sectional, case-control and cohort studies. They involve use of questionnaires, performing physical or laboratory investigations and do not involve interventions.

6.3 Experimental epidemiological studies

Experimental epidemiological studies on the other hand involve studies where the investigators alter one or more variables under control and studies the effects of such alterations. They also include randomized controlled studies whereby randomization is aimed at reducing 'bias' attributable to individual or group influence. Results from the categories are then compared. Epidemiological studies of that nature usually raise ethical issues; and are generally unethical except where genuine reasons have been advanced to convince IREC to grant ethical clearance.

6.4 Potential for physical and psychological damage

Epidemiological studies have been shown to have potential physical and psychological damage. The potential may arise from data and specimen collection, storage and utilization of the results. The emergence of HIV/AIDS and large number

of People Living with AIDS (PLWA) in communities has to a greater extent increased the community's concern on damage. Therefore in all forms of epidemiological studies special consideration should be given to the rights of individual participants, communities and the researchers.

6.5 Existing guidelines on epidemiological studies

Guidelines on epidemiological studies now exist (e.g. the CIOMS). The guidelines are aimed at enhancing sensitivity of researchers and IRECs to ethical issues, adoption of standards ethics starting from the designing of the epidemiological studies, and encourage high professional standards, humane attitudes and high quality research.

It is however, unfortunate that the guidelines do not answer all the questions related to dilemmas that arise when applying them in different communities with different social-cultural backgrounds. Therefore, in reviewing proposals on epidemiological studies, special attention should be given to ensure that:

- (i) Research proposal provides adequate process of ensuring that consent is obtained;
- (ii) Respect for persons is considered;
- (iii) Beneficence is considered;
- (iv) The study will do no harm (Non - maleficence); and
- (v) There will be justice in sharing the benefits and risks.

6.6 Guidelines for informed consent in epidemiological studies

Cases have been reported where informed consent in epidemiological studies have been challenged. In accordance with these Guidelines informed consent shall be obtained from all subjects recruited for the study. Studies that propose not to seek informed consent should be critically scrutinized and the principal investigators of the proposals should be directed to provide satisfactory reasons to IRECs as to why the proposal should be granted ethical clearance in absence of informed consent. However, where subjects to be recruited in the study are well informed through the

media that is generally an acceptable practice that personal data is made available for epidemiological studies, informed consent may not necessarily be required.

6.7 Consent of the community

There are circumstances where it may not be feasible to obtain informed consent from individual subjects recruited for epidemiological studies. In such situation:

- (i) An agreement of the community representation may have to be sought from the community where the planned study is to take place;
- (ii) Selection of the representative should be carried in a manner that conforms with the traditions and culture of the community;
- (iii) Approval proved for by the community has to be assessed and to conform with ethical norms;
- (iv) There may be need to establish the authenticity of the community approval; and
- (v) Individual refusal to participate in the study must be respected regardless of the community consent.

6.8 Inducement and pressure to subjects

Community concern has been expressed on the use of inducement and pressure during recruitment of subjects for epidemiological studies. The common question asked is whether a person who has authority over the individual or the community should make recruitment of subjects into the study. For example a member of the parliament recruiting study subjects in his/ her constituency, schoolteacher on students, army officer recruiting research subjects etc.

Emergence of vulnerable groups in communities including pregnant women, children, HIV infected persons, the sick, prisoners, adolescents, disabled and physically challenged individuals are strong points for instituting strict measure on ethical consideration. It should be the responsibility of the researcher using the expected outcomes and benefits to convince subjects to participate in the study

without necessarily having to exert pressure or suggest inducements. In accordance with these Guidelines, Institutional Research Ethics Committees or Board are required to:

- (i) Critically review the proposal on the recruitment procedures;
- (ii) Recruiting officers should be scrutinized to ascertain their influences on the community;
- (iii) Subjects or communities should not be subjected to pressure during recruitment; and
- (iv) Scrutinize the proposal for any clues of inappropriate inducement or promises.

6.9 Provision of health care to community under study

In Tanzania, like in many developing countries, the health system has, between late 1970s to the 1990s, been affected by a declining economy, poverty, emerging new diseases, re-emerging diseases and rapidly growing population. Health facilities are faced with shortages of essential supplies and materials as well as trained human resources. Carrying research studies in such communities may create a sense of relief and expectations that the community will be provided with health care during the period of study and in some cases even after the study has come to an end. In accordance with these Guidelines and where possible:

- (i) Arrangements should be made to provide the care that the community needs; and
- (ii) Provision for a referral system should be established.

6.10 Training and support to local personnel

Health knowledge has from the beginning of the 20th century been growing rapidly and health personnel in developing countries have found difficult to keep pace. Economic crisis has contributed to lack of current reading materials in libraries etc., and health personnel especially those in rural areas are left far behind. Health

research in communities brings along with it knowledge, skills and capacity building in terms of hardware, materials and supplies which should be optimized during the study. Research studies proposed to be carried out to such communities should:

- (i) Include in the protocol aspects of imparting knowledge to local personnel; and
- (ii) Provide opportunity to train local health personnel in skills which can be used after the study has come to an end.

6.11 Multi-centre research

Multi-centre research involves studies of the same nature carried out at different stations in more than one country. Studies are required where global results are pooled and analyzed to provide a global view of a health condition e.g. WHO Cardiac Study which involves about sixty countries of the world. Research in Multi-centre studies has in some countries faced difficulties in obtaining ethical clearance because of absence of a national body to approve the protocol. To avoid delays in implementing multi-centre study:

- (i) A single IREC with a good range of expertise may examine the protocol in depth and share its views with other IRECs;
- (ii) A mechanism whereby one committee is selected to analyze the ethics of the protocol, leaving the other IRECs to concentrate on local aspects e.g. suitability of the investigators etc;
- (iii) The principal investigator should be well informed of the procedures and running of the research; and
- (iv) At all times, the interest of research subjects must be given priority.

CHAPTER SEVEN

7. GUIDELINES ON RESEARCH OUTPUT

7.1 Introduction

The primary objective of health research is to search for cure, better management of health conditions and advancing knowledge and skills in health. Research information should therefore be made available to stakeholders including the community where the study was carried. Because of the community concern on research involving human subjects, the commonest question asked include who owns research results?

It is now generally accepted that the research sponsor has the right to receive the full results of the research, and in studies involving close and sustained cooperation with patients or research subjects, both the sponsor and the research subjects should be informed of the results. Problems arise when the sponsor owns the results and dissemination of research results was not part of the research protocol. Results from such research may not be published and may not be available to medical library. This is serious especially where research protocol was prepared from outside and local personnel were only involved in data collection and linkages between local and outside research are not assured of sustainability. It should be the responsibility of the IREC to scrutinize the protocols and ensure that:

- (i) Research protocol contains procedures for information dissemination to stakeholders, including communities where research subjects were recruited;
- (ii) Research is free from commercial bias;
- (iii) Research results with proven advantages are widely disseminated and be put to use; and
- (iv) The protocol contains provisions to ensure that in the cause of dissemination of research results, confidentiality of third party is not compromised.

7.2 Receiving gifts and hospitality in health research

The growing research interest of researchers from developed world to developing countries may bring along with financial or other packages that might influence research. Bearing in mind that a number of researchers in developing countries are lowly paid, gifts and hospitality might be inducement for researchers to engage in researcher that do not conform with internationally accepted standards. The CMA as well as MAT has provided guidelines, and a joint advice has been issued by the BMA and other on subjects such as 'Clinical Trials in General Practice' and "Post Marketing Surveillance". The views of the GMC are that.

"It may be improper for a doctor to accepted per capita or other payments from a pharmaceutical firm in relation to a research project such as the clinical trial of a new product, unless the payment have been specified in a protocol for the project which has been approved by the relevant national or local ethical committee. It may be improper for a doctor to accept per capita or other payments under arrangements for recording clinical assessments of a medicinal product, whereby he is asked to report reactions which he has observed in patients for whom he has prescribed the product, unless the payments have been approved by the relevant national or local ethical committee. It is improper for a doctor to accept payment in money or kind which could influence his professional assessment of the therapeutic value of the new product".

While this seems to be directed at the doctor, the principle is equally applicable to non-medical researchers as long as they are carrying out research involving human subjects. Therefore:

- (i) Researchers should be transparent by indicating in their protocols gifts and other forms that would be associated with their carrying out the study;
- (ii) IRECs should assess the per capita payment which should not exceed a reasonable estimate of the cost of studying a subject plus any legitimate profit; and

- (iii) IRECs should provide guidance on what constitutes legitimate profit on the basis of acceptable practice.

7.3 Compensation (No fault)

As earlier stated, research may be cause of harm to research subjects in the physical or psychological sense. The risks are however, minimal but cannot be completely neglected. The question that is commonly asked is whether there are guidelines on the form acceptable for compensation. It should be stressed that motives driving research subjects to participate in the research may be variable. However, there is agreement that the benefits that society stands to gain outweigh the risks. Therefore, research subjects who develop illness as a result of participating in a research project are only legally entitled to compensation if they can show evidence of negligence on the part of:

- (i) Investigator;
- (ii) The host institution;
- (iii) The sponsor of the research; or
- (iv) Respective staff.

From the preceding paragraph, it can be concluded that research subjects have no legal right if they are unable to demonstrate negligence, a concept that raises questions of justice to research subjects. The BMA considers this lack of automatic compensation measure unacceptable and has called for more consideration especially where;

- (i) The research protocol carries high risks because it involves invasive procedures; and
- (ii) There is sufficient evidence that the procedures carry risks, arrangements for compensation should be made regardless of whether there may or may not have been negligence.

In Tanzania there are provisions in the Insurance Act of the necessity for compensation to research participants who develop illness as a result of participating to a research project. The Act clearly states that the insurance cover should be in accordance with local laws and regulations. In 2007, the Ministry of Health and Social Welfare through the Tanzania Food and Drug Authority directed full implementation of the provisions. Therefore in accordance with these Guidelines, it shall be required that:

- (iv) All clinical trial proposals shall provide statements on how participants will be compensated in the event of adverse effects;
- (v) The name(s) of insurance companies or brokers be provided in the proposal;
- (vi) The terms of compensation shall be clearly stated in the proposal; and
- (vii) The mode of compensation shall be clearly stated.

CHAPTER EIGHT

8. ETHICAL ISSUES UPON COMPLETION OF A STUDY

8.1 Introduction

It has become apparent that there are ethical issues involved when research on human subjects comes to an end, and the matter has attracted attention of researchers in many scientific fora. The questions often asked include post research obligations to:

- (i) Research subjects and researchers.
- (ii) Communities
- (iii) Institutions.
- (iv) Sponsors

Also commonly asked is “who should bear the responsibility”? Experience in developed countries has shown that more often the responsibility rests with the researchers, sponsors and the health authorities, taking into consideration for the benefits of communities or those with the studied condition. Similarly, the contribution of market forces in collaboration with health professionals and others have been recognized as those factors which make the outcomes of the study reasonably available to all stakeholders. Experience in the developing countries on the other hand is different, as in many cases consideration of what happens when the study comes to an end is often left un-addressed.

8.2. Guidelines on what to do at the end of a study

8.2.1 *The CIOMS Guidelines*

CIOMS recognizes the need for guidelines on this issue, and Guideline 15 states:

“As a general rule, the sponsoring agency should agree in advance of the research that any products developed through such research will be made reasonably available to the inhabitants of the host community or country at the completion of successful testing”.

CIOMS further stresses capacity building of the host country and requires that external research sponsors should help develop the host countries capacity to be able to carry out similar studies independently, including the review process.

8.2.2 US National Bioethics Advisory Commission

The US National Bioethics Advisory Commission recommends that *“Arrangements should be put in place to continue to provide to all participants (including members of a controlled group) any research intervention that was proven successful along the research, and the agreed upon details regarding post-trial treatment must be included in the informed consent process”*.

However, other schools of thought argue against this and advocate that such conditions should not in any way constitute general requirements of health research in developing countries because they are unrealistic and generally not achievable.

In the case of Tanzania, it is in accordance with these Guidelines recommended that arrangements regarding post-study treatment are included in the proposal and informed consent form to the extent that available resources allow.

8.2.3 Ethical issues related to the post-study period

There are numerous ethical issues to be considered after the trial has come to an end which when not addressed carefully constitute dilemmas in health research. For example researchers have encountered dilemma on deciding who should be informed of the results and in what order. As a general rule:

- (i) Research results should be disseminated to stakeholders including individuals, communities, and policy and decision makers;
- (ii) Research results should be repackaged and disseminated in a manner and language that stakeholders regardless of education and cultural background will understand.

8.4 What to do with the human resources involved in the study?

More often in Tanzania, staffs are recruited from either institutions or communities hosting the study. At the end of the study it is uncommon that staff from institutions return to their routine work while those from local communities where the studies were carried out are left on their own. This has in many cases caused anxiety and in the long run may erode the trust on research and compromise future results.

In accordance with these Guidelines and as a matter of principle research protocols should provide capacity buildings of staff involved in the study to enable them to be able to carry out similar studies independently. This may be in the form of training, faculties and continuing education.

8.5 Sustainability of health improvement

Often health research is associated with health improvement, which may not be easily sustained after the study has come to an end. As a general rule, research protocols should provide strategies to sustain the health of the research subjects.

8.6 Disposal of residual resources

Researches bring to the host communities large pools of resources including vehicles, equipment, supplies, chemicals and pharmaceutical products, etc. Questions arise on appropriate disposal of such resource at the end of the study. As general guidelines:

- (i) Prior consideration should be given to resources that may be beneficial to the host communities.
- (ii) Research protocols should detail how residual resources will be disposed of;
- (iii) Contract agreement should be entered between researchers and host communities on the disposal of residual resources.
- (iv) Disposal should aim at capacity building; and
- (v) National legal regulations on such disposal of residual resources should be taken into account.

8.7 Availability of products

Health research in patients may involve provision of therapeutic products. Researchers may encounter dilemmas where a trial product has proven benefits to the studied subjects. In this regard:

- (i) Research protocols should provide details on how to handle research subjects on a product if it proves to benefit the patients;
- (ii) Contract agreement should be drawn to ensure that a product with proven beneficial effect is made available to the community as soon as possible, at an affordable price.
- (iii) Agreement should be made to ensure that a product, which has been shown to be effective, is made available to all research subjects as well as to other population at risk.

8.8 Archived specimens

Often researchers store specimen long after the study has come to an end. Ethical issues related to archived specimens like blood, organs, tissues, etc, are becoming subjects of discussion. The questions often asked include whether researchers may use archived specimens for studies other than the study consented to by the research subjects. It is important to note that consent is provided for the intended study, and it is unethical to use specimens for purposes other than those consented for. As general guidelines on this matter:

- (i) Research protocols should detail the purpose and use of research specimens;
and
- (ii) Archived specimens should be commitment that if the specimens will be required in another experiment, researchers must provide a new protocol;

8.9 Patient rights and sharing of benefits

Researchers in developing countries, including Tanzania, have in recent years complained of research piracy by researchers from developed countries. As a result, Intellectual Property Rights and the sharing of benefits from commercial products are raising ethical issues. For example, an ethno-botanical study has demonstrated a

pharmacological effect of a product. However, because of lack of facilities for further product development, collaborators from overseas went ahead to isolate the active ingredient, patented and later commercialized in without the involvement of the local collaborators. It is therefore, recommended that local researchers involved in collaborative health research with external researchers should draw contract agreement detailing:

- (i) How intellectual property rights matters shall be dealt with;
- (ii) Anticipated benefits and risks that may have to be shared;
- (iii) How benefits and risks shall be shared between researchers, sponsors and society;
- (iv) The contributions of each researchers; and
- (v) The methods of dissemination of research result, including publication.

8.10 Capacity building

There in need to ensure that all forms of research funding should include provision for capacity building of the host institution. Strategies for capacity building should be developed so as to include:

- (i) Early involvement of the study community in the design, development and implementation processes;
- (ii) Scientific exchange, knowledge and skills transfer;
- (iii) Support for development of local ethical review capacity;
- (iv) Support for education, information technology; and
- (v) Support for consensus building.

8.11 Community participation

Involvement of community representatives should neither be seen a single encounter, not as one-directional. The orientation of community involvement in research should be one of partnership towards mutual education and consensus building regarding all aspects of the research. To ensure the ethical and scientific quality of the proposed research, its relevance to the community and its acceptance

by the study population, community representatives should be involved in an early and sustained manners in the:

- (i) Design of the study
- (ii) Development and implementation stages
- (iii) Dissemination of research results.

8.12 Conclusion

In this chapter an attempt has been made to address what should be done when the research has come to an end and the dilemmas that researchers, research subjects and communities are likely to encounter. The list however, is not exhaustive and researchers are advised to update themselves on their experiences. Clear approaches and frequent exchange of ideas between researchers and other stakeholders are essential and will enrich our understanding of the intricacies and ethical matters related to what should happen when the research has come to an end.

CHAPTER NINE

9. ETHICAL ISSUES REGARDING ANIMAL EXPERIMENTATION

9.1. Introduction

The role of animals in advancing health science has long been established. Animal experimentation has provided knowledge on the understanding of human physiology and pathophysiologic basic of diseases. Similarly, animal experimentation has in numerous ways provided models for training and others scientific knowledge. It is important therefore, that animals involved in research should be respected and cared for. Good care improves the welfare of the animals and consequently will yield better, dependable and reproducible results than animals that are poorly kept or suffer from diseases. Experimental animals are any non-human living vertebrates or any other animal which according to the National Ethics Committee for Research on Animals has a nervous system which is so sophisticated that the animals is capable of experiencing pain in much the same way that any vertebrate might experience. An animal experiment therefore, is any procedure or procedures whereby a live animal or animals are used for the purpose of testing a hypothesis, answering research questions, collecting information for purpose of advancing knowledge or teaching or registering the effects of a certain procedure on an animal.

9.2. The National Health Research Ethics Committee recommendation

With respect to ethical issues in research involving laboratory animals, the National Health Research Ethics Committee wishes to:

- (i) Recognize the contribution of animals to knowledge and that future use of animals are necessary;
- (ii) Urge researchers to exercise humane care to animals during experimentation;
- (iii) Stress that during animals experimentation, care must be exercised to ensure as much as possible that the animal is free from pain, stress, and discomfort, suffering and permanent damage; and

- (iv) Stress that any institution carrying out animal experiments should establish Committee for Research Involving Animals (ICRIA) or Animal Use and Care Committees.

9.3 Composition of ICRIA

The size of the committee must not be too large or too small but should consist of members with the following qualities:

- (i) Researchers with long experience in animal experiments;
- (ii) One member representing a recognized organization involving in monitoring animal welfare in Tanzania but not involved in the proposed research;
- (iii) One member representing veterinary sector (a registered veterinarian) but not involved in the proposed research;
- (iv) One lay member vested with interest in research, but not involved in the proposed research.

9.4 Appointment of members of ICRIA

The management of the institution should make appointment of membership to ICRIA, and the functions of ICRIA should include:

- (i) To prepare institutional guidelines on the conduct of animal experiment and clinical care within the institution;
- (ii) To keep register of the variety of animal species used for experiments;
- (iii) To ensure that the animals are well fed, kept and free from discomfort, suffering of diseases by making frequent examinations;
- (iv) To ensures that procedures for experiments conform to acceptable standards;
- (v) To ensure that experimental procedures are done by competent persons;
- (vi) To ensure that decisions made by the Committee are complied upon by researchers;
- (vii) To hold regular meetings aimed at reviewing suitability of submitted proposal for clearance; and
- (viii) To make regular reports to the management of the institution.

9.5 Shipment of drugs for investigational use in laboratory animals

There are cases where laboratory animals in Tanzania are and or will be used in investigation of a trial product (drug). The drugs will in most cases be shipped from outside the country. It is important that such information be contained in the submitted protocol for review by IREC or NHREC. IRECs and NHREC must ensure that a person:

- (i) May ship into Tanzania a drug intended solely for tests *in vitro* or laboratory animals if it is labelled as follows:
 - **CAUTION:** Contains a new drug for research use only in laboratory animals, or for test *in vitro*. **Not For Use in Humans.**
- (ii) May ship a biological product for research *in vitro* diagnostic use if it is labelled as follows:
 - **CAUTION:** Contains a biological product for research *in vitro* diagnostic tests only.
- (iii) Shipping into Tanzania a drug under paragraph (i) of this section shall use due diligence to assure that the consignee is regularly engaged in conducting such tests and that the shipment of the new drug will actually be used for tests *in vitro* or animal used only for laboratory research;
- (iv) Shipping a drug under paragraph (i) of this section shall maintain adequate records showing the name and post office address of the expert to whom the drug is shipped and the date, quantity, and batch or code mark of each shipment and delivery. The records of shipment and deliveries shall be maintained for period not less than **TWO** Years.

9.6 Disposition of unused drugs

As a matter of principle the person who ships into Tanzania:

- (i) Drugs under section 9.5 of this chapter shall assure the return of all unused supplies of the drug(s) from individual investigators whenever the research discontinues or is terminated.

- (ii) Drugs, may authorize alternative disposition of unused supplies of the drug or drugs provided that the alternative disposition does not expose humans to risks from the drug(s), either directly or indirectly, and the shipper shall maintain record of the alternative disposition.

CHAPTER TEN

10. PROCEDURES FOR CONDUCTING HEALTH RESEARCH IN TANZANIA

10.1 Role of the National Institute for Medical Research (NIMR)

The responsibility for controlling, coordinating, conducting and promoting the conduct of health research and dissemination of research results in Tanzania is vested upon NIMR by the Act of Parliament No.23 of 1979 (Appendix III). It follows therefore that in order to conduct health research in Tanzania permission must be sought from NIMR and under no circumstances can any research involving human beings be conducted or initiated in Tanzania without the permission of NIMR. This permission is given in the form of research clearance certificate signed by or on behalf of the Director General of NIMR who is the chairman of the Medical Research Coordinating Committee (MRCC). The same certificate will, as from August 2001, also carry the approval of the Ministry of Health to conduct the research by NIMR in health facilities of the Ministry of Health and in communities under the national health authorities in Tanzania, signed by or on behalf of the Chief Medical Officer.

10.2 The Medical Research Coordinating Committee (MRCC)

The MRCC of NIMR is the National Health Research Clearance body responsible for receiving, reviewing and granting research clearance to all health research proposals, submitted for the purpose of conducting research in Tanzania or elsewhere but for the benefit of Tanzania citizens (Appendix III). Once the Committee is satisfied with the scientific and ethical considerations of a research proposal, and has issued an Ethics Clearance Certificate, it will be co-signed by the Director General of the NIMR (as MRCC Chairperson), and the Chief Medical Officer of the Ministry of Health and Social Welfare. In case the research involves Tanzanians. For non Tanzanian after getting Ethical clearance they proceed to Tanzania Commission for Science and Technology (COSTECH) to get further approvals.

10.3 Tanzania Commission for Science and Technology

The Tanzania Commission for Science and Technology is a body mandated to issue research permit and research clearance to conduct research in the country, for all foreign researchers seeking to conduct or collaborate in conducting research in Tanzania. In order to issue any such permit for the conduct of health research, the commission requires the confirmation by NIMR that the research has been cleared and hence scientifically and ethically sound.

In order to enhance efficiency and reduce delays in issuing the clearance certificates, NIMR has authorized institutions mandated to conduct health research, to form Institutional Health Research Ethics Review Committee whose function will be to review research proposals for health research intended to be conducted within or by the institution and which will be conducted by a research team which involves only Tanzania nationals. Any research, whose team either involves foreign nationals or has the intention of conducting the research in collaboration with external individuals or institutions, has to be submitted to NIMR for clearance, unless the institution has been mandated to control and monitor such research by the Tanzania Government. It is emphasized that Institutional Committees of Health Research in Tanzania may issue research permits only for research proposals which do not involve foreigners. All copies of research proposals reviewed and cleared by the Institutional Health Research Committees must be submitted to NIMR for scrutiny and for record keeping. NIMR charges US \$ 300 for clearance of a research proposal. This charge is currently applicable only to research proposals involving external collaboration.

10.4 Functions of the different institutions involving in health research clearance

10.4.1 Tanzania Commission for Science and Technology (COSTECH)

- (i) The body that coordinates all research in Tanzania;
- (ii) The only institution that may provide research permits to foreign research after ascertaining that the research has been cleared by NIMR;

- (iii) Receives copies of the clearance certificates and corresponding proposals of health research proposal that have been cleared by NIMR.

10.4.2 *The National Institute for Medical Research (NIMR)*

- (i) The body mandated to control and monitor health research conducted in Tanzania.
- (ii) Receives health research proposals from individuals and institutions for ethical clearance.
- (iii) Reviews the proposals and issues clearance certificate, demands modification of proposals before clearance or denies clearance if not satisfied with the scientific and ethical soundness of the proposal.
- (iv) Sends clearance certificated to the Ministry of Health for permission to conduct research within the premises of the facilities of the Ministry of Health.
- (v) Sends copies of the clearance proposals and corresponding certificates to COSTECH for the issuance of research permits to foreign researchers or collaborators.
- (vi) Monitors the conduct of research according to protocol.

10.4.3 *Other Health Research and Academic Institutions*

- (i) Receive research proposals.
- (ii) Review the proposal and issues research clearance to proposals from its staffs, which do not involve foreign researchers or collaborators.
- (iii) Submit all research proposals involving foreign researchers or collaborators to NIMR for national ethical clearance.
- (iv) May review research proposal involving foreign researchers or collaborators but can not issue research clearance and must therefore submit the proposal and reviewers comments to NIMR for clearance.

If mandated by law to issue clearance to research proposals involving foreign researchers or collaborators, the institutions must send a copy of such proposals and

corresponding clearance certificates to NIMR for records and for further scrutiny. In any case NIMR may revoke such a clearance certificate or demand necessary amendments to the proposal before it is conducted in Tanzania, if it is not satisfied with the scientific and ethical integrity of the proposal.

CHAPTER ELEVEN

11. THE TANZANIA NATIONAL HEALTH RESEARCH FORUM

11.1 Background

The Tanzania National Health Research Forum is a forum of partner institutions involved in health research and their representatives. It is an inclusive body which ensures that each partner has a clearly defined role, is considered an asset and share in the ownership of the mechanism. Its functions are based on the Essential National Research (ENHR) strategy, which ensures that evidence based information, is utilized correctly in the policy and decision making process, enhancing the provision of better and equitable health to the population.

The Forum is a consultative and advisory body to policy and decision makers as regards to health research coordination, undertaking collaboration, dissemination of health research and enhancing the utilization of research results for policy and decision making. It is a non-political, non-religious, voluntary body dealing only with issues of health research and development in the country.

11.2 The genesis of TANHER Forum

The genesis of the TANHER Forum may be traced to:

- (i) 1985, the Health System Research Unit was established in the MoH with the support of the World Health Organization;
- (ii) 1991, the Essential National Health Research Strategy was developed, and was supported by MoH, NIMR and COHRED;
- (iii) 1996, The National Health User's Trust Fund was established under the support of MoH, NIMR and Swiss Agency for Development Cooperation.
- (iv) 1998:
 - (a) Ghana held ENHR Conference under the support of COHRED and National Health Research Forum was first proposed as a mechanism for WNHR.
 - (b) Proposal for NHRF was approved by the NIMR Council.

- (c) ENHR Strategy Workshop was held and an interim NHRF Chairman was appointed.
- (v) 1999, ENHR Priority Setting Workshop was held using the Three Pronged Approach. It was during the workshop that elections for the NHRF Chairman, Secretary and the Secretariat were made;
- (vi) The NHRF was launched officially by the Minister for Health on 26th February, 1999;
- (vi) The NHRF Secretary became the Council Member of the Global Forum for Health Research in March 1999; and
- (vii) The NHRF held its First Annual Meeting on February 2000.

11.3 The terms of reference of the Forum include:

- (i) To discuss and recommended a mechanism for National Health Research (NHR) priority setting;
- (ii) To establish and revise periodically NHR Priorities;
- (iii) To receive and approve the report of the NHRCC;
- (iv) To receive and approve the report of the NHREC.
- (vii) To recommend to the MoH for approval of ethical guidelines for scientific content and ethics of health research in Tanzania.
- (viii) To promote the establishment of networking and coordinating between centres and institutions.
- (ix) To advise policy and decision makers on the allocation of funds for NHR activities; and
- (x) To provide guidelines for partnership in health research.

The forum is therefore an independent body, which supports NIMR in its role in health research coordination and ethics review without actually taking these functions away from NIMR. Its functions are with respect to defining policies and guidelines for the conduct of health research and making it possible that all stakeholders actively participate in the formulation of such guidelines.

It ensures that harmonization of guidelines for the conduct of health research in Tanzania and the review process including the health research review guidelines. It also provides checks and balances in the processes and outputs of research monitoring bodies like NIMR, functions towards ensuring the development and maintenance of health research priorities in Tanzania, as well as that funds are made available for financing of such health research priorities.

In addition, the Forum works to enhance the translation of health research results into action. The approach is to set strategies for enhancing the utilization of such results by policy and decision makers, and stimulate the application of such strategies. In this regard, the Forum acts as a catalyst for the reactions of all stakeholders in this process, ensuring participation and ownership of the processes by the stakeholders themselves. The Forum is therefore an essential organ for strengthening the conduct of health research in Tanzania, and as a stimulant for development of research capacities.

11.4 Mode of operation

Depending on the mandate, each partner institution is a vehicle for passing on the Forum recommendations to policy and decision makers for policy and decision-making. It is the aim of the Forum to develop better strategies for research coordination, ensuring the maintenance of quality research and setting priorities for national research activities.

11.5 Conclusion

This booklet is the first national initiative in providing guidelines to health researchers and other stakeholders for the conduct of health research involving human subjects has been necessitated by the concern of the Tanzania society. It is intended to increase the level of awareness of all stakeholders on the need to comply with ethical standards in health research.

It is now accepted that health research carries the potential to cause physical and/ or psychological harm. This work draws the attention of researchers on ethical issues that have to be given consideration before, during, and after the study period. This however, is by no means exhaustive. Several issue, which are due to recent advancements in medical science and technology, which though important, may not have been included in this work. Such areas include the ethics of gene therapy, embryo research, the use of radiation in research. These important areas will nevertheless have to be addressed in the future.

In preparing these guidelines, emphasis was directed at ensuring that the interest of individual research subjects must always come first and be respected. In recruiting subjects into the study, adequate information on the aims methods, anticipated benefits; potential hazard and any discomfort that the research may entail must be given to all subjects in a manner that will empower them to make informed consent.

The rights if individual subjects to refuse participation in the study and or withdraw from the study at any stage of the study must be respected. In the process of obtaining consent, the consent will only be valid if it is given freely, and without undue pressure or inducements. No research which could equally be carried out on competent persons with their consent should be allowed to be carried out on people who cannot give valid consent.

To enable monitoring of health research in Tanzania, institutions engaged in research and training of health personnel must establish Research Ethics Committees (IREC). The composition of IRECs should include competent people in their areas of specialization, but also people from outside with the capacity to contribute towards enhancing ethical consideration in health research. The functions of the IRECs include receiving and scrutinizing research protocols, monitoring the research processes and keeping the records of research outputs. IRECs will be expected to provide advice and guidance to authors on the scientific and ethical soundness of their research proposals.

For smooth running and proper record keeping on the trends of health research in Tanzania, the NHREC should establish stronger linkages with collaborating institutions. The composition of the NHREC should be optimal and lay people should be included and encouraged to participate in activities of the NHERC.

These guidelines should be considered in line with acceptable community socio-cultural norms so as to avoid transgressing societal value. Where in doubt, existing guidelines e.g. the guiding principles and those earlier cited should be consulted.

APPENDIX ONE

DECLARATION OF HELSINKI

Human experimentation

In 1964, the WMA drew up a code on human experimentation. This code is since then known as the Declaration of Helsinki, as amended by the 29th World Medical Assembly, Tokyo, Japan, in 1975, the 35th World Medical Assembly, Venice, Italy, in 1983, 41st World Medical Assembly, Hong Kong, 1989 and the General Assembly, Somerset West, Durban, South Africa, in 1996 reads:

It is the mission of the medical doctor to safeguard the health of the people. His or her knowledge of conscience are dedicated to the fulfilment of this mission.

The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration", and the International code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient".

The purpose of biomedical research involving human subjects must be to improve diagnostic, therapeutic and prophylactic procedures and the understanding of aetiology and pathogenesis of disease.

In current medical practice, most diagnostic, therapeutic or prophylactic procedures involve hazards. This applies especially in biomedical research.

Medical progress is based on research, which ultimately must rest in part on experimentation involving human subjects. In the field of biomedical research a fundamental distinction must be recognized between medical research in which the aims is essentially diagnostic or therapeutic for a patient, and medical research, the

essential object of which is purely scientific and without implying directed diagnostic or therapeutic value to the person subjected to the research.

Special caution must be exercised in the conduct of research, which may affect the experiment, and the welfare of animals used for research must be respected. Because it is essential that the results of laboratory experiments must be applied to human beings to further scientific knowledge and to help suffering humanity, the WMA has prepared the following recommendations as a guide to every physician in biomedical research involving human subjects. They should be kept under review in the future. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Physicians are not relieved from criminal, civil and ethical responsibilities under the laws of their own countries.

1. Basic Principles

- (a) Biomedical research involving human subjects must conform to the generally scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.
- (b) The design and performance of each experiment procedure involving human subjects should be clearly formulated in an experimental protocol, which should be transmitted to a specially appointed independent committee for consideration, comment and guidance.
- (c) Biomedical research involving human subjects should be conducted only by scientifically qualified persons under the supervision of a clinically competent medical person. The responsibility for human subjects must always rest with the medically qualified person and never rest on the subject of research, even though the subject has given his or her consent.
- (d) Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

- (e) Every biomedical research involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable to the subject or to others. Concern for the interest of the subject must always prevail over the interest of science and society.
- (f) The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
- (g) Physicians should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazard involved is believed to be predictable. Physicians should cease any investigation if the hazards are found to outweigh the potential benefit.
- (h) In publication of the results of his or her research, the physician is obliged to preserve the accuracy of the results.
- (i) In any research on human being, each potential subject must be adequately informed of the aims, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The physician should then obtain the subject's free-given consent, preferably in writing.
- (j) When obtaining informed consent for the research project the physician particularly should be cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a physician who is not engaged in the investigation and who is completely independent of this official relationship.
- (k) In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation. Whenever the minor

child is in fact able to give consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.

- (l) The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

2. Medical research combined with professional care (Clinical Research)

- (a) In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgment it offers hope of saving life, re-establishing health or alleviating suffering.
- (b) The potential benefits, hazard and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.
- (c) In any medical study, every patient including those of a control group, if any should be assured of the best-proven diagnostic and therapeutic method.
- (d) The refusal of the patient to participate in a study must never interfere with the physician-patient relationship.
- (e) If the physician considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee.
- (f) The physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

3. Non-therapeutic biomedical research involving human subjects (Non-clinical biomedical research)

- (a) In the purely scientific of medical research carried out on a human being, it is the duty of the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.

- (b) The subjects should be volunteers; either healthy persons or patients for whom the experimental design are not related to the patient's illness.
- (c) The investigator or investigating team should discontinue the research if in his or her judgment it may; if continued, be harmful to the individual.
- (d) In research on man, the interest of science and society should never take precedence over considerations related to the well being of the subject.

APPENDIX TWO

SCIENTIFIC AND ETHICAL REVIEW GUIDELINES

The guidelines have been drawn to provide as a checklist which would assist IRECs to review proposals submitted for ethical clearance. The checklist also serves as a standard for harmonizing proposal review. On reviewing the proposal the review committee should look for the following:

1. Title

- 1.1. Is there a title for the proposed study?
- 1.2. Is the title clear and explains the intended research?
- 1.3. Should not be too long?

2. Authors and Institutional Affiliations

- 2.1. Who are the authors?
- 2.2. Are they qualified for the intended research?
- 2.3. Any previous experience in research of similar nature?
- 2.4. Adequacy of the research team for the proposed study?
- 2.5. Is multi-disciplinary approach addressed?
- 2.6. To which institutions are they affiliated?

3. Summary

- 3.1. Does the proposal carry a summary?
- 3.2. Adequacy of the summary in providing important elements of the study (Background, Rationale, Objectives, Methodology, Timeframe and Total Budget)?

4. Background and literature review

- 4.1. Has the subject of research been adequately reviewed?
- 4.2. Will the proposed study bring new knowledge?

5. Problems statement

- 5.1. Is there a problem warranting the study?
- 5.2. What research questions would the study answer?
- 5.3. What hypothesis is being tested?
- 5.4. What is to be gained from the study?
- 5.5. Will the study design provide answers to the raised question?

6. Objectives of the study

- 6.1. Are objectives clear and address the problem to be researched?
- 6.2. Will the objectives attempt to answer the raised research questions?
- 6.3. Are objectives realizable?

7. Study area and population

- 7.1. Where is the study going to be carried out?
- 7.2. Is the selected study area and population appropriate for the proposed study?
- 7.3. Given the available capacities, is it feasible to carry out the study in the selected area and population?
- 7.4. Is the study population well defined?
- 7.5. What sampling methods have been proposed for selecting study population?
- 7.6. Would the selected population be representative of the community from which the sample has been selected?

8. Methodology

- 8.1. Are proposed methods clearly explained?
- 8.2. Will the proposed methods provide answers to the research question?
- 8.3. Are there advantages of using one method over the other or combination of methods?
- 8.4. How will collected data be handled?
- 8.5. Does the proposal address issues of capacity building of local collaborator (s)?

9. Ethical consideration

- 9.1. Is it ethical to carry out the proposed study?
- 9.2. Have ethical issues related to the study been considered?
- 9.3. Have the risks to benefit been considered?
- 9.4. Are social and cultural factors that may transgress individual privacy been considered?
- 9.5. Is the procedure for seeking consent clear?
- 9.6. Has autonomy of research subjects been considered?
- 9.7. Are the necessary instruments available?

10. Compensation

In case of clinical trials:

- 10.1. Is there a description of how research participants will be compensated?
- 10.2. What are the levels of compensation?
- 10.3. To what extent compensation is in accordance with local laws?
- 10.4. Which company(ies) will be involved in providing insurance cover?

11. Safety data monitoring

In the case of clinical trials, establish:

- 1.1. Is there a Data Safety Monitoring Board proposed?
- 1.2. Have the functions of the DSMB clearly defined?
- 1.3. Has at least one member from Tanzania been included?

12. Constraints

- 12.1. Are there constraints that might require social attention?
- 12.2. What strategies have been proposed to address the constraints?
- 12.3. Is there assurance that the effects of the constraints on the study output will be minimal?

13. Dissemination

- 13.1. Are there proposals of how the research results will be disseminated?

13.2. Do the proposed dissemination strategies target stakeholders?

14. Budget

14.1. Is the budget realistic?

14.2. Is a budget justification satisfactory?

14.3. Is there balance on how funds will be shared between collaborating institutions?

14.4. are the potential participants been considered for their time and travel

14.5. Is the payment appropriate for their circumstances

APPENDIX THREE

Research provisions of the National Institute for Medical Research Act No. 23 of 1979

1. The National Institute for Medical Research (NIMR) was established by Act of Parliament No. 23 of 1979. Section 4 (1) of the NIMR Principal Act prescribes the NIMR functions relevant to research to include among other things:
 - (i) To carry out, and promote the carrying out of, medical research designed to alleviate disease among the people of Tanzania.
 - (ii) In collaboration with the Government of any person or body of persons, to promote, or provide facilities for, the training of local personnel for carrying out scientific research into medical problems.
 - (iii) To carry out, and promote the carrying out of research into various aspects of local traditional medical practices for the purpose of facilitating the development and application of herbal medicine.
 - (iv) To monitor, control and co-ordinate medical research carried out within Tanzania, or elsewhere on behalf of or for the benefit of the Government of Tanzania, and evaluate the findings of that research.
 - (v) To establish a system for the registration of, and to register, the finding of medical research carried out within Tanzania, and promote the practical application of those findings for the purpose of improving or advance the health and general welfare of the people of Tanzania.
 - (vi) To establish and operate a system of documentation and dissemination of information on any aspect of the medical research carried out by or on behalf of the Institute.

2. Section 4 (2) further stresses that, in particular, but without prejudice to the generality of Subsection (1) NIMR may:

- (i) Carry out, and promote the carrying out of, research and investigation into the cause, and the ways of controlling and preventing the occurrence in Tanzania of particular diseases or a category of them.
 - (ii) In co-operation with the Government or any person or body of persons, carry out and promote the carrying out of, basic, applied and operational research designated to provide effective measure for the control of disease endemic in Tanzania.
3. The Act. No, 23 of 1979 further mandates NIMR, under Section 11, to require in writing any hospital, health centre, dispensary or other medical establishment or category of them to furnish to its such information relating to such disease or disease as the Institute may specify.
4. Further, Section 12 empowers NIMR to call for information on medical research by requiring every person or body of persons engaged in medical or other allied scientific research within Tanzania to furnish to it such information relating to medical or other allied scientific research as the Institute may specify. The section spells out condition to be complied that, every person or body of persons required to furnish information under Section 12 (1) shall comply with the requirement and any person or body or persons, who refuses or fails to comply with that requirement shall be guilty of an offence.

In conclusion, NIMR is the National Institute with mandate to carry out, promote and monitor the conduct of health research in Tanzania. In order to enhance smooth operations and research environment in Tanzania, institutions with mandates to carry out health research in Tanzania should therefore, familiarize themselves with the relevant provisions of the NIMR Act.

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