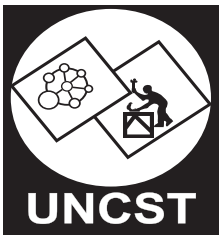

THE REPUBLIC OF UGANDA

NATIONAL GUIDELINES FOR RESEARCH INVOLVING HUMANS AS RESEARCH PARTICIPANTS

Uganda National Council for Science and Technology
Kampala - Uganda

March 2007

These guidelines were prepared by a Task Force set up by the Uganda National Council for Science and Technology (UNCST).

Additional information about the guidelines may be obtained from:

The Executive Secretary
Uganda National Council for Science and Technology
P. O. Box 6884, Kampala - Uganda.
Telephone: + 256 (0)414 - 250499
+ 256 (0)414 - 705500
Fax: + 256 (0)414 - 234579
E-mail: uncst@starcom.co.ug
Internet: http: www.uncst.go.ug

Recommended citation:
Uganda National Council for Science and Technology 2007. National Guidelines for Research involving Humans as Research Participants. Kampala - Uganda: UNCST

Table of Contents

Table of Contents

Table of Contents

MEMBERS OF THE UNCST TASK FORCE

Professor Nelson K. Sewankambo, (Chair)
Faculty of Medicine, Makerere University

Dr. David Guwatudde, (Vice Chair)
Institute of Public Health, Makerere University

Dr. Banson Barugahare,
Joint Clinical Research Centre

Dr. Joseph Olobo,
Department of Microbiology,
Faculty of Medicine, Makerere University,

Professor Edward Kasuja Kirumira,
Faculty of Social Sciences, Makerere University

Dr. Philippa Musoke,
Department of Paediatrics and Child Health,
Makerere University

Dr. Frederick Nelson Nakwagala,
Department of Medicine,
Mulago Hospital, Ministry of Health

Professor Elly Katabira,
Faculty of Medicine, Makerere University

Dr. Stella Neema,
Makerere Institute of Social Research, Makerere University

Dr. Joseph Ochieng,
Department of Anatomy,
Faculty of Medicine, Makerere University

Dr. Edward Katongole Mbidde,
Uganda Virus Research Institute

Dr. Irene Lubega,
Department of Paediatrics and Child Health,
Makerere University

Dr. Betty Kwagala,
Makerere Institute of Social Research, Makerere University

Mr. Julius Ecuru, (Secretary)
Uganda National Council for Science and Technology

ACKNOWLEDGEMENT

The contribution of the UNCST Task Force in preparing these guidelines is very much appreciated.

The UNCST is grateful to the International AIDS Vaccine Initiative, in particular Ms. Leslie Nielsen, Mr. Emmanuel Mugisha and Dr. Samuel Kalibala for providing logistical support to the Task Force meetings, and the Makerere University – Walter Reed Project for offering to print initial few hundred copies of the guidelines.

The UNCST is also grateful to its staff namely: Mr. Edward Tujunirwe, Ms. Jane Nabbuto and Ms. Leah Nawegulo for the administrative support they rendered to the Task Force.

Finally, UNCST is thankful to all the stakeholders for their inputs which enriched these guidelines.

Acronyms

CAB	Community Advisory Board
DSMB	Data and Safety Monitoring Board
IBC	Institutional Bio-safety Committee
IRC	Institutional Review Committee
MTA	Materials Transfer Agreement
NDA	National Drug Authority
R&D	Research and Development
SAE	Serious Adverse Event
S&T	Science and Technology
SC	Scientific Committee
SOP	Standard Operating Procedures
UCG	Uganda Clinical Guidelines
UNCST	Uganda National Council for Science and Technology

Preface

The purpose of research is to generate or contribute to generalisable knowledge that could benefit present and future generations. In order to achieve this purpose, some people have to bear the burden of research. It is necessary to ensure that the people who bear this burden of research also benefit in some way or that their rights and welfare are not compromised during the course of research. Therefore, these National Guidelines for Research involving Humans as Research Participants have been formulated to provide a system in Uganda that facilitates the carrying out of important research without compromising the rights and welfare of individual research participants.

These National Guidelines for Research involving Humans as Research Participants are a revised version of the 1997 Guidelines for Health Research involving Human Subjects in Uganda. The changes and new material in these revised guidelines is in keeping with the belief that the guidelines are subject to modification with changing conditions and new information. As new information in the field of research ethics emerged, it became necessary to revise the 1997 guidelines to reflect the current norms of scientific research practice and ethical conduct.

To this end, the UNCST appointed in November 2005 a Task Force to review the then Guidelines for Health Research Involving Human Subjects in Uganda. The Task Force accomplished its work through a series of meetings, consultations and literature review; and prepared these revised guidelines with a new title, "National Guidelines for Research involving Humans as Research Participants". The revision broadened the guidelines to cover all aspects of research involving humans as research participants, including social and behavioural research, research in alternative medicine and research with stored human biological specimens. They also emphasise the role of Institutional Review Committees in conducting initial and continuing review of research projects involving humans as research participants.

These guidelines are intended to guide individuals and institutions to conduct research in Uganda in a scientifically and ethically appropriate manner. They should assist investigators to fulfil their obligations to plan and conduct research in accord with sound scientific and ethical principles.

Readers who detect errors of omission or commission are invited to send corrections and suggestions to the Uganda National Council for Science and Technology, P. O. Box 6884, Kampala. E-mail: uncst@starcom.co.ug.

Professor Nelson K. Sewankambo
Chairman, Task Force

Dr. Peter Ndemere
Executive Secretary, UNCST

1. GENERAL PROVISIONS

1.1 Introduction

Uganda has unique health, environmental, social and economic problems that attract both local and international research interests. Since 1990 the number of research projects involving humans as research participants in Uganda has more than tripled. This increasing quest for knowledge and the search for novel remedies to health, environmental, social and economic challenges is beneficial but could involve exposing research participants to a spectrum of risks. These guidelines provide a national framework for harnessing the benefits of research while ensuring that the rights, interests, values and welfare of research participants are protected.

1.2 Rationale

Ideally, research is conducted for the benefit of society. However, research also presents burdens to the individuals and communities who volunteer as research participants. The research participant's rights and welfare could be compromised when researchers develop conflicts of interest because of their quest for new knowledge. In other instances, communities may be unfairly denied the benefits of research or be unjustifiably exposed to potentially risky research. It is thus imperative to develop a system that promotes beneficial research and guards against unethical research.

1.3 Objectives

The overall objective of these guidelines is to facilitate the conduct of research without compromising the rights and welfare of research participants.

Specifically, these guidelines are to:

a. Protect the rights and welfare of research participants;
b. Provide ethical standards and procedures for the conduct of research involving humans as research participants;
c. Ensure that research takes into account social and cultural sensitivities of participating communities.

1.4 General Policy

Research and development including scientific investigations and technological trials involving humans as research participants shall be conducted for the benefit of communities in Uganda and abroad without causing unnecessary harm or inconvenience to human research participants, and shall not compromise the rights and welfare of research participants.

1.5 Scope of Application

The aforementioned general policy and other provisions of these guidelines apply to (1) all research involving humans as research participants in Uganda, including research in social sciences and humanities, conventional and alternative medicines and research conducted in or by public institutions, private, inter-governmental and non-governmental organizations, and (2) research conducted in a foreign country on human biological materials collected from Uganda.

2. RIGHTS AND WELFARE OF RESEARCH PARTICIPANTS

2.1 Research involving humans as research participants

Research involving humans as research participants includes:

a. Clinical investigations, that is, any experiment or study on one or more persons which involves a test product/ article, whether a drug, treatment, procedure, or device;
b. Social-behavioural studies which involve interaction with or observation of people; and
c. Basic scientific research to study the biology of persons or organs and specimens thereof;
d. Systematic collection, storage and analysis of data on humans.

2.2 Rights and welfare of human research participants and their communities

Research should be conducted in a manner that does not violate the rights and welfare of human research participants.

The rights of human research participants include, but are not limited to, the rights to:

a. Participate in ethically acceptable research;
b. Be respected, including the right of their autonomy, culture, beliefs and values;
c. Information about the research (it is important to ensure that information is communicated in understandable language, format and in a conducive environment at all stages of the research);
d. Protection against research related injuries, harm, exploitation, and any other forms of abuse related to the research;
e. Privacy and confidentiality of their participation, during and after the research;
f. Decide whether to participate in the research or not, or withdraw at any time without penalty;
g. The standard of health care that is available nationally;
h. Compensation for research related injuries and costs; and
i. Report any abuses of ones rights and welfare to the Principal Investigator, IRC, UNCST or any other relevant legal authority.

Research should aim at improving the well being of research participants and their communities. This can be attained through:

a. Provision of health care beyond research related care;
b. Optimization of collateral benefits to the research communities;
c. Provision of good client care during study investigations and procedures;
d. Taking measures to ensure easy access by the community to the test drug/device, if proven beneficial.

2.3 Research Ethics Principles

In order to protect the rights and welfare of human research participants, research should be conducted in accordance with the four basic research ethics principles, namely: respect for persons, beneficence, non-maleficence and justice. It is generally observed that these principles guide the conscientious preparation of proposals for scientific studies. They may be expressed differently and given different moral weight in different settings, and their application may lead to different decisions or courses of action in those particular settings. These principles are briefly described as follows:

a. ***Respect for persons*** incorporates at least two fundamental ethical considerations, namely: respect for autonomy, which requires that those who are capable of deliberation about their personal choices should be treated with respect for their capacity for self-determination; and protection of persons with impaired or diminished autonomy, which requires that those who are dependent or vulnerable be afforded security against harm or abuse.

b. ***Beneficence*** refers to the ethical obligation to maximize benefits and to minimize harms. This principle gives rise to norms requiring that the risks of harm by research be reasonable in light of the expected benefits, that the research design is sound, and that the investigators are competent both to conduct the research and to safeguard the welfare of the research participant.

c. ***Non-maleficence*** (to do no harm) proscribes the deliberate infliction of harm, or evil on research participants.

d. ***Justice*** refers to the ethical obligation to treat each person in accordance with what is morally right and proper, to give each person what is due to him or her. In the ethics of research involving humans as research participants the principle refers primarily to ***distributive justice***, which requires the fair and equitable distribution of both the burdens and the benefits of participation in research.

3. REGULATORY OVERSIGHT OF RESEARCH PROJECTS

3.1 The Regulatory Process

The oversight of research involving humans as research participants in Uganda is presently carried out at two levels: at the institutional level by the Institutional Review Committees (discussed in detail in Chapter 4), and at the national level by the Uganda National Council for Science and Technology (UNCST). The UNCST liaises with the Research Secretariat in the Office of the President, for national security reasons, to clear researchers to undertake their projects in Uganda. For clinical trials, an additional requirement is to obtain the National Drug Authority's authorization to import and/or use the trial drug/device in Uganda. The legal responsibilities of the UNCST and the National Drug Authority for oversight of research are briefly explained below.

3.2 Oversight by the UNCST

The UNCST is a semi-autonomous government agency established in 1990 (CAP 209 of the Laws of Uganda) to develop and implement strategies for integrating science and technology (S&T) into the national development process, provide advice to the government of Uganda on policy matters necessary for advancing S&T and, oversee and coordinate research and development (R&D) in Uganda.

The UNCST has specific functions for R&D coordination and oversight under Sections 4 and 5 of the UNCST Act (CAP 209). The functions are stated as follows:

Section 4:

a. To advise and coordinate the formulation of an explicit national policy on all fields of science and technology;
b. To act as a clearing house for information on research and experimental development taking place in scientific institutions, centres and other enterprises and on the potential applications of their results;
c. To work in close co-operation with and co-ordinate all scientific and technological activities of persons, institutions, sectors and organizations;

Section 5:

a. To establish specialized committees, research councils, organizations and experimental and developmental activities or other scientific and technological services;

In executing the above functions, the UNCST registers and, in liaison with the Research Secretariat in the Office of the President, clears all research intended to be carried out in Uganda. In so doing, the UNCST receives and reviews research protocol for their scientific

merit, safety and ethical appropriateness, and thereby issues permits to conduct the research in Uganda1. The research permit is granted at a national level to facilitate the carrying out of research within the country.

Thus, all persons intending to carry out research in Uganda are required to register their research activities with the UNCST, and obtain UNCST approval of the intended research activities. Research project proposals submitted to UNCST for registration and approval should be well written and fully developed. Draft research proposals shall not be accepted for registration. A research proposal should have a title and, at least, sections on objectives, methodology, significance/justification for the study, work plan and budget and references/ bibliography. In addition, the research project proposal should have a version and date, names and brief biographical sketches of the investigators and their institutions of affiliation, and data collection instruments, such as questionnaires.

3.3 Oversight by the National Drug Authority

The National Drug Authority (NDA) regulates the safety, quality, efficacy, handling and use of drugs or drug related products in research. Part IV, section 40 of the National Drug Policy and Authority Act (Chapter 206) states that, with respect to clinical trials:

a. The authority (NDA) may issue a certificate to any person for the purpose of carrying out clinical trials in respect of a drug that may be specified in the certificate.
b. No person may carry out any clinical trial in respect of any drug unless he or she is in possession of a certificate issued under subsection (1).

It is the responsibility of each trial sponsor and/or investigator to obtain such authorization certificate for all experimental drugs/devices, irrespective of whether the drug/device has previously been licensed for use in humans or not. Investigators must file a copy of the NDA certificate authorizing the importation and/or use of the trial drug/device in Uganda with the UNCST. The NDA shall also verify the continued use and eventual disposal of unused trial drug/device.

Applicant shall, *inter-alia*, provide the following information about the drug/device to the NDA:

a) Investigator's brochure
b) A description of the drug/device (physical characteristics);
c) Dosage form of the drug/device;
d) Composition (complete formula);
e) Active ingredients;
f) Other ingredients (adjuncts, exipients, preservatives, colour, flavour etc);
g) Pack size (weight or volume);
h) Quality control processes done;

1. *Research proposals received and registered by the UNCST are reviewed by the UNCST Specialized/Ethics Committees, Task Forces and peer reviewers for their scientific merit, safety and ethical appropriateness.*

i) Certificate of analysis;
j) Batch release certificate;
k) Stability studies done on the drug/device;
l) Good Manufacturing Practice certificate of plant from which drug/device was manufactured;
m) Containers in which products is packaged;
n) Labelling;
o) Relevant published literature on the drug/device;

3.4 Oversight by Institutional Review Committees

Institutional Review Committees (IRCs) are established by institutions whose mandate includes carrying out research. Their primary function is to conduct initial and continuing review and approval of research projects, with the aim of protecting the rights and welfare of human research participants. IRCs operating in Uganda must receive accreditation from the UNCST. IRCs have a special role of monitoring research activities to ensure compliance with scientific and ethical requirements in accordance with these guidelines. Details about the operations of IRCs are described in Section 4.0 below.

3.5 Oversight by other Committees

Besides the UNCST, NDA and IRCs, there are a number of other Committees that are involved in one way or the other in the oversight of research projects. These committees include:

3.5.1 Scientific Committees

3.5.1. Establishment

Scientific Committees (SCs) are sometimes set up within institutions as an internal review mechanism for research proposals. Where such committees formally exist, they should approve research protocol prior to submission to an IRC. SCs shall be objective, multi disciplinary, and shall have a programme for continuing education for SC members.

SCs shall be constituted by at least 3 experts. They shall have standard operating procedures (SOPs) to guide their functions, membership requirements, internal procedures and quorum requirements. The SOPs should specify, at least, the following:

a. Format of research protocol to be submitted for review;
b. Frequency of SC meetings;
c. Time allowance for members to read research protocol before the meeting date;
d. Number of research protocol that can be reviewed each time;
e. How decisions will be arrived at (by consensus or vote);
f. Records of the meetings (minutes) and distribution requirements;

g. Procedure for re-submission of research protocol after revision;
h. Ways of communication decisions (with reasons for every decision clearly stated in writing).

Members of the SCs shall protect confidentiality of all information given to them in the course of their work, and sign confidentiality agreements with their institutions. In addition, they shall not to use information supplied in the research proposals under their consideration for their own research projects or personal gain.

3.5.1.2 Functions

The primary function of a SC is to review and evaluate all scientific aspects of research projects with emphasis on suitability, relevance and feasibility of the study.

Specific issues that shall be scrutinized by the SC include, but are not necessarily restricted to: study design, objectives of the study, methodology, appropriate controls, statistical methods, and feasibility of the study.

The SC shall also build lines of communication between the various departments within the institution and IRCs;

3.5.2 Data and Safety Monitoring Boards

3.5.2. Establishment

A Data and Safety Monitoring Board (DSMB) is an independent group of experts established by the study sponsors to review safety data during a clinical trial. It ensures that the study is conducted and the data are handled in accordance with the provisions of the research protocol and monitors adverse events and safety data. A DSMB shall be established before the commencement of a clinical trial and its composition submitted to the IRC and the UNCST for record purposes.

All Phase I, Phase II, and Phase III, including drug efficacy trials, and all clinical trials conducted in Uganda shall have a safety monitoring plan and a DSMB. Other interventional studies, such as community trials, may be required to set up DSMBs on a case by case basis.

The membership of the DSMB shall include:
a. Individuals knowledgeable in the processes of conducting the trial, including requirements for research protocol amendments;
b. Individuals with adequate medical, pharmaceutical, scientific, and/or ethics qualifications and clinical trial experience. The qualifications most appropriate for a specific DSMB will depend on the nature of the clinical trial and of the product under investigation;
c. At least three members including a clinician with competence in the research field of the trial and a bio-statistician;

3.5.2.2 Functions

The functions of a DSMB are to:

a. Ensure safety of study participants;
b. Preserve the integrity and credibility of the trial;
c. Ensure availability of definitive and reliable results in a timely manner;
d. Make decisions related to safety, based on the submitted results and adverse event reports and recommend whether the study should continue or not.

The DSMB shall report to the sponsor(s) of the trial:

a. Any concerns over differences in serious adverse events between study arms;
b. Any serious social harms;
c. Any concerns about the conduct of the trial;
d. Any concerns about data integrity;
e. Whether the study should be terminated or continued based on safety and interim data;

The DSMB shall determine before the commencement of the study, the following:

a. Mode and time frame for receiving adverse events reports;
b. Frequency of receiving data;
c. Frequency of meetings to review the data and adverse event reports at hand. (Where there may be any element of concern, the DSMB may chose to review the data more frequently);
d. Channels of communication with the study and the IRC.

3.5.3 Community Advisory Boards

3.5.3.1 Establishment

Community Advisory Boards (CABs) are established by the study investigators. They are important forums for facilitating dialogue between community members, study volunteers and researchers.

CAB members shall be largely identified from communities where research is to be undertaken through a stake holder consultative process. The CAB's role and expectations should be clearly stated in their terms of reference. Members of the CAB may include but are not limited to the following:

a. Individuals with understanding of local laws, cultural values and gender issues
b. Peer leaders
c. Religious leaders
d. Representatives of the study population
e. Media
f. Professionals who understand research or science issues
g. Community leaders

3.5.3.2 Functions

The primary function of a CAB is to assist investigators understand and incorporate community concerns into their research activities. This happens through different ways like advising on issues central to the informed consent process, achieving successful volunteer recruitment and retention, among others.

The responsibilities of the CABs may vary according to the study location, size, and other factors, but generally, they are to:

a. Provide information on traditional beliefs and needs of the study population and their concerns regarding the research project;
b. Provide input into the design of the research protocol as appropriate including the informed consent process;
c. Advise on effective methods for disseminating information about the research project and its outcomes;
d. Provide advice and support regarding recruitment and retention of research participants including gender equity.

3.5.4 Institutional Bio-safety Committees (IBC)

3.5.4.1 Establishment

Institutional Bio-safety Committees (IBC) are established by institutions that undertake research on potentially hazardous substances of a physical, chemical, biological, or any other nature. Any institution involved in or planning to conduct research with potentially hazardous substances is required to set up or designate a competent IBC. Each IBC once formed shall consist of a bio-safety officer and at least three other officers with appropriate expertise. The IBC shall be certified by the UNCST.

It is the responsibility of the Principal Investigator to notify and provide the IBC with the research proposal involving potentially hazardous substances of a physical, chemical, biological, or any other nature.

Members of the IBC shall protect confidentiality of all information given to them in the course of their work, and shall sign confidentiality agreements with their institutions. In addition, they shall not use information supplied in the research proposals under their consideration for their own research projects or personal gain.

3.5.4.2 Functions

The IBC's function is to minimize potential human and environmental harm that may be associated with research on or with potentially hazardous substances such as pathogens, radioactive material and applications of bio-technology, especially recombinant DNA techniques and processes.

Specifically, IBCs shall:

a. Notify the IRC and UNCST of any research with potentially hazardous substances in their institutions;
b. Conduct bio-safety review of research proposals on potentially hazardous substances;
c. Ensure the provision of suitable and safe storage and disposal facilities for all materials involved in work with potentially hazardous substances;
d. Ensure that all appropriate technical personnel of the institution have adequate training in bio-safety;
e. Establish a health-monitoring plan for all high-risk personnel involved in application, use and production of potentially hazardous substances;

4. ESTABLISHMENT, FUNCTIONS AND REVIEW PROCEDURES OF INSTITUTIONAL REVIEW COMMITTEES

4.1 Introduction

Institutional Review Committees (IRCs) are committees established in an institution to conduct initial and continuing review of research projects with the primary goal of protecting the rights and welfare of research participants. All institutions in Uganda that conduct research involving humans as research participants should set up IRCs in accordance with these guidelines. Where an institution cannot set up an IRC that institution may rely on an IRC of another institution to review their research projects, provided the IRC is recognized by the UNCST.

4.2 Establishment

An institution that wishes to establish an IRC shall inform, in writing, the Executive Secretary of the UNCST of the institution's intention to set up an IRC. In the communication, the institution shall provide assurance to the UNCST that it will comply with the requirements set forth in these guidelines. Assurance shall at the minimum include:

a. A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human research participants of research conducted at or sponsored by the institution. This may include an appropriate existing code, declaration, or statement of ethical principles, or a statement formulated by the institution itself.

b. Assurance of availability of meeting space and sufficient staff and resources to support the IRCs review and record-keeping duties.

c. A list of IRC members identified by name, qualifications, profession, representative capacity, indicators or experience such as board certification, licenses, etc. sufficient to describe each member's anticipated contributions to IRC deliberations; and any employment or other relationship between each member and the institution; for example, full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant, etc. Any changes in IRC membership must be reported to the UNCST.

d. Written procedures for monitoring the conduct of studies approved by the IRC;

e. Written procedures which the IRC will follow for:

    i. Conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution;

ii. Determining which projects require review more often than annually and which projects require verification from sources other than the investigators that no material changes have occurred since previous IRC review; and

iii. Ensuring prompt reporting to the IRC of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRC approval has already been given, may not be initiated without IRC review and approval except when necessary to eliminate apparent immediate hazards to the research participant.

iv. Written procedures for ensuring prompt reporting to the IRC and appropriate institutional official of any unanticipated problems involving risk to research participants or others or any serious or continuing noncompliance with these guidelines or the requirements of the IRC; and suspension or termination of the IRC approval. Reports required under this section must be provided to the IRC having review authority no later than 30 days following the risk to the research participant(s) or first occurrence of non-compliance.

The UNCST shall review the institution's application, and if satisfied, will authorize in writing, the establishment of the IRC. The IRC shall not commence its activities until authorization has been received from the UNCST. The UNCST reserves the right to establish IRCs within its institutional framework, when necessary.

4.3 Composition and Integrity of IRC members

a. Each IRC shall be composed of at least five (5) members, with varying backgrounds to ensure complete and adequate review of research activities commonly conducted by the institution. The IRC shall be sufficiently qualified through the experience and expertise of its members, and the diversity of members, including consideration of gender, region, religion, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of research participants. In addition to possessing the professional competence necessary to review specific research activities, the IRC shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRC shall, therefore, include persons knowledgeable in these areas. If an IRC regularly reviews research that involves a vulnerable category of persons, such as children, prisoners, pregnant women, members of the armed forces or persons with disabilities, the IRC shall include or co-opt one or more individuals who are knowledgeable about and experienced in working with these research participants.

b. Every nondiscriminatory effort shall be made to ensure that no IRC consists of entirely men or entirely women, including the institution's consideration of qualified persons of both sexes. No IRC may consist entirely of members of one ethnic group, religion, or

social or economic class. No IRC may consist entirely of members of one profession, e.g. physicians. Lack of formal education shall not be a reason for excluding an individual from IRC membership.

c. Each IRC shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in non-scientific areas.

d. Each IRC shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

e. No IRC member may participate in the IRC's initial or continuing review of any project in which the member has a conflict of interest, except to provide information as may be requested by the IRC.

f. Each IRC member shall undergo at least one basic training in research ethics within one year of appointment, and thereafter, should undergo continued ethics education at least once every two years.

g. An IRC may, in its discretion, invite individuals with competence in special areas to assist in the review of issues, which require expertise beyond, or in addition to that available in the IRC. These individuals do not vote with the IRC.

h. Membership in any IRC shall not exceed a term of three years. After serving for three years, a member is eligible for reappointment.

i. IRC members must guard against any tendencies of unethical conduct on their own part, for example, they must protect the confidentiality of research projects, documents and discussions; where there is an actual or potential conflict of interest with respect to a particular research proposal, the IRC member should not participate in the review of such a proposal, except to provide information or clarifications; an IRC member shall not appropriate the submitted proposal for his or her own use; and IRC members shall not compel investigators to submit to unnecessary repetition of review.

j. IRCs have a special responsibility to determine whether the objectives of the research are responsive to the health needs and priorities of the proposed study population, in particular and of Uganda in general. The ability to judge the ethical acceptability of various aspects of a research proposal requires a thorough understanding of a community's customs and traditions. The IRC, therefore, must have competent members or consulting persons with such understanding. It will then be in position to determine the acceptability of the proposed means of obtaining informed consent and otherwise respecting the rights of prospective research participants as well as of the means proposed to protect

the welfare of the research participants. Such persons should be able, for example, to indicate suitable members of the community to serve as intermediaries between investigators and research participants, and to advise on whether material benefits or inducements may be regarded as appropriate in light of a community's gift-exchange and other customs and traditions.

4. 4 Functions

IRCs act as independent reviewers of any proposed study on human research participants, to ensure ethical conduct of research, and that participant's rights and welfare are not violated. Therefore, the major responsibility of IRCs is to safeguard the rights, safety, and well being of research participants. It is important for IRCs to review the scientific soundness of the research proposals. In view of this, the functions of any IRC in Uganda shall be to:

a. Maintain ethical standards of practice in research;
b. Protect research participants and investigators from harm or exploitation;
c. Preserve the research participants' rights and welfare;
d. Provide assurance to society of the protection of the rights and welfare of research participants; and
e. Ensure adherence to ethical conduct of research protocol approved by the IRC;

4. 5 Review Mechanisms

As previously mentioned, each IRC must have written procedures, including procedures to be followed in their review mechanism. The following are the minimum requirements for an IRC review mechanism.

4.5.1 General Requirements

a. The IRC shall review proposed research at convened meetings at which at least fifty percent (50%) of the members of the IRC are present, including at least one member who represents the interests of the community;

b. In order for the research project to be approved, it shall receive the approval of a simple majority of those members present at the meeting. The only exception to this procedure shall be in the case of expedited review as provided in Section 4.5.2;

c. The IRC shall meet as often as possible, but at least once every three months;

d. An IRC shall require that information given to research participants as part of informed consent complies with the general requirements for informed consent as prescribed by these guidelines. However, the IRC may require that more information be given to the research participants, provided such additional information would meaningfully add to the protection of the rights and the welfare of the research participants.

e. An IRC shall generally require documentation of informed consent process. For certain types of research, however, the IRC may require the investigator to administer a comprehension test (or test of understanding) to ensure that prospective research participants have acquired adequate understanding of the relevant facts and consequences of participation in the study.

f. An IRC shall notify investigators in writing the outcome of the review of the investigators research project. Such notice shall be provided to the investigator within 14 days from the date of IRC review of the research project. In case the IRC does not approve a research activity, it shall include in its written notification a statement of the reasons for its decision.

g. An IRC shall conduct continuing review of research covered by these guidelines at intervals appropriate to the degree of risk, but not less than once a year, and shall have authority to observe or have a third party observe the informed consent process.

4.5.2 Expedited Review Procedures

a. The IRC may use an expedited procedure to review minor changes in previously approved research protocol during the period of one year or less for which approval is authorized. Minor changes include such changes as the addition of a collaborator or a small change in the number of research participants, or spelling corrections. Major changes include, but are not limited to, significant changes in the research methodology or a change in the procedures for the research participants. Each IRC shall develop standard operating procedures to define eligibility for expedited review;

b. Under an expedited review procedure, the review may be carried out by the IRC chairperson or by one or more experienced reviewers designated by the chairperson from among the members of the IRC. In reviewing the research, the reviewers may exercise all of the authorities of the IRC except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the standard procedure outlined above.

c. Each IRC that uses an expedited review procedure shall adopt a procedure for keeping all members advised (no later than at the full IRC meeting following the expedited review), of research proposals which have been approved under this procedure.

d. The UNCST may restrict, suspend, terminate, or choose not to authorize an IRC use of the expedited review procedure when deemed necessary to protect the rights and welfare of research participants.

4.5.3 Exemption from IRC Review

The following categories of research are exempt from the requirements of IRC review specified in these guidelines:

a. Use of publicly available unlinked data that does not identify individuals or communities;
b. Emergency use of a test article provided that such emergency use is reported to the IRC within 5 working days. Any subsequent use of the test article at the institution is subject to IRC approval.

If an investigator believes that his/her research project would satisfy the requirements for exemption by IRC review, the investigator shall apply to the IRC for his/her study to be exempt from IRC review. The IRC shall review the application to ensure that the proposed study satisfies requirements for exemption from IRC review, and will, thereafter, grant exemption.

4.5.4 Review of Collaborative Research Projects

a. Collaborative research projects are those projects that involve more than one institution, some of which might be international. In the conduct of collaborative research projects, each participating institution is responsible for safeguarding the rights and welfare of research participants and for complying with these guidelines, and this involves securing IRC approvals in their institutions as appropriate. However, with the approval of the UNCST, an institution participating in a collaborative research project may enter into joint review arrangements for that particular research project in order to streamline the review process. Such joint IRC review should ensure that the proposed research is responsive to the needs and priorities of Uganda and meets the requisite ethical standards described in these guidelines.

b. An international collaborative research project should have a co-principal investigator in Uganda who must be employed and/or affiliated to a recognized local institution that is relevant to the area of the proposed research.

c. The local IRC overseeing an international collaborative research project is the IRC of record in view of its better understanding of the cultural sensitivities of the population in which the proposed research is to be conducted. It is also better placed to monitor compliance in the course of a study.

d. In addition, the local IRC shall require approvals of the research project by the co-principal investigator in the collaborating institution and the sponsoring agency.

e. The guidelines for reporting SAEs as stipulated herein shall have precedence over any other guidelines.

4.5.5 Suspension or Termination of IRC Approval of Research

a. An IRC shall have authority to halt, suspend or terminate approval of research that is not being conducted in accordance with the IRC's requirements or that has been associated with unexpected serious harm to research participants or that contravenes these guidelines. The IRC may suspend research when, for instance:

i. It finds that the investigator has implemented major changes in the research protocol without the prior approval of the IRC,
ii. When the investigator has failed to follow specific procedures or requirements enunciated by the IRC in its initial review of the research protocol, or
iii. When there is unexpected serious harm to the participants including, but not limited to, serious physical injury or death.

b. Any suspension or termination of approval shall include a written statement of the reasons for the IRC's action and shall be reported promptly to the investigator(s), appropriate institutional officials and the UNCST.

4.6 IRC Records

The institution shall ensure that the IRC prepares and maintains adequate documentation of IRC activities, including the following:

a. Detailed written procedures for the IRC.
b. Copies of all research proposals reviewed, scientific evaluations that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, reports of injuries to research participants, etc.
c. Minutes of IRC meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRC; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controversial issues and their resolution.
d. Records of continuing review activities.
e. Copies of all correspondence between the IRC and investigators.
f. Statements of significant new findings provided to research participants.

The records required by these standards shall be retained for at least five (5) years after completion of the research project. All records shall be accessible for inspection and copying by authorized representatives of the UNCST.

4.7 Basic Requirements for Approval of a Research Protocol

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

a. Risks to research participants are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose the research participants to risk and whenever appropriate by using procedures already being performed on the research participant for diagnostic or treatment purposes.

b. Risks (if any), are reasonable in relation to anticipated benefits to the research participants, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits the IRC should consider only those risks and benefits that the research participants would receive even if not participating in the research. The IRC 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.

c. The selection of research participants is equitable. In making this assessment the IRC shall 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 especially vulnerable populations.

d. Informed consent will be sought from each individual prospective research participant or the individual participant's authorized representative.

e. Informed consent will be appropriately documented in accordance with the provisions of these guidelines.

f. The research plan makes adequate provision for monitoring the data collection to ensure the safety of the research participants.

g. When appropriate, there are adequate provisions to protect the privacy of research participants and to maintain confidentiality of data.

h. When some or all of the research participants are likely to be vulnerable to coercion or to undue influence, additional safeguards have been included in the study to protect the rights, welfare and interests of these research participants.

4.8 Requirements for Submission to an IRC

All research protocol submitted to an IRC for review and approval must at the least include the following information:

a. A clear statement of the objectives of the research, with regard to the present state of knowledge and a justification for undertaking the investigation;
b. A precise description of all proposed procedures and interventions, including the duration of the study;
c. A statistical analysis plan;
d. Description of the study population including the number of research participants to be recruited;
e. The inclusion and exclusion criteria for study participants and procedures for the withdrawal of individual participants;

f. Complete details of the informed consent process, including the proposed means of obtaining informed consent;
g. Evidence that the investigator is appropriately qualified and experienced and has adequate facilities for the safe and efficient conduct of the research; and
h. The provisions that will be made to protect the confidentiality of information/data obtained from research participants;
i. Study instrument e.g. questionnaires, case report forms, videos, flip charts and other data collection tools/forms;

4.9 Obligations of an IRC

The IRC is obliged to:
a. Conduct initial and continuing/periodic review of research projects, including site monitoring visits;
b. Review the investigators research protocol in a timely manner but in any case within 60 days from the date of receipt of the research protocol. In the case of annual continuing review, the IRC shall maintain the same anniversary date of approval for any given research protocol;
c. Communicate the outcome of the review within 14 days from the date of IRC review of research protocol;
d. Respond to any allegations of misconduct in research projects approved or rejected by the IRC;
e. Liaise with other IRCs within and outside the country for better carrying out of its functions;
f. Prepare annual reports of IRC performance to the UNCST;

5. ETHICAL CONSIDEREATIONS IN THE REVIEW OF RESEARCH PROTOCOLS[2]

5.1 Scientific validity

Any research project asking valuable questions, if it is designed or conducted poorly will yield scientifically unreliable or invalid results. Scientifically unsound research on humans is unethical in that it may expose research participants to risks or inconvenience to no purpose. For research to be ethical, the methods must be valid and practically feasible, the research project must have a clear scientific objective, be designed using acceptable scientific principles, methods and reliable practices; have sufficient power to definitely test the objective and offer a plausible data analysis plan.

5.2 Science and social value

The major objective of research using humans is the anticipated benefit, which could be in a form of new intervention that could improve the quality of life of a community, or it could be generalisable knowledge to benefit the entire scientific world or it could be a step towards a major break through in terms of health care delivery. A research project should demonstrate value in terms of new information to be added to the scientific community and probably improvement in health care provision and general social well being. There should be foreseeable benefits to the individuals and community that is going to be studied, and the risks should be minimized.

5.3 Favourable risk-benefit ratio

For a research project to be ethically acceptable, it should have a favourable risk/benefit ratio to the individual research participant and to society generally in terms of the knowledge that will be gained from the research project. IRCs should undertake a systematic analysis of the risks and benefits of a research project to individual research participants and society; and ascertain that the anticipated benefits justify the risks. Risks may include psychological, mental, social, physical and economic harms. Benefits may include such aspects as medical care and treatment. In balancing these elements, the risks and benefits to the individual research participant will normally carry special weight.

5.4 Community involvement

Where appropriate, there should be a provision for involvement of the community in the research process right from the inception to the post research period. The community in this context may be geographical or study population specific. Community involvement includes

2 *Adapted from Emmanuel E. et al (2000) Ethical Requirements for Clinical Research. JAMA May 24/31, 2000-Vol 283, No. 20*

participation in planning and implementation of the research project and dissemination of research findings. Community involvement shall not override the rights of individuals to provide voluntary consent for participation in the research project.

5.5 Fair selection of research participants

Selection of research participants should be justified by the scientific hypothesis or research question, but not by the convenience of obtaining research participants. The risks/burdens and benefits of research should be equitably distributed among both disadvantaged and privileged communities. Vulnerable groups should not be targeted for risky research and they should not be denied potentially beneficial research. Consideration shall be made of the socio-economic factors, gender, age, ethnic and racial differences, where applicable. Exclusion of a category of research participants who should have otherwise been included in the study should be justified.

5.6 Informed consent process

The purpose of informed consent is to ensure that individuals control whether or not they wish to enrol in the study and participate only when the research project is consistent with their values, interests and preferences. To provide informed consent, individuals must be accurately informed of the purpose, methods, risks, benefits and alternatives to research; understand this information and its bearing on their own situation, and make a voluntary and uncoerced decision whether or not to participate.

6. THE INFORMED CONSENT PROCESS

6.1 Introduction

Respect for persons requires that research participants be given the opportunity to make choices about what should be done to them. Consent is not just a form or a signature/mark but a process of information exchange between the researcher and research participants on the whole research process. Information provided should be adequate, clearly understood by the research participant with decision making capacity and the research participant should voluntarily decide to participate.

6.2 General Requirements for the Informed Consent Process

Except as provided elsewhere in these guidelines, no investigator shall involve an individual person as a research participant unless the investigator has obtained informed consent of the individual or the individual's authorized representative. As an example, a community leader may not consent for the participation of community members in research without the individual research participants' informed consent.

An investigator shall seek such consent only after ascertaining that the prospective research participant has adequate understanding of the relevant facts and of the consequences of participation. For certain types of research, the IRC may require the investigator to administer a comprehension test (or test of understanding) to ensure that prospective research participants have acquired adequate understanding of the relevant facts and of the consequences of participation. Seeking consent shall be carried out under circumstances that provide the prospective research participant 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 research participant or the representative, whether it is conveyed orally, in writing or other delivery mechanism, shall be in a language and form understandable to the participant or the representative. No informed consent, whether oral or written, shall include any exculpatory language through which the research participant or representative is: (1) made to waive or appear to waive any of the research participant's rights, or (2) appears to release the investigator, the sponsor, the institution, or its agents from liability.

The investigator shall ensure that there is initial monitoring at the start of the study and continued adequacy of the informed consent process and renewal of informed consent if there are significant changes in the conditions or procedures of the research project or if new information becomes available that could affect the research participant's willingness to continue in the research project.

6.3 Elements of an Informed Consent Form

The elements which must be included in the information provided to each potential research participant in order for the consent to be valid include the following:

a. A statement that this is a study rather than the provision of clinical care; that the study involves research; an explanation of the research project; an estimate of the duration of the research project and the research participant's participation in that research project; a description of the procedures to be followed in the research project, and the identification of any procedures, including the use of medication or devices, that are experimental.
b. A description of any reasonably foreseeable risks or discomforts that the research participant may experience.
c. A description of the benefits to the research participants or to others that may reasonably be expected to result from the research project.
d. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the research participant.
e. A statement describing the extent, if any, to which privacy and confidentiality of the research participants will be maintained.
f. For research involving more than minimal risk, a statement as to whether any compensation and any medical treatments are available if injury occurs and, if they are, what they consist of and where further information may be obtained.
g. Identification by name and contact details of the individual(s) who should be contacted for answers to questions about the research project and the research participants' rights and the name of the individual(s) to contact in case of a research-related injury to the research participant. The designated individuals must be able to communicate with the research participant in the language of the research participant or must have the capability and authority to promptly secure the services of an interpreter to assist in responding to the research participant's questions.
h. A statement that participation is voluntary, that refusal to participate will not result in a penalty or a loss of benefits to which the research participant is otherwise entitled, and that the research participant may discontinue participation at any time without penalty or loss of benefits to which the research participant is otherwise entitled.
i. A statement of the extent of the investigator's responsibility, where applicable, to provide medical services to the research participant.
j. A statement of the nature, form and extent of compensation for study participation, e.g. reimbursement for transport, time and meals.
k. A brief description of the sponsors of the research project and the institutional affiliation of the investigators.
l. A statement that research participants will get feedback on findings and progress of the study, and that any new information that affects the study or data that has clinical relevance to the research participants, will be made available to the research participants or their health care providers.

m. Where necessary, for example, illiterate, mentally incapacitated or physically handicapped research participants, the provision for a witness at appropriate specific stages of the informed consent process.
n. A statement that the study has been approved by a specified recognized Ugandan based IRC.

Any of the following elements shall be provided to the research participant when appropriate based on the nature and conduct of the study:

a. A statement that a particular treatment or procedure under study may involve risk to the research participant, or to the embryo or fetus if the research participant is or may become pregnant, and that the risk is currently unforeseeable.
b. An explanation of circumstances under which the investigator may terminate the research participant's participation, whether or not the research participant consents to such termination.
c. An explanation of any additional costs to the research participant that may result from his or her participation in the research project.
d. A statement explaining the consequences of a research participant's decision to withdraw from the research project. Research participants may withdraw at any time without further notice. However, research participants' should be provided with a description of the procedures that are to be followed in order to give notice of their withdrawal.
e. A statement that significant new findings that are made during the course of the study, whether by the study's investigators or others that may relate to the research participant's willingness to continue his or her participation, shall be provided to the research participant in a timely manner.
f. The approximate number of individuals participating in the research study.
g. Whether, when and how any of the products or interventions proven by the research project to be safe and effective will be made available to the research participants at the end of the study and whether they will be expected to pay for them.
h. With regards to research involving the collection of biological/genetic materials, an explanation should be provided on how specimens will be managed at the end of the study. If the samples will be stored for future use, separate consent should be obtained. See section on storage of biological materials.

6.4 Documentation of Informed Consent

The research participant may imply consent by voluntary actions, express consent orally, or sign a consent form.

Except as provided in section 6.5 below, informed consent shall be documented by the use of a written informed consent form approved by an IRC and signed by the research participant or the research participant's representative and the person obtaining the consent. A copy shall be offered to the research participant or the research participant's representative signing the form.

The consent form shall contain all of the elements listed in section 6.3 above. This form may be read to the research participant or the research participant's representative. The research participant or the research participant's representative must be given sufficient time to read the consent form before the research participant or the research participant's representative signs the form or places his or her thumbprint on the form indicating that he or she has read and understood and agrees to participate in the study.

IRCs shall determine whether the investigator's proposal to obtain verbal informed consent is appropriate or not.

6.5 Waiver of informed consent and/or documentation of informed consent

An IRC may waive some of, or all of the requirements for the investigator to obtain an informed consent and/or a signed /thumb printed consent form for some or all of the research participants of a particular study if the IRC determines that:

a. The research project carries no more than minimal risk, that is, risk that is no more than the risks encountered in normal daily life in a stable society;
b. The research project could not practicably be carried out without the waiver or alteration (whenever appropriate the research participants will be provided with additional pertinent information after participation);
c. In situations where deception needs to be applied to achieve the objectives of the study;
d. The only record linking the research participant and the research project would be the consent document and the principal risk to the research participant would be potential harm resulting from a breach of confidentiality;
e. The research participant presents in an emergency situation and informed consent can not be reasonably obtained from the individual or his/her representative.

If a waiver of written informed consent is granted by the IRC, then each research participant should be asked whether he or she wishes to have documentation that links him or her with the study; and the research participant's wishes shall govern. In situations in which the research participant prefers not to execute a written informed consent form, the investigator must obtain oral informed consent and document that it has been obtained.

6.6 Assent

A child's affirmative agreement to participate in research shall be sought from all children eight (8) years of age and above. If the informed consent given by the parent/guardian is written, the assent from the child shall be written, and if the informed consent given by parent/guardian is verbal, the assent from the child shall also be verbal.

7. STANDARD OF CARE DURING RESEARCH

7.1 Standard of care for research participants

A care package for research participants should be stated before initiation of a research project. Care and treatment for research participants should be provided with the ideal aim of providing the best established effective intervention and, at the least, should be in accordance with the current Uganda Clinical Guidelines (UCG) and other national health guidelines and standards. In the absence of these national health standards, the investigator, IRC, UNCST and Sponsor shall agree on the care and treatment package to be provided.

The duration and sustainability of care and treatment for the research participant after the study should be negotiated before initiation of the study. Sponsors are encouraged, but not obliged, to provide care for concurrent illnesses not associated with the research project. Investigators should provide relevant follow up procedures for research participants for an appropriate period of time after the trial.

7.2 Standard of care for research participants in control groups

Research participants in a control group of a research project of a diagnostic, therapeutic, or preventive intervention should receive an established effective intervention or as may be determined with reference to the applicable national health standards. Sponsors may, where possible, provide care and treatment beyond what is recommended in the national health guidelines taking into consideration sustainability issues. Only in certain circumstances, as may be advised by an IRC and/or UNCST, would it be acceptable to use an alternative comparator such as a placebo or no treatment. However, in general, placebo-controlled trials may be conducted provided that:

a. Based on knowledge that is available at the commencement of the trial, the new drug or device to be tested does not confer any significant benefit compared to the placebo, and a proven prophylactic, diagnostic or therapeutic method or established effective intervention does not exist.
b. Withholding an established effective intervention would expose the research participant to at most temporary discomfort or delay in relief of symptoms;
c. Use of an established effective intervention as comparator would not yield scientifically reliable results and the use of a placebo would not add any significant risk or irreversible harm to the research participants.

Once the intervention being studied has been demonstrated to be superior, the Sponsor(s) shall promptly offer to research participants in the placebo arm the intervention treatment free of charge. However, Sponsors shall not be obliged to provide lifelong care and treatment for chronic and relapsing illnesses.

7.3 Care for research related injuries

The sponsor should provide care until complete cure or stabilization of a research related injury. The research participant shall be entitled to the highest attainable standard of care within the country for the research related injury. Research participants shall not be required to waive their legal rights for redress in courts of law.

7.4 Referral of research participants

The Investigator shall undertake to refer all research participants whose conditions may not be managed adequately within the expertise and licensure of the medical professionals at the study site, and/or where facilities or supplies at the study site do not allow adequate handling of the condition. The referral process should be adequately documented and all referral guidelines should be adhered to as stipulated in national guidelines on referral. Research participants should always be informed of all options available for management of their conditions including those outside the country.

7.5 Compensation for research related injury

Injury related to research participation may be physical, social or psychological, and may be classified as follows:

a. *Definitely:* When the injury is directly caused by participation in the research project;
b. *Probably*: When the injury is most likely explained by participation in the research project but when no definite proof of causality is evident;
c. *Possibly*: When explanation for the injury is equally due to participation in the research project or other cause;
d. *Unlikely*: When the injury is more likely explained by another cause other than participation in the research project;
e. *Not related*: When the injury is clearly due to another cause other than participation in the research project.

Subject to applicable laws in Uganda, research participants shall be entitled to compensation when the injury is classified as "Probably" or "Definitely" related to their participation in the research project. Sponsors shall ensure that research participants who suffer injury as a result of their participation in the research project are entitled to free medical treatment for such injury and to such financial or other assistance as would compensate them equitably for any resultant impairment, disability or handicap. In the case of death as a result of their participation, their next of kin are entitled to compensation.

Research participants shall not be asked to waive the right to compensation, and shall retain the legal rights to seek monetary compensation for research related injuries including settlements out of court, in accordance with applicable laws in Uganda.

7.6 Compensation for participation in research

Research participants may be reimbursed for lost earnings, travel costs, lunch and other expenses incurred in taking part in a study; they may also receive free medical services. Research participants, particularly those who receive no direct benefit from the research project will be compensated for inconvenience and time spent. The compensation or medical services shall not be out of proportion so as to induce prospective research participants to consent to participate in the research against their better judgment.

7.7 Incentives

Incentives to research participants for their participation in research projects shall not be considered a research benefit, but a recruitment incentive, and should not present undue influence to potential research participants.

8. RESPONSIBILITIES OF INVESTIGATORS, SPONSORS AND HOST INSTITUTIONS

8.1 Investigators

The Investigator is responsible for the overall conduct and supervision of the research project. Specifically:

a. The investigator must sign the research protocol and shall be responsible for ensuring that it is strictly followed. The investigator shall not implement changes in the research protocol without prior approval of an IRC, except when necessary to eliminate an apparent immediate hazard or danger to research participants. Any change in the research protocol must be in the form of an amendment, appended to the original research protocol and signed by the investigator and where necessary, the sponsor.

b. The investigator, must promptly investigate all serious adverse events, take appropriate measures to ensure the safety of all research participants, and report these and any other information that is likely to affect the safety of the research participants or the conduct of the research events, to the IRC, UNCST, collaborating institutions and sponsor.

c. The investigator must provide adequate and safe medical or dental care, where appropriate, to research participants during the research, within the expertise of the investigator, and must ensure that appropriate medical care and follow-up procedures are maintained after the research project for a period of time that is dependent upon the nature of the disease, the research project, and the intervention(s).

d. If the investigational product is found to be beneficial, the investigator should assist to secure its provision, without charge, to participants in the research project following the conclusion of the research project.

e. In the event of early termination of the research project, the investigator must advise, in writing, the appropriate IRC, the UNCST, the National Drug Authority, and the research sponsor of the early termination and the underlying reason for such termination.

f. The investigator is responsible for the documentation of all steps in data management to allow step-by-step retrospective assessment of the quality of the data and the performance of the research project.

g. The investigator shall ensure appropriate and timely feedback on the research process and findings.

8.2 Sponsor

The sponsor is responsible for providing all the necessary financial support for initiation and completion of the research project. Specifically:

a. The sponsor is responsible for the preparation and approval of a comprehensive final

study report that is suitable for regulatory purposes, whether or not the research project has been completed.

b. The sponsor is responsible for the provision of special forms for the reporting of any adverse events that occur during the course of the research project, and to monitor the investigation and management of adverse events until resolution or stabilization.

c. The sponsor is responsible for providing compensation or indemnity in the event of research-related injuries, disability, or death, in accordance with applicable Ugandan laws and regulations.

For research involving investigational new drug/device, the sponsor:

a. Must provide to the IRC and all other regulatory authorities, a description of the investigational and comparator drugs/devices;

b. Must provide a dossier (research protocol and Investigator's Brochure);

c. Must ensure that the investigational product and any comparator products are of appropriate quality and are subject to quality assurance procedures. This information must be accurate and adequate to justify the nature, scale, and duration of the clinical trial;

d. Must promptly provide the investigator with any relevant new information that arises during the course of the trial, including information relating to product safety;

e. Is responsible for the proper packaging and labeling of the investigational product(s) or medical device. The investigational and comparator products must be labeled in conformity with the research protocol and the labeling must state that the product is for investigational purposes only;

f. Must retain sufficient samples of each batch of the investigational products under study and a record of analyses and characteristics so that, if necessary, an independent laboratory may check the product for quality control or bio-equivalence.

8.3 Host Institution

The institution must work closely with, and monitor research activities of the investigator(s) at the institution. Specifically, host institutions shall:

a. Establish, and/or designate a functional IRC(s) to review their research protocol in accordance with the provisions of these guidelines;

b. Ensure that they have qualified and competent investigators to carry out the research studies at their institution.

c. Facilitate the smooth implementation of research studies conducted at their institution;

d. Take appropriate disciplinary action against investigators for non-compliance with these guidelines.

9. ADDITIONAL PROTECTION FOR VULNERABLE GROUPS

9.1 Introduction

Vulnerable groups are those categories of people who are relatively (or absolutely) incapable of protecting their own interests. Such groups may have insufficient power, intelligence, education, resources, strength, or other requisite attributes to protect their own interests. Classes of individuals conventionally considered vulnerable are those with limited capacity or freedom to consent or decline consent. These include children, mature and emancipated minors, street children, prisoners, the homeless, substance abusers, handicapped (mentally and physically), armed forces, and pregnant women. In some cases willingness to volunteer to participate in research is unduly influenced by expectation of benefits associated with their participation, or fear of retaliation from interested senior members of the hierarchy in case of refusal to participate.

Characteristics that constitute vulnerability with reference to communities include one or more of the following:

a. Limited economic empowerment;
b. Inadequate protection of human rights;
c. Discrimination on the basis of health status;
d. Inadequate understanding of scientific research;
e. Limited availability of health care and treatment options;
f. Limited ability in the community to provide informed consent.

Research among vulnerable groups requires additional attention to ensure their protection. Where factors relating to vulnerability are an aspect of the research project, researchers should specify how that particular vulnerability would be addressed. In particular, IRCs must ensure that:

a. Selection of the particular communities is justified by the research goals;
b. Research is relevant to needs and priorities of the community in which it is to be conducted;
c. Research is beneficial to that community;
d. The community can access products of the research;
e. Where appropriate, feedback of results relevant to the community;
f. Research participants must be fully aware that they are participating in the research, and should provide informed consent. Special attention to the content and language of the consent document as well as the procedures for obtaining informed consent and precautions such as monitoring the process and testing comprehension are essential.

9.2 Children

Research involving greater than minimal risk but presenting the prospect of direct benefit to the child may be conducted only if:

a. The risk is justified by the anticipated benefit to the child;
b. The relation of the anticipated benefit to the risk is at least as favourable to the research participants (children) as that presented by available alternative approaches; and
c. Adequate provision has been made for the solicitation of the child's assent and their parents'/guardians' permission.

Research that involves greater than minimal risk and entails no prospect of direct benefit to the individual child participant but is likely to yield generalizable knowledge about the child's disorder or condition may not be conducted unless:

a. The risk represents a minor increase over minimal risk;
b. The intervention or procedure presents experiences that are 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 generalizable knowledge about the child's disorder or condition that is of vital importance for the understanding or amelioration of that disorder or condition; and
d. Adequate provisions have been made for the solicitation of the child's assent and their parents'/guardians' permission.

Children should only participate in (clinical) research when their participation is indispensable and where participation is not contrary to the child's best interest.[3]

The child's assent takes precedence over the parent's or guardian's consent.

For all research involving children, there must be no financial or other inducements to participate for the parent, guardian or child, although reimbursements and a token for the child after completion of the study may be acceptable.

9.3 Mature and Emancipated Minors

Mature minors are individuals 14-17 years of age who have drug or alcohol dependency or a sexually transmitted infection; while emancipated minors are individuals below the age of majority who are pregnant, married, have a child or cater for their own livelihood. Mature and emancipated minors may independently provide informed consent to participate in research if:

a. In the view of the IRC the research is not objectionable to parents or guardians (established by the IRC with evidence from the community);
b. The research protocol include clear justification for targeting mature and emancipated minors as participants; and a clear justification for not involving parents or guardians in the consent process.

3 *It is advisable to define a child's best interest according to health/survival outcomes.*

9.4 Prisoners

It is possible that prisoners may be under constraints because of their incarceration and these constraints could affect their ability to make a voluntary decision regarding their participation in research. Therefore, any IRC reviewing proposed research to be conducted, which involves prisoners as research participants shall ensure that:

a. A majority of the IRC members have no association with the prison(s) involved other than their status as members of the IRC reviewing the proposed research;
b. Where possible, a prisoner or an ex-prisoner co-opted in to the IRC reviewing the proposed research project;

Research involving prisoners must conform to the following requirements:

a. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such magnitude that the prisoner's ability to weigh the risks of the research against the value of these advantages in the prison environment is impaired;
b. The risks involved in the research are commensurate with the risks that would be accepted by non-prisoner volunteer research participants;
c. Procedures for the selection of participants from within the prison are fair to all prisoners and insulated from arbitrary intervention by prison authorities or by prisoners. Research participants in the control arm are to be selected randomly from among eligible prisoners;
d. The information conveyed to the prisoners is presented in a language that is understandable to them; and
e. There is adequate assurance that a prisoner's participation or refusal to participate will not be considered in decisions regarding his or her release or further detention and each prisoner is clearly informed in advance that his or her participation in the research project will have no effect on his or her release.

Research involving prisoners may not be approved unless:

a. The proposed research has the intent and a reasonable probability of improving the health and well-being of the research participants; and
b. Appropriate knowledgeable persons in penology, medicine, and ethics have been consulted in the course of reviewing the research protocol.

9.5 The Homeless

This category includes street children, adults staying on the street, refugees and internally displaced persons. To the extent that these and other classes of people have attributes resembling those classes identified as vulnerable, the need for special protection of their rights and welfare shall be considered.

9.6 Handicapped (Mentally and Physically)

Disabled persons require special attention because they are prone to being social marginalized. Therefore, their dignity, rights and well being in research must be respected. Careful consideration should be made where proxy consent is to be used, and where the use of signed consent forms is not feasible, alternative viable methods should be employed.

Persons with disabilities (mental or physical) should not be unfairly excluded from participating in research; researchers should make efforts to address communication, disability and comprehension constraints are often the excuse for exclusion.

For research specifically addressing disability issues, a representative of disabled persons or a disabled person should be co-opted into the IRC. If the IRC routinely reviews research protocol on disabled persons, it advisable for such an IRC to have as a members a person conversant with and committed to the enhancement of the well being of disabled persons

People with mental disabilities or substance abuse related disorders include those people with psychiatric, cognitive or developmental disorders. These groups of people are usually institutionalized; and institutionalization may further compromise their ability to make voluntary decisions to participate in a research project. Therefore, research on people with cognitive disabilities or with substance abuse related disorders should:

a. Provide sufficient justification for involving such people;
b. Have appropriate evaluation procedures for ascertaining research participants' ability to give informed consent. If research participants are deemed unable to understand and to make an informed decision, then an appropriate proxy should be identified;
c. Have an informed consent process that is free from coercion;
d. Be of no more than minimal risk; or if minimal risk is involved, the risk is outweighed by the anticipated benefits of the research project to the research participants.

9.7 The Mentally ill and Behaviorally Disordered

Mentally ill or behaviorally disordered persons involved in research are unable to fully comprehend the nature of the research and the informed consent process. Therefore, research involving mentally ill or behaviorally disordered persons must conform to the following requirements:

a. Consent of each potential research participant shall be obtained to the extent of his or her capabilities; and
b. In the case of incompetent research participants, informed consent shall be obtained from the individual's guardian, conservator, or other duly authorized person and evidence of such authority should be presented to the IRC.

Research shall not be conducted with individuals who are mentally or behaviorally incapable of giving informed consent if:

a. Such research could be equally well carried out with individuals who are in possession of their full mental faculties;
b. The purpose of the research is not relevant to the particular health needs of persons with mental or behavioural disorders; or
c. Alternative interventions exist which are at least as advantageous to the individual research participant as that under study.

9.8 Armed Forces

Soldiers involved in research may be under constraints because of the conditions of their military service and these constraints could affect their ability to make a voluntary decision regarding their participation in research. Any IRC reviewing proposed research on soldiers must meet the following additional requirements:

a. A majority of the IRC members shall have no association with the soldiers involved other than their status as members of the IRC reviewing the proposed research project;
b. At least one member of the IRC must be an enlisted soldier on command.

Research involving soldiers on command must conform to the following requirements:

a. Any possible advantages accruing to the soldier through his or her participation in the research project (when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings) are not of such magnitude as could impair the soldier's ability to weigh the risks of the research against the value of these advantages in the military environment;
b. The risks involved in the research are commensurate with the risks that would be accepted by non-soldier volunteer research participants;
c. Procedures for the selection of research participants from within the military are fair to all military personnel and insulated from arbitrary intervention by military authorities or by other soldiers;
d. The information conveyed to the soldiers is presented in language that is understandable to them; and
e. There is adequate assurance that a soldier's participation or refusal to participate in the research project will not be considered in decisions regarding his or her promotion, pay, or any other career opportunities.

Research involving soldiers may not be approved unless:

a. The proposed research has the intent and a reasonable probability of improving the health and well-being of the research participants; and
b. Appropriate experts in human rights, medicine and ethics have been consulted in the course of reviewing the research protocol.

9.9 Pregnant Women and Fetuses

Additional safeguards are necessary in reviewing activities relating to research involving fetuses and pregnant women in order to assure that they conform to appropriate ethical

standards and relate to important societal values. No research relating to pregnant women or fetuses may be undertaken unless:

a. Appropriate studies on animals and non-pregnant individuals have been completed;
b. The risk to the fetus is minimal and is the least possible risk for achieving the objectives of the research project, except where the purpose of the research project is to meet the health needs of the mother and the fetus and the foreseeable benefits outweigh the potential risks; and
c. Individuals engaged in the research project have no part in deciding the timing, method, and procedures to be used to terminate the pregnancy or in determining the viability of the fetus at the termination of the pregnancy.

No procedural changes that could cause greater than minimal risk to the fetus or to the pregnant woman may be introduced into the procedure for termination of the pregnancy, solely in the interest of the research project.

No inducements, whether financial or of another form, may be offered to terminate the pregnancy for the purposes of the research project.

Pregnant women may not be involved as research participants in clinical research unless:

a. The purpose of the research is to meet the health needs of the mother and the fetus will be placed at risk to the minimum extent necessary to meet these needs or the risk to the fetus is minimal; and
b. The mother and the father are both legally competent and have been fully informed of the possible impact on the fetus and have given their informed consent to proceed. However, the father's consent shall not be required if (i) the purpose of the research is primarily to meet the health needs of the mother; (ii) the father's identity and/ or whereabouts are unknown; (iii) the father is not reasonably available; or iv) the pregnancy resulted from rape or incest.

No fetus in utero may be involved as a research participant unless:

a. The purpose of the research project is to meet the health needs of the particular fetus and the fetus will be placed at risk to the minimum extent necessary to meet these needs; or
b. The additional risk to the fetus imposed by the research project is minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means; and
c. The mother and the father are legally competent and have given their informed consent. However, the father's consent will not be required if (i) the purpose of the research project is primarily to meet the health needs of the mother; (ii) the father's identity and/or whereabouts are unknown; (iii) the father is not reasonably available; or (iv) the pregnancy resulted from rape or incest.

Until it has been ascertained whether or not a fetus *ex utero* is viable, a fetus *ex utero* may not be involved in research unless:

a. There will be no additional risk to the fetus from such research and the purpose of the research project is the development of important biomedical knowledge which cannot be obtained by other means; or
b. The purpose of the research project is to enhance the possibility of the particular fetus' survival to the point of viability.

No nonviable fetus may be involved as a research participant in the research project unless:
a. The vital functions of the fetus will not be artificially maintained;
b. Experimental activities which themselves would terminate the heartbeat or respiration of the fetus will not be employed;
c. The purpose of the research project is the development of important biomedical knowledge which cannot be obtained by other means; and
d. The mother and father are legally competent and have given their informed consent. However, the father's consent shall not be required if
   (i) The purpose of the activity is primarily to meet the needs of the mother;
   (ii) The father's identity and/or whereabouts are unknown;
   (iii) The father is not reasonably available; or iv) the pregnancy resulted from rape or incest.

No provision of this subsection shall be construed as authorization to terminate a pregnancy where such termination would not otherwise be in conformity with current laws of Uganda relating to the termination of pregnancy.

9.10 Terminally ill Patients

Terminally ill patients are those individuals who have an incurable condition and are likely to die in the short term. The desperate state of terminally ill patients may affect their ability to make voluntary decisions regarding their participation in research projects. Any IRC reviewing a research project involving terminally ill patients as research participants must meet the following additional requirements:

a. The research can only be conducted in this group; if the objectives of the research project cannot be addressed using another non-vulnerable group;
b. The risk-benefit ratio should be favourable to the patients;

10. MONITORING AND REPORTING

10.1 Introduction

These guidelines give criteria for prompt reporting of certain categories of adverse events to an IRC and the UNCST. When the health related intervention is a drug, the National Drug Authority shall also be notified. An *adverse event* is any unfavorable and unintended sign, symptom or condition temporally associated with the administration of a health related intervention, whether or not considered related to the intervention.

The Investigator undertakes prime responsibility for monitoring and reporting of adverse events to the regulatory authorities. While the Investigator undertakes to monitor and manage all adverse events during the conduct of the investigation, not all adverse events are reportable to the regulatory bodies.

The requirement to report adverse events to regulatory authorities shall not apply to events that are observed among participants who are in observational studies in which no health related intervention is being administered.

10.2 Defining seriousness of adverse events

An adverse event shall be deemed serious if it:

a. Results in death;
b. Is life threatening;
c. Requires in patient hospitalization or prolongation of existing hospitalization;
d. Results in significant and persistent incapacity;
e. Is a congenital anomaly or birth defect;
f. Is an important medical condition in the opinion of the Investigator.

Severity of an adverse event shall be graded as follows:

Mild: Includes events that do not interfere with activities of daily living and do not require treatment;

***Moderate*:** Includes events that have minimal effect on activities of daily living and usually require out patient treatment;

***Severe*:** Includes activities that significantly affect activities of daily living and may require inpatient hospitalization;

***Very severe*:** Includes all events that are life threatening and usually require emergency procedures.

An adverse event shall be deemed unexpected if:

a. It is previously unobserved or undocumented in humans under the health research intervention (or one substantially similar);
b. The nature or severity is not consistent with information in the investigators brochure or other safety information known at the time;
c. The event is observed with higher frequency or severity than previously documented.

Unexpectedness shall not include events that may reasonably be extrapolated from *in vitro* and animal studies.

The following grading shall be used to define the relation of adverse event to a health related intervention:

Definitely: When the event is directly caused by the intervention.
Probably: When event is most likely explained by the research intervention but when definite proof of causality is not evident.
Possible: When explanation for event is equally due to research intervention or other cause.
Unlikely: When the event is more likely explained by another cause.
***Not related*:** When the event is clearly due to another cause.

10.3 Adverse events monitoring and reporting

10.3.1 Adverse events monitoring and reporting during the research

Events requiring prompt reporting to regulatory bodies include:

a. All serious adverse events irrespective of relationship to the health related intervention;
b. All unexpected events of greater than moderate severity irrespective of relationship to health related intervention;
c. All events associated with protocol violations irrespective of severity and relationship to health related intervention;
d. When criteria for stopping or pausing a study as stipulated in the protocol are met;
e. Any event mandated by regulatory authorities;
f. Any event stipulated in the protocol as reportable to the regulatory bodies.

All serious adverse events must be reported to the local IRC as soon as possible and in any case no later than seven (7) calendar days of becoming aware of the event. Thereafter, a detailed report of the SAE should be submitted within eight (8) days.

All other reportable adverse events should be reported to the IRC as soon as possible and in any case not later than fifteen (15) calendar days.

Other issues to consider are that the Investigator must clearly outline in the protocol how management of both foreseeable and unforeseeable adverse events will be done. This outline should clearly show:

a. How adverse events will be recognized promptly.
b. How immediate harm or risk would be managed.
c. Plans for management of events till recovery/or stabilization.
d. Reporting procedures, timelines and documentation of events.

10.3.2 Adverse events monitoring and reporting after the research has been concluded

Certain categories of interventions whose long term effects are not known or cannot reasonably be extrapolated will require extended monitoring for adverse events. This may include genetically modified substances, gene therapy and DNA-based therapies.

10.4 Compliance monitoring

Compliance monitoring shall be within the mandate of the IRC, UNCST and the NDA. Capacity for carrying out monitoring activities by the respective bodies shall be established. The Investigator shall be required to comply with monitoring requests by these regulatory bodies. Certificates of non-compliance shall be issued to non-complying Investigators and Institutions.

10.5 Protocol violations and deviations

Any change in the stated procedure, activity or any provision of the protocol without prior approval except for the purposes of intervening when a person's life is in danger constitutes a protocol violation or deviation. Violations tend to be more serious than deviations. When any of these occur, the Investigator shall notify the IRC and the UNCST. Where the health related intervention is a drug, the NDA shall also be notified.

The report should contain the following information:
a. Title of the study,
b. Name of Investigator,
c. Organizational affiliation,
d. Date of report,
e. Date(s) when violation occurred,
f. Brief description of what happened,
g. Any effect on the study,
h. Any adverse events arising from the violation,
i. Management and follow up of violation and steps to avoid recurrence of the violation.

Notification to the IRC, UNCST, and where applicable the collaborating institution IRC or any other regulatory bodies should be made by the Investigator within seven (7) working days of having become aware of the event.

11. HUMAN BIOLOGICAL MATERIALS

Human biological materials include any substance obtained from a human research participant including, but not limited to: blood, urine, stool, saliva, hair, nail clippings, skin, and microorganisms and other associated bio-products obtained from human research participants.

11.1 Acquisitions, storage and future use

The acquisition, storage and future use of human biological samples from research participants in Uganda shall be guided by the following procedures:

a. There should be a separate informed consent process for obtaining human biological samples for storage and for future use. This process includes the use of a consent form separate from that used for enrollment of research participants into the study. Research participants should know the purpose of sample storage, quantities of samples to be stored, place where samples will be stored, measures to protect confidentiality, policies that will govern use of the samples in future research, potential risks and benefits of storing samples for future research and any other information deemed necessary by the Investigators, IRCs or the UNCST. After explaining the need to store the samples, the research participant should be offered to choose whether their samples should or should not be stored for future studies.

b. The host institution in Uganda should hold the samples in trust on behalf of the research participant. Research participants should reserve the right to withdraw their samples from storage if the samples are linked. The host institution is entrusted with custodianship over the samples, and shall have the authority to decide use, transfer, storage and future use of the samples taking into consideration the rights and welfare of the research participants.

c. Where samples have not been obtained as part of research (for example as part of routine surveillance, emergency procedures, laboratory quality control, notifiable diseases, routine counseling and testing, etc), the institution that collected the samples takes custodianship of the samples. Any future research study on such samples is subject to review by an IRC.

d. When it is necessary to transfer samples for storage abroad, the host institution shall negotiate appropriate contract with the recipient institution. This Contract shall be in the form of a Materials Transfer Agreement (MTA). The specific details of the MTA should include, *inter alia*, purpose for the transfer/export, clear arrangements for collaboration and benefit sharing, a framework for accessing and sharing data, restrictions to third party transfer, and annual reports to the host institution and the UNCST on the status of the samples.

e. It is required that a Ugandan scientist must be included as co-investigator in all future studies using the human biological materials collected from Uganda.

f. IRCs in Uganda shall review all research studies on stored human biological samples.

11.2 Procedures for Exchange/ Transfer of Human Biological Materials

Investigators, their sponsors and collaborators must ascertain that in-country capacity to perform the required investigations/testing does not exist or is inadequate before considering transfer of human biological materials abroad. The only exception to this is when samples are being transferred for quality assurance purposes. Investigators, their sponsors and collaborators are encouraged to build, develop or strengthen local capacity for any investigative testing to fulfil the objectives of the proposed research. All exchanges and transfers (including importation) of materials for research purposes shall require clearance from the UNCST. The UNCST shall oversee the negotiation processes for the MTAs, and maintain a depositary of all MTAs. Applications for permission to exchange or transfer human biological materials shall be made to the UNCST. These applications must be accompanied by a MTA.

The following are the necessary steps for the exchange or transfer of materials for research purposes:

a. The research project that involves the exchange or transfer of human biological material shall first be registered and approved by the UNCST through the established procedures for research approvals in Uganda.
b. The applicant must be a legal resident of Uganda or be affiliated to a local legally recognized institution in Uganda.
c. A request for the exchange or transfer of human biological material shall be made in writing to the Executive Secretary of the UNCST.
d. An MTA and any other document related to the exchange or transfer of human biological material shall accompany the request for the exchange or transfer of the material.
e. The applicant shall receive feedback from the UNCST on the status of his/her request within fourteen (14) days from the date of submitting the request in (c) above. The feedback may be an approval/clearance, reject/disapproval or comments to improve the quality of the application for the exchange or transfer of the human biological material.
f. Subject to other necessary legal requirements as the case may be, approval/clearance of the UNCST shall be sufficient to facilitate the exchange or transfer of the human biological material.

12. PUBLICATION AND DISSEMINATION OF RESEARCH

The Investigator shall submit to the local institution with which the research project is associated and to the UNCST, or to the UNCST alone if there is no such local institution, a copy of the prepared manuscript or publication arising from the research work. The local institutions and the UNCST shall reserve the right to review the manuscript or publications and provide their comments for the author's consideration.

A manuscript submitted for review pursuant to this section shall be confidential. No portion of the manuscript may be released by the UNCST or the relevant local institution or entity to a third party, either orally or in writing, without the prior written consent of the unauthorized author of such manuscript. No portion of the manuscript may be appropriated, borrowed, copied, transmitted, or otherwise used or disseminated for any purpose other than for review, without the express written consent of the author(s) of the manuscript.

The Investigators shall, as appropriate, make all reasonable efforts to share findings of research project with the communities in which research was done.

13. PENALTIES FOR NON-COMPLIANCE

Non-compliance with these guidelines may be identified by any person or IRC or institution or the UNCST and may be graded as non-serious or serious.

The UNCST shall require documentation of non-compliance whenever it is identified. This shall be in writing.

The UNCST shall subsequently communicate the non-compliance to the IRC, the host institution and to the NDA, when applicable. The UNCST will require that the IRC or the host institution respond to this communication within a specified time period and describe the corrective actions that should be taken by the IRC, the institution, or both to achieve compliance with these guidelines.

On the basis of the IRC's or the institution's response UNCST (and where applicable the NDA) may schedule an audit to confirm the adequacy of corrective actions taken. In addition, until the IRC or the host institution takes appropriate corrective action, the UNCST may:

a. Withhold approval of new studies to be conducted at the institution or reviewed by the IRC;
b. Direct that no new research participants be added to ongoing studies;
c. Terminate ongoing studies when such termination would not harm research participants;
d. Stop an institution from carrying out a research project;
e. Withdraw the research permits of Investigators involved in repeated non-compliance;
f. Close all health related investigations at the institution in cases of serious non-compliance that results in grave consequences to human research participants;
g. Disqualify IRC's that have failed to take adequate steps to correct the non-compliance stated in the letter sent by the UNCST or where applicable, the NDA. IRC's may also be disqualified if they repeatedly fail or refuse to comply with these guidelines.

GLOSARRY

Adverse event is any untoward medical occurrence in a participant in a clinical trial who has been administered a pharmaceutical product or a medical device. The event may or may not be casually related to the treatment or procedure.

Adverse reaction is (a) a response to a pharmaceutical product that is noxious and unintended, that occurs at doses normally used or tested in humans for prophylaxis, diagnosis, or therapy of the disease, or for the modification of physiological function (b) a response to a medical device that is noxious and unintended, that occurs with the use of the device in the manner intended for use in humans for prophylaxis, diagnosis, or therapy of the disease or for modification of the physiological function. Adverse reactions include injuries caused by overdosing, abuse, dependence, and interactions with any other product.

Assent means a child's affirmative agreement to participate in a research project. Failure to object does not constitute assent.

Child is a person below the age of eighteen years.

Clinical trial is a systematic study of pharmaceutical products or medical devices in human research participants in order to discover or to verify the beneficial or adverse effects, to identify any adverse reaction in the investigational product, and/or to study the absorption, distribution, metabolism, and excretion of the product with the objective of ascertaining its safety and efficacy.

Dead fetus means a fetus *ex utero* that does not exhibit a heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, and pulsation of the umbilical cord if it is still attached.

Fetus means the product of conception from the time of implantation as indicated by any of the presumptive signs of pregnancy, including missed menses or a medically accepted pregnancy test, until a determination is made, following expulsion or extraction of the fetus, that it is viable.

Guardian means a person having parental responsibility for a child.

Institution means any entity or agency, whether public or private. The institution should have adequate capacity to conduct the proposed research project.

Investigational labeling refers to labeling developed specifically for products involved in a clinical trial.

Investigational product or study product is any pharmaceutical product or medical device or placebo being tested or being used as a reference in a clinical trial.

Local Investigator is an individual who is employed by an institution in the host country, who is qualified by training and has experience as an appropriate expert who conducts a research project.

Medical device is any device that has a therapeutic, prophylactic, or diagnostic use or is intended to modify physiological functions and is attached, implanted, or inserted for use in humans.

Minimal risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives or in the routine medical, dental, or psychological examination of healthy persons.

Parent means the biological mother or father or adoptive mother or father of a child.

Parental responsibility means all rights, duties, powers, responsibilities and authority which by law a parent of a child has in relation to the child.

Permission means the agreement of the parent(s) or guardian(s) to the participation of their child or ward in the research project.

Pharmaceutical product is any substance or combination of substances that has a therapeutic, prophylactic, or diagnostic use or is intended to modify physiological functions and is presented in a dosage form suitable for administration to humans.

Pregnancy refers to the time period from confirmation of implantation through any of the presumptive signs of pregnancy including, for instance, missed menses or a medically accepted pregnancy test, until expulsion or extraction of the fetus.

Principal Investigator is an individual who is qualified by training and has experience as an appropriate expert who conducts a research study, and where appropriate, under whose immediate direction the investigational agent under investigation is administered or dispensed. When a team of individuals conducts an investigation, the responsible leader of the team would be the Principal Investigator.

Prisoner means any individual who is involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil provision or ruling, 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 a final disposition of their case.

Research means any type of systematic investigation, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Research involving humans as research participants is defined as any study involving persons, and directed to the advancement of biomedical or other knowledge, that cannot be regarded as an element in established clinical management, public health or social practices and that involves either physical or psychological intervention or assessment, or generation, storage, and analysis of records containing biomedical or other information referable to identifiable individuals and communities. Research involving humans as research participants also includes research on any material obtained from a research participant, whether the participant is still living or has died.

Glosarry

Research participant means a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or identifiable private information.

Serious adverse event is an adverse event associated with death, hospital admission, prolongation of a hospitalization, persistent or significant disability or incapacity, or otherwise life-threatening condition in connection with a clinical trial.

Soldier means any individual who is on active duty in the military service of the government of Uganda, regardless of where that individual is located, the nature of his or her duties, and whether that particular assignment is temporary or permanent in nature. Soldier encompasses all military personnel regardless of rank.

Street children and orphans are persons who have not yet attained the legal age of majority under the applicable law and have no identifiable parent or guardian or have been abandoned by their parent(s) or guardian (s), are in wards of government or governmental entity, institution, organization, ministry, department, or subunit thereof, or are under the care of any governmental entity, institution, organization, ministry, department or subunit thereof.

Viable means being able, after spontaneous or induced delivery, to survive, given the benefit of available medical therapy, to the point of independently maintaining heart beat and respiration. If a fetus is viable after delivery, it is a premature infant.

Vulnerability refers to a substantial incapacity to protect one's own interests owing to such impediments as lack of capability to give informed consent, lack of alternative means of obtaining medical care or other expensive necessities, or being a junior or subordinate member of a hierarchical group.

Notes:

Notes: