REPUBLIQUE DU RWANDA

NATIONAL ETHICS COMMITTEE / COMITE NATIONAL D'ETHIQUE

(RNEC)

FWA No: 00001973
IRB 00001497 of IORG 0001100

Ministry of Health
Po Box 84
Kigali-Rwanda

E-mail : info@rnecrwanda.og
Web-site: www.rnecrwanda.org

Rwanda National Ethics Committee Guidelines

Research Ethics Guidelines on Functioning, Protocol Application, Analysis and Approval Procedures

Table of Contents

1 INTRODUCTION

The ethical and scientific standards for carrying out biomedical research human subjects have been developed and established in international guidelines, including the Declaration of Helsinki, the CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects, and the WHO and ICH Guidelines for Good Clinical Practice. Compliance with these guidelines is a requirement and helps to ensure that the dignity, rights, safety, and well-being of research participants are promoted and that the results of the investigations are credible.

For the purposes of these guidelines, biomedical research includes research on pharmaceuticals, medical devices, medical radiation and imaging, surgical procedures, medical records, and biological samples, as well as epidemiological, social, and psychological investigations.

1.1 Rwanda National Ethics Committee (RNEC)

The Committee is an independent national body (an ethics review committee), constituted of medical/scientific professionals and non-medical/non-scientific members, whose responsibility it is to ensure the protection of the rights, safety and well-being of human subjects involved in any research or in a clinical or non-clinical trial involving human participants. To provide public assurance of that protection, by, among other things, reviewing and approving/providing favorable opinion on, the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

The legal status, composition, function, operations and regulatory requirements pertaining to RNEC allows the Committee to act in agreement with Good Clinical Practice (GCP).

The Rwanda National Ethics Committee (RNEC) hereinafter "the Committee," is pleased to provide this guidance on information about using this Guideline by all persons i.e. physical or moral with ethical guidance on how to apply for and receive research ethical clearance that involves .

The information is intended to provide practical guidance about submission questions, review process and oversight, and other topics that may be of interest to you and your research staff. Please use the information in any way that will serve to assist your research efforts as we join together in protection of the human research subject.

3 OBJECTIVE

The objective of these Guidelines is to contribute to the effective functioning of the Committee, so that a quality and consistent ethical review mechanism for health and biomedical research is put in place for all proposals dealt with by the Committee as prescribed by international ethical guidelines for biomedical research on human participants.

2 ROLE OF THE COMMITTEE

The role of the Committee is to safeguard the dignity, rights, health and wellbeing of those participating in biomedical research, to ensure that informed consent is granted, and to approve protocols and research projects which meet international ethical standards.

The Committee's mission is to examine all the human research projects to be conducted anywhere within Rwanda and any modifications to be made to them, regardless of the nationality of the promoters. It also is the approval authority for such projects. Any decision must be properly justified.

To promote the principle of equity, whereby the weight and benefits of the research must be equitably distributed among all groups and classes of society, the purpose of the ethics committee is to bring to research projects competent independent analysis in the area of ethics. The Committee also oversees quality assurance of biomedical research.

3 PROTOCOL APPLICATION REQUIREMENTS

4.1 Submitting a complete file

An ethics approval application for a biomedical research project must be requested by a qualified researcher, who is responsible for the ethics and scientific monitoring of the research. All research conducted in Rwanda have the ethical responsibility to ensure that the research projects address the field of health, the country's development needs and the individual needs of those suffering from the pathologies being addressed.

The following documents must be submitted to the secretariat of the ethics committee (15) Fifteen working days before the meeting:

1. Copy of the request letter.
2. Copy of the summary and protocol,
3. Copy of the patient informed consent and the patient information sheet in English or French and Kinyarwanda,
4. CVs of all investigators and their respective roles in the study,
5. Approval from National Health Research Committee (NHRC) if the study is a medical research,
6. The study budget,
7. Review Fees of amount of 1,500,000 FRW (One Million five hundred thousand Rwandan francs) for Research projects funded by research Institutions or other international organizations. The fees are paid to the following account number: Rwanda National Ethics Committee 00001-013010 53 298-63in COGEBANQUE. The proof of payment must be enclosed with the file submitted,
8. The above stated documents are submitted to the official email of Rwanda National Ethics Committee i.e. info@rnecrwanda.org (save all documents in PDF format and separate the documents).
9. The Principal Investigator (PI)/ Co-investigator must be present or request for a virtual presentation of the protocol at the Committee meeting.
10. Any other document or information that the researcher may considered relevant to the application and the Committee.

4 PROTOCOL ANALYSIS AND APPROVAL PROCESS BY THE COMMITTEE

The Committee examines all the aspects of the research protocol or clinical trial and ensures that:

1. The protocols are conducted to answer specific questions that the assumption is scientifically valid and that it offers a realistic possibility to bring greater benefit to the standard care.
2. The methodology clearly shows the criteria for selection of the participants, and provides adequate and easily understandable information for obtaining an informed consent of the participants, as well as a clear description of the interventions and observations to be carried out, and a statistical estimate of the anticipated results.
3. The goal of each trial must be precisely established and each project must be led by qualified researchers with the necessary experience and qualifications.
4. The ethics committee approves the amendments made or can reject a research project for ethical reasons. The decisions are noted in writing and also specify the reasons for the rejection.
5. When considering a research protocol, the committee can ask for the assistance of an expert in a given subject area but the committee should ensure that such experts do not have any conflict of interest in relation to the research project.
6. Health research projects carried out in the community must include a clear plan on the way in which the communities will be consulted or involved in the research process, and how they will generally be kept informed.
7. Communication between the sponsors of the research project and the ethics committee shall to be via the principal researcher.
8. A research project must include a statement of the ethical considerations used. The ethics committee must make sure that the research protocol gives adequate consideration to social values, such as beliefs, the law and the cultural heritage.
9. All documents and other material used to inform potential participants in the research project must be approved by the committee, including the language used for the information, the consent form, the questionnaires and other items.

5 PARTICIPATION OF PROTOCOL INVESTIGATOR IN THE COMMITTEE MEETINGS AND VOTING PROCEDURE

6.1 The researcher's participation

Ethics committee meetings are not public and are held behind closed doors. The committee can invite qualified people who are not members to deliver their technical opinions on rather specific fields. Such persons will not take part in the deliberations and cannot obtain voting rights. The committee can hear the promoter and/or the researcher of a research project. These persons must comply with all the quality standards and best practices in both ethics and the technical field. The committee reserves the right to request from the researcher any additional information about the research. In this case, the researcher is also to bring these data to the committee meeting. The decisions are caught by consensus and if there is no consensus, a vote is taken.

The following instructions describe the conditions for participation of protocol investigator in the Committee meetings when their protocols are being reviewed.

1. The Secretary/Administrator shall notify all PIs of the meeting scheduled to consider their submissions at least two weeks before the meeting date. The Secretary/Administrator shall also notify all PIs about their protocol's place in the agenda. An Associate Investigator may attend on the PI's behalf if necessary.
2. The PI may be invited into the meeting room during consideration of his or her protocol.
3. The PI may be invited to make a 15-20-minute presentation on the protocol under consideration. After the presentation, the PI shall remain in the meeting to answer any questions, concerns and suggestions from members.
4. After the question and answer session, the PI and any other attendees with a potential conflict of interest with the protocol or institution submitting shall leave the meeting during the decision/voting period.

5. Each Committee member shall vote/have a say for or against a protocol or abstain. An absentee member is allowed to send in his/her comments but cannot vote.
6. In order for a protocol to be approved, it shall receive the approval of a simple majority of those members present at the meeting. The Committee may also decide to postpone decisions on a protocol if more information or consideration is required.
7. If the Committee decides to disapprove a research proposal, the Committee shall include in its written notification to the investigator a statement of the reasons for its decision, and shall give the investigator an opportunity to respond in person or in writing.

If the PI is not satisfied with the committee's decision, the arbitration mechanism shall involve the PI presenting an appeal to the Arbitration Board, which in this case is the Ministry of Health.

Voting procedure

1. Only those members who are not affiliated with the promoter or researcher of a research project have voting rights or may render an opinion on the research in question.
2. Only the members who took part in the study and the discussion of a research project will vote or deliver their opinion and/or recommendation.
3. The researcher will provide information on all the aspects of his research project but will not take part in the deliberations of the ethics committee or the vote/opinion of the ethics committee.
4. Any member present has the right to demand a secret vote.
5. Opinions are rendered by simple majority of the members present on reports
6. delivered by one of the members of the committee designated by the chairman
7. or a qualified person.
8. The chairperson casts the deciding vote in the event of a tie.

The ethics committee functions on the principle of autonomy.

7 RESEARCH PROTOCOL EVALUATION

The Committee is responsible for ensuring that the research projects which has been approved are monitored and evaluated. The monitoring will be done in accordance with the protocol initially approved. The Committee will require that the lead researcher submits an annual report on the following:

1. The current progress of the study or the results of studies already completed;
2. Information connected with maintaining data confidentiality;
3. The proof that the research protocol is being properly followed; and
4. Proof that each condition of the agreement has been observed.

The Committee adopts adequate additional evaluation mechanisms, including the inspection of the data collected by research centers, recording interviews and signed consent forms compared to the initial consent given to the participants.

It is important that the researchers report any event or change to the protocol, which could affect the ethical acceptability of the project. They must inform the committee if the research project may be interrupted and provide justification.

7.1 RNEC Ethical Review Process

All members of the Committee are afforded sufficient time to review the research project file or clinical trial in advance of the meeting. The protocol and the patient information sheet in English or French and Kinyarwanda as well as informed consent form will be analyzed.

The following elements are taken into account:

1. The scientific scheme and monitoring of the study;
2. Inclusion criteria;
3. Exclusion criteria,
4. The dignity and the protection of the participants in research;
5. Maintenance of the participants' confidentiality;
6. The informed consent process;
7. Society's moral considerations;
8. The qualifications of the lead researcher and the co-researcher are to be analyzed.

All required documents must be submitted and the members must agree before any study is approved or amended.

The vote is taken by show of hands. The person in charge of the project will be informed of the rejection, amendment or approval of the research. The decision of the Committee is forwarded to the person in charge for the project within 10 (ten) working days after the meeting.
The Committee will pay special attention to the following:

7.2 Scientific design and conduct of the study

The Committee ensures that the protocol submitted meets national and international standards. In particular the study design must contain:

1. Adequate background information and literature review;
2. The appropriateness of the study design in relation to the objectives of the study, the methodology, the statistical analysis including sample size calculation and the potential for reaching sound conclusions with the smallest number of research participants;
3. The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants and the concerned communities;
4. The justification for the use of control arms;
5. The criteria for prematurely withdrawing research participants;
6. The criteria for suspending or terminating the research as a whole;
7. The adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a Data and Safety Monitoring Board (DSMB) or Oversight Committee;
8. The adequacy of the site including the supporting staff, available facilities and emergency procedures;
9. The manner in which the results of the research will be reported and published.

7.3 Recruitment of research participants

A researcher must demonstrate to the Committee that research participants will be recruited in conformity with agreed upon and scientifically sound standards and practices. The protocol must indicate that the following conditions were satisfied:

1. The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status);

2. The means by which initial contact and recruitment is to be conducted;

3. The means by which full information is to be conveyed to potential research participants or their representatives;

4. Inclusion criteria for research participants;

5. Exclusion criteria for research participants.

7.4 Care and protection of research participants

1. The competence of the investigator(s) (qualifications, experience, etc) to carry out the proposed study;

2. Any plans to withdraw or withhold standard therapies for the purpose of the research and the justification for such action;

3. The medical care to be provided to research participants during and after the course of the research;

4. The adequacy of medical supervision and psychosocial support of the research participants;

5. Steps to be taken if research participants voluntarily withdraw during the course of the research;

6. The criteria for extended access to, the emergency use of, and/or the compassionate use of study products;

7. The arrangement, if appropriate, for informing a research participant's general practitioner, including procedures for seeking the participant's consent to do so;

8. A description of any plans to make the study product available to the research participants following the research;

9. A description of any financial cost to the research participant;

10. The rewards and compensations for research participants (including money, services and /or gifts);

11. The provisions for compensation/treatment in the case of injury/disability/death of a research participant attributable to participation in the research.

12. The insurance and indemnity arrangements, if required.

7.5 Protection of research participants' confidentiality

1. The people who will have access to personal data of the research participants, including medical records and biological samples;

2. The measures taken to ensure the confidentiality and security of personal information concerning research participants.

7.6 Biological specimens

1. A full description of any specimens that will be collected (blood, body fluids, tissue biopsies , etc);

2. Plans for obtaining consent and clearance from participants and the Committee, for long-term storage, export, and future research;

3. Arrangements for disposal.

7.7 Informed consent process

1. A full description of the process for obtaining informed consent, including the identification of those responsible for obtaining the consensus;

2. The adequacy, completeness and understandability of written and oral information to be given to the research participants, and, when appropriate , their legally acceptable representative(s);

3. Clear justification for the intention to include in the research individuals who cannot consent, and a full account of the arrangements for obtaining consent or authorization for the participation of such individuals;

4. Assurance that research participants will receive information that becomes available during the course of the research relevant to their participation (including their rights, safety and well-being);

5. The provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project;

7.8 Community considerations

1. The impact and relevance of the research on the local community from which the research participants are drawn and on the wider concerned communities and the environment;

2. The steps taken to consult with the concerned communities during the course of a designing the research;

3. The influence of the community on the consent of the individuals;

4. Proposed community consultation during the course of the research;

5. The extent to which the research contributes to capacity –building, such as the enhancement of local healthcare, research, and the ability to respond to public health needs;

6. A description of the availability and affordability of any successful study product to the concerned communities following the research;

7. The manner in which the results of the research will be made available to the research participants and the concerned communities.

7.9 Vulnerable populations

- Documentation on how the researcher will protect the rights and welfare of special categories of the population, i.e. children, pregnant women, refugees, prisoners, elderly persons, orphans, etc.

8 MAIN AMENDMENTS TO THE PROTOCOL

8.1 Submission of required documents

All main amendments to the protocol are entered on the meeting's agenda and will be discussed in the meeting that follows the one in which initial comments are made, then approved or rejected during a meeting of the Committee.

A main amendment is any substantial amendment which has an impact on the safety or the integrity of the participants, decreases the scientific interest of the trial or the interpretation of the results, the effective validity of the data, study scheme, the statistical analysis planned, or other considerable changes to the trial.

8.1.1 Examples of substantial changes can include:

1. Changes to the scheme or the methodology of the study;
2. Modifications to the effectiveness or safety measures;
3. Change of the sample size, reduction or increase in the measurement tests;

4. Change in the number of patients planned to be included, the age range or other
   inclusion criteria.
5. Duration or dose of drugs for the study.

8.1.2 The following documents are to be sent to the Secretariat of the Committee within fifteen (15) working days.

i. Application form;
ii. Letter of request;
iii. The main amendment to the protocol;
iv. Document justifying the amendment;
v. The summary of modifications made to the protocol;
vi. The revised version of the patient informed consent;
vii. A check for submission fees, in favor of the Committee must be enclosed with the file submitted.

If a pro forma invoice is needed, please contact the Committee's administrator. Payment may also be wired directly to the following account: "Rwanda National Ethics Committee 130-10 53 298 in COGEBANQUE." No important amendment is reviewed unless the amount stated above is fully paid.

9 CONTINUOUS ANALYSIS / ANNUAL APPROVAL

Continuous review of a research project takes place at regular intervals but no less than once a year. When research is in progress, members of the Committee receive and review the summary of the protocol report. A research progress report is sent to the Committee at the end of the first year. The research progress report will include the following elements:

1. Number of participants included by center;
2. A summary of the major undesirable events and the problems not anticipated by the center, including the side effects which have occurred and their relationship to the treatments used in the study;
3. The number of persons who dropped out and the reason for their doing so.
4. Any new significant incident.

10 RESUBMISSION

More than one gap in a research protocol will result in the project's being rejected or amended. This requires that the protocol be resubmitted. Conditional approval can still be granted if there are minor omissions when submitting a protocol/amendment. The correction or addition of supplemental information will be reviewed by a committee member, such as the chairperson.

11 EXPEDITED ANALYSIS PROCEDURES

The committee provides expedited study of certain categories of the research projects if the research concerned involves only a minimum risk for the subjects and if the situation involves review and approval of minor modifications to research that had already been approved in the previous year. This expedited review can be performed by the chairperson of the committee or one or more members appointed in advance who have particular experience in the matter. This designated person has all the authority of the committee. However, he may only reject a research study provided that the normal non-expedited research project analysis procedure is used.

The report of this expedited analysis will be drafted and a letter of approval drawn up. Then, the remainder of the members of the committee will be informed of the review and the decision in question must be upheld by the whole committee at its next meeting.

In its offices, the committee will post an official statement listing the categories of research, which are eligible for the expedited processing.

In general, research projects likely to cause psychological or physical damage are not eligible for this procedure. This includes drug trials, research involving invasive procedures and sensitive cultural or personal subjects.

12 RECORDING DECISIONS

The Committee documents all research protocols received and studied. Hence, it keeps a copy of each research protocol and each research project requiring approval. The registered file for each project includes an information sheet on the research concerned, the consent forms and all correspondence relating to the research. All documents are noted in the form in which they had been approved by the ethics committee. A list of the members of the Committee

present at the time of the deliberation and the final decision-making is also appended.

13 COMMUNICATING A DECISION

A decision is communicated in writing to the applicant within ten days of the meeting at which the decision was made. The communication of the decision includes the following:

i. The name and title of the applicant;

ii. The exact title of the research proposal reviewed;

iii. A clear identification of the protocol of the proposed research or amendment, including the date and version number, where applicable, on which the decision has been made;

iv. The names and (where possible) specific identification numbers (version numbers/dates) of the documents reviewed, including the potential research participant information sheet/material and informed consent form;

v. The date and place of the decision;

vi. A clear statement of the decision reached;

vii. Any advice by the Committee;

viii. In the case of a conditional decision, any requirements of the Committee including suggestions for revision and the procedure for having the application resubmitted;

ix. In the case of a positive decision, a statement of the responsibilities of the applicant: for example, confirmation of acceptance of any requirements imposed by the Committee, submission of Progress Report(s), the need to notify the Committee in cases of protocol amendments, the need to report adverse events related to the conduct of the study, the need to report unforeseen circumstances, the termination of the study, or significant decisions by other ethics committees;

x. In the case of a negative decision, clearly stated reasons for the negative decision;

xi. Signature (dated) of the Chairperson (or other authorized persons) of the Committee.

14 COMPLAINTS, SUSPENSION OR TERMINATION OF RESEARCH

The contact information for the Ethics Committee shall be provided to research participants and researchers in the event they should wish to file a complaint. All complaints will be investigated and both parties will receive a response from the Committee. If required, a formal investigation may be considered if the Committee deems the dispute is important enough to justify it.

If the committee concludes that the research project is not carried out as prescribed in the protocol approval and/or that the dignity and rights of the subjects have been compromised, the committee reserves the right to cancel its approval.

The Committee informs the lead researcher or the sponsor of its decision and will recommend the suspension or the termination of research. In these cases, the researcher must stop his project and meet the new conditions required by the Committee.

15 SAFETY REPORTING

All serious adverse events (SAEs) must be reported immediately to the sponsor who in turn will forward the information to the ethics committee within 24 hours. The reports must be followed promptly by detailed, written reports. The follow-up reports should identify subjects by unique code numbers assigned to the trial subjects rather than by the subjects' names, personal identification numbers, and/or address.

The investigator should also comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to the regulatory authority (ies) i.e. the Rwanda FDA and the Committee. A specific Standard Operating Procedure determines the process for reporting and actions that the Committee undertakes.

Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol. For reported deaths, the investigator shall provide the sponsor and the Committee with any additional requested information (e.g. autopsy reports and terminal medical reports).

The sponsor is responsible for the ongoing safety evaluation of the investigational product(s). The sponsor should promptly notify all concerned investigator(s)/institution(s) and the regulatory authority(ies) of findings that could affect adversely the safety of subjects, impact the conduct of the trial, or alter the Committee's approval/favorable opinion to continue the trial.

The sponsor should expedite the reporting to all concerned investigator(s)/institution(s), to the Committee, where applicable, and to the regulatory authority (ies) i.e. the Rwanda FDA, of all adverse drug reactions (ADRs) that are both serious and unexpected. Such expedited reports should comply with the applicable regulatory requirement(s) and with the ICH Guideline for Clinical Safety data management.

The sponsor must submit to the regulatory authority (ies) all safety updates and periodic reports, as required by applicable regulatory requirement(s). Any relevant information relating to safety must be reported to the committee as quickly as possible.

Any **unexpected or suspected Adverse Drug Reaction** occurring at research centers outside of Rwanda but related to the trial must be reported to the Committee in the form of a list appended to the annual re-approval request.

The Committee may accept reasonable deviations the deadlines due to special procedural conditions. Nevertheless, all important data (for example: application file, follow-up, CIOMS, etc.) must be forwarded within a reasonable time.

15.1 Following information must be available when an adverse event occurs:

1. Number of the protocol;
2. Title of the protocol;
3. Number of the subject;
5. Diagnosis (more precisely the SAE reported);
6. Initials of the subject;
7. Date of birth;
8. Name of the principal Researcher;
9. Product of the study;
10. Description of the undesirable event;
11. Action taken in connection with the produced study;
12. Treatment;
13. Causality link with the produced study;

A designated member (safety) of the committee will analyze all SAEs.
The lists of these will be reviewed as part of the annual re-approval process.
The ethics committee will acknowledge receipt of the SAE and the lists in writing.
Please send all SAEs & lists to the administrator, email: info@rnecrwanda.org

16 RIGHTS OF THE VOLUNTEERS/PATIENTS IN THE STUDY

The universal statement on bio-ethics and human rights has introduced general principles on the rights of persons involved in biomedical research:

1. Human dignity and human rights: Fundamental liberties must be respected. The interests and wellbeing of the individuals must supersede the sole interest of science or society.
2. Beneficial and harmful effects: The direct or indirect benefits to the patients must be maximized and any harmful effects that could impact on these persons are to be minimized.
3. Autonomy and individual responsibility: Decision-making must include the assumption of responsibility and respect for the independence of others. Specific measures may be taken to protect the rights and interests of persons who cannot exercise their independence.
4. Consent: The advance, free and informed consent of the person involved, based on sufficient information, is require for any medical intervention of a preventative, diagnostic or therapeutic nature. The individual in question reserves the right to
    a. retract his/her consent at any time without reason or consequence to him/herself.
5. Inability to express consent: For these persons, the health benefit must be direct,
    a. provided there are authorizations and measures established to protect them.
6. Respect for human vulnerability and personal integrity: Protection of groups that are particularly vulnerable.
7. Privacy and confidentiality: Information about the persons in question may not be
    a. released without their consent, in accordance with international laws on human
    b. rights.
8. Equality, equity and justice: Fundamental equality of all human beings with regard

a. to dignity and under the law requires that they be treated fairly and equitably.

9. Non-discrimination and non-stigmatization: No individual shall be subjected to
    a. discrimination or stigmatization for any reason whatever.

17 PATIENT INFORMATION AND INFORMED CONSENT REQUIRMENTS

The committee requires the following information on informed consent forms:

1. A description of the procedure used for obtaining informed consent, to include
   identification of those who are tasked with doing so.
2. Complete, understandable and adequate information, both in writing and orally,
   provided to the participants in the study and, where necessary, to their legally acceptable representatives.
3. A clear explanation of the intent to include in the research persons who cannot consent to it, and a compete set of the arrangements implemented to convince these persons.
4. Mechanisms put in place to receive and respond to questions and complaints from participants in the research or their representatives during the study.

In all cases, verbal and written informed consent must be obtained.
Verbal consent alone is required when the participant is illiterate. This must be given in the presence of a witness who will co-sign the consent form.
For minor participants under the age of 21, consent must be obtained from a parent or legal guardian. No other person is authorized to give consent for a child to participate in any study.
Appropriate steps must be followed to gain the inclusion of a child, if it is deemed appropriate to make such a decision. The consent may be granted if, in the estimation of the parents or the researcher, the child is capable of giving its own consent (+/- 9 years old). Maturity, psychological condition and age enter into consideration in this case.

18 CONTROL USING PLACEBOS

As a general rule, the Ethics Committee does not, as a matter of course, support control using placebos for preventative, diagnostic and therapeutic intervention. This is usually used for assessing the effectiveness of a reference treatment versus a placebo.

Nevertheless, the committee will consider use of a placebo in the following circumstances:

1. There is no already established effective intervention.
2. The lack of therapeutic effectiveness could expose the subject to transitory illness or a period of reduced symptoms
3. Using effective intervention as a control measure could not lead to scientifically
4. valuable results and using a placebo will not add any risk or produce serious irreversible damage to the subjects.

In all cases where a placebo is intended to be used as a control, the Committee must receive a letter justifying the use of the placebo included with the rest of the application file.

19 SITE EVALUATION/INSPECTION

The research site must be authorized by the Ministry of Health, or at a minimum approved by competent governmental authorities. The procedures for approving a research center meet certain requirements. These sites may be hospital establishments or centers that must meet strict safety requirements to receive patients.

Some organizations may be afforded relaxed conditions for simple actions such as taking blood samples or an act commonly practiced in family medicine. This measure is particularly useful for studies relating in particular to the fields of epidemiology, pharmacoepidemiology and genetics. Certain studies falling under these categories actually become outdated before they are completed since the time it takes to obtain such authorization is extremely long if the research is conducted outside of hospital environments.

19.1 Joint Inspections

The Committee and the Rwanda FDA may conduct separate or joint inspections of trial sites upon receiving reports from the researcher or on their own

initiative aimed at ensuring compliance with the approved protocol, or research standards.

20 SELECTING INDEPENDENT CONSULTANTS

The more accentuated the diversity of promoters and protocols, the more variable the Committee's role becomes. The Committee may be required to approve a technical protocol that may require the Committee to use expertise on the matter in question, in which case it will require that more expert advice be given.

Here, it will appoint an expert based what technical skills are specific to the research undergoing evaluation. Also, his ethics must be beyond doubt and his integrity above reproach. The consultant in question must not have any tie to the promoter of the research project. He remains anonymous. He is called upon to explain the scientific and methodological quality of the research, its clinical interest, the qualifications of the researchers, and the information they have submitted in the report, using language that is the most understandable for the entire Committee.

21 PROTOCOL SUSPENSION

If the chairperson of the Committee, or in his absence, the vice-chairman deems that the sponsor, the researcher or any other person involved in conducting the research is no longer satisfying his obligations, he will send a warning to the promoter or any other person in charge of the research prescribing the corrective measures to be taken by a particular deadline.
The promoter is to send a response immediately to the committee on individual protection, which rendered an opinion on the research in question.

The promoter has one week either from the time he received the demand to modify the protocol, or the date of the decision to suspend or prohibit the research, to submit his observations. Once this deadline has passed, the project is suspended.
Within one year from the time that the research was terminated, a report is to be compiled, which is signed by the promoter and researcher (or researchers in

the case of a multicentric study or of there is no coordinating researcher). This report is kept at the disposal of any competent authority.

22 RETENTION OF STUDY FILES

The Committee will retain at least one copy of all documents submitted to it for at least 15 years, to track the future of each study approved. The researcher and promoter must retain all trial documents (preparatory documents, individual observations of each patient, trial report, correspondence and product accounting) for no less than 10 years or as long as the medication is authorized.

This storage requirement also applies to source documents, i.e. the individual patient records that may contain information confirming or supplementing the data collected for the trial. This must last for as long as the hospital or physician's office permits. On the other hand, a list of patient identification codes must be retained for at least 15 years.
In order to propagate best practices and thereby improve protections for persons participating in studies, a database archiving the studies and committee rulings will be created.

23 ESTABLISHING STANDARD EVALUATION PROCEDURES

Trials or experiments set up and performed on humans for the purpose of enhancing biological or medical knowledge are authorized under prescribed conditions and identified by the term “biomedical research".

In order to preclude any assault on the individual's integrity during such studies that are critical to medical progress, clear and precise provisions have been defined to oversee how biomedical research is organized. It is based on these standardized provisions that the Ethics Committee renders its rulings on approving research projects.
The conditions under which a research protocol can be started are very specifically defined. No biomedical research may be performed on a human being:

1. If it is not based on the latest state of scientific knowledge and sufficient pre-clinical

    a. experimentation;
2. If the potential risk to persons participating in the research is disproportionate to the
    a. anticipated benefit to them or their interests;
3. If it is not aimed at expanding scientific knowledge of the human body and means that are likely to improve the human condition.

The conditions for completing protocols are also strictly regulated.
In fact, biomedical research can only be performed:

1. Under the direction and supervision of a physician with demonstrated appropriate experience;
2. Under material and technical conditions that are suitable for the trial and compatible with accepted scientific imperatives, as well as the safety of the individuals participating in the studies.

Even more restrictive conditions on imposed for pregnant women, convicts and the infirm who cannot give their consent, as well as for minors and protected adults.

The promoter, i.e. “the individual or legal entity that takes the initiative in a biomedical research study on humans” must ensure compensation for any injurious consequences the study may have on individuals participating in it. Also, the promoter must take out an insurance policy guaranteeing his civil liability for such biomedical research.

There are precise rules to be observed with regard to obtaining consent. Before any biomedical research can be done on a person, his/her free express and informed consent must be obtained after the researcher, i.e. “the individual(s) directing and supervising the conduct of the research, or a physician representing said individual(s)” has informed the person of the following:

1. The goal of the study;
2. The benefits expected, the limitations and potential risks, including those from the research being terminated early
3. The Ethics Committee's opinion on the biomedical research.

Some arrangements are possible for research in the field of psychology and in cases where, in the interests of a sick person, the diagnosis of the illness could not be revealed to him/her. The information provided must be summarized in writing and given to the individual whose consent is being sought. The consent must be obtained in writing.

In emergency situations, the protocol may state that the consent has not been sought and only the consent of the family members, if any, has been requested. The interested party is then informed as soon as possible and his/her consent is requested so the research may be conducted.

24 DISTRIBUTION OF STANDARD EVALUATION PROCEDURES

In order to better meet the expectations of researchers and study promoters, as well as to provide proper protection for individuals participating in biomedical research, the Ethics Committee is compiling a compendium of standard practices for evaluating research projects.
It will ensure wide distribution of this document, which will present the procedures to be followed in order to obtain the Committee's approval before beginning a biomedical research project. These Guidelines will be available at the Committee's secretariat and placed at the disposal of researchers. They may also be accessed at the Committee's web site ww.rnec.gov.rw.

25 REVIEWING THE STANDARD EVALUATION PROCEDURES

By examining biomedical research projects, the Ethics Committee strengthens the scientific quality of research projects that are critical to medical progress, using a clear and precise procedural framework while being ever mindful of its primary mission: to protect the dignity and integrity of the individual.

These standard procedures define the various steps to be taken in order to obtain the Ethics Committee's approval and must be adapted to suit the needs of scientific progress and the demands of our society. It is for this reason that these standard procedures must be reviewed every 2 years to ensure they remain suited to the general context of protecting individuals participating in biomedical studies.

26 CONFIDENTIALITY

All issues debated by the Ethics Committee are to be kept confidential for all committee members and are not to be disclosed to third parties unless required by law. Each committee member is obliged to keep confidential the

deliberations of committee meetings and any other information concerning research projects submitted for the committee's approval. Moreover, the committee shall take care to protect the privacy of individuals involved in research projects.

27 MULTICENTRIC RESEARCH

Multicentric research is when a promoter assigns several researchers at different locations to perform the study. The promoter names one of them to act as the coordinating researcher. The coordinating researcher has an important task: to obtain for the entire multicentric research project the approval of a committee on protecting the rights of individuals, which is located in the region where he or she is performing his or her job.

For the rest, the respective functions of the coordinator and the other researchers depend on the will of the parties and are defined in the research protocol. Their obligations under the law are the same. Each is responsible for that portion of the research that he must actually direct and for which he must oversee the compliance of the participants. It is incumbent upon the ethics committee to ensure the researchers are qualified.

In a multicentric study, it is the coordinating researcher's responsibility to:

1. Consult the ethics committee to obtain its ruling before the study is launched,
2. Forward this ruling to the promoter,
3. Wait for the promoter to send the "letter of intent" before beginning the study,
4. Request an additional opinion from the ethics committee if a "substantial" change is made to the protocol during the study (the promoter, for his part, will notify the relevant oversight authority of this),
5. Inform the promoter of the start and end dates of the study so that they may be forwarded to the insurer and the term for which the participants will be covered under the guarantee can be determined exactly.

All researchers in a study share the following responsibilities:

1. To obtain (signed) consent from the participants, after informing them verbally and in writing,
2. To retain (with the greatest care) copies of the consent forms for at least fifteen (15) years after the study has ended;

3. To adhere scrupulously to the terms of the trial protocol (inclusion and exclusion criteria, administration procedure, evaluation procedure, among others.)
- To notify the promoter or the appropriate designated point of contact if any serious adverse event should occur during the study as quickly as possible. The promoter must, in turn, inform the Ministry of Health or the drug agency of this within a relatively short period of time.

Lastly, by signing the agreement to participate in a study, researchers assume medical liability towards the participants, as well as any civil liability there may be and "commercial “liability towards the promoter. Thus, any deliberate violation of the protocol may constitute breach of contract and result in litigation with the promoter.
At the end of the trial, the researcher must compile a signed and dated report.

28 INSURANCE AND INDEMNITY

Biomedical studies require that their promoters take out in advance an insurance policy covering their own civil liability, as well as that of anyone involved, regardless of the nature of the ties between the promoter and the involved parties. For biomedical studies that have no direct individual benefit, the promoter assumes responsibility for compensating the participants and their assigns for any injurious consequences the research has, even if there is no fault, provided they did not result from the action of a third party or the voluntary withdrawal of an individual who had initially consented to participating in the study.

For biomedical studies that have direct individual benefit, the promoter assumes responsibility for compensating participants and their assigns for any injurious consequences the research has, unless he satisfies his burden of proof that the damage was not his fault or the fault of any person involved in the study or show that it was due to the action of a third party or the voluntary withdrawal of an individual who had initially consented to participating in the study.

The Committee can only validly examine and issue an opinion on a research project if the certificate of insurance is enclosed with the file. This certificate from the insurer serves as presumption of coverage and it is required to include the following items:

1. References to the applicable regulatory and legal provisions,
2. Company name of the insurer,
3. The insurance policy number,
4. The name and address of the person/entity, who took out the policy,
5. The exact name of the study that the policy covers.
6. The policy must indicate the minimum coverage amount for a biomedical study.

29 ADMINISTRATIVE PPEALS PROCEDURE

29.1 Time limit to make an administrative appeal

Within 15 days from being notified of an unfavorable ruling by the Committee, the sponsor may file an administrative appeal with the Executive Organ of the Committee to have his or her project re-examined or reconsidered. In this case the researcher states the grounds that he or she requires to be examined and addresses the key issues raised in the Committee. If he or she is not satisfied by the decision of the Executive Organ of the Committee he or she may address the matter to the Minister of Health who is required to give general guidance to the Committee to reconsider, approve, reject or suspend the research. The file for administrative appeal must contain the following:

- An administrative file,
- A file on the biomedical study, which specifically contains the date of the protocol and in writing, where necessary the appeal may include any subsequent modifications thereto and,
- May describe the objective(s), concept, method, statistical aspects and organization of the research, as well as a brochure for the researcher.

The Minister of Health may also appoint an ad hoc committee of experts in the academic or professional area that is contested, to examine the appeal using the standard evaluation procedure for biomedical research projects and its ruling may contain the following:

1. Identification and title of the study,
2. The name of the researcher or
3. The coordinating researcher, as the case may be,
4. The name of the promoter,
5. Dated identification of the documents on which the committee has already ruled,
6. Where applicable, identification of the modifications made when the file was examined or after the research began,

7. The place where the study is to be conducted, if it is subject to authorization,
8. The date of the session during which the opinion was issued and the names of the individuals who deliberated on the project, the category to which they belong, whether they are permanent or substitute members,
9. The Committee's justification.

The Ad hoc committee submits its copy of any opinion it renders to the Minister and reserves a copy to the chairperson of the Committee. If the study has not started within one year from the Committee's ruling, the ruling becomes invalid. However, the Ad hoc committee may extend said deadline if proper justification is produced before it expires.

30 RESEARCH IN GENETICS

The ethics committee analyzes the progress of human genetics. It handles issues on ethics and the consequences it produces on human health and the health care services, as well as any social, legal ethical and economic implications.

It takes care to centralize the data and promote vigilance over the development and use of human genetics. It must draft recommendations on computerization, protection and use of personal genetic data.

Furthermore, the researcher must ensure that family member consent freely to the research, that the results of genetic tests are not divulged to third parties (unless properly authorized) and that the privacy of individuals is protected. The ethics committee is to remain abreast of any damage to which the participants could be subjected, and the precautions researchers should have taken to prevent this (e.g. genetic counseling, etc.).

31 USE OF HUMAN TISSUE OR ORGAN SAMPLES

Due to fundamental values on human reproduction, studies where new reproduction techniques are used raise important moral concerns for researchers and the general public. When human tissue samples are taken for purposes of biomedical, ethnographic or anthropological research, there is a fundament ethical principle that seeks for the researcher to respect individual and collective notions of human dignity and physical, spiritual and cultural integrity. The data and information obtained from human tissues must be

handled as confidential personal information and, to the extent possible, be collected with the free and informed consent of the interested parties. Consent must be obtained even if the tissue is obtained as part of patient care and even if it is handled anonymously.

Organ samples from deceased persons may be taken only for therapeutic or scientific purposes after the individual has been properly pronounced dead. This sampling can be performed provided the person did not make it known while alive that it was against his/her wishes. Such wishes may be expressed via a national register intended for this purpose. It may be revoked at any time. If the physician does not know what the wishes of the deceased are, he must make every effort to find them out from the family.

No samples may be taken for scientific purposes, except for investigating the cause of death, without the directly expressed consent of the deceased or the advice of his/her family.
Physicians who have taken samples from a deceased person must ensure that the body is properly restored.

However, organs may only be removed from living persons who are organ donors in the direct therapeutic interest of the recipient. The donor must give his consent, after being informed in advance of any consequences or risks from the removal. No organ may be removed as a donation from a living minor or from a living adult who is covered by a legal protection measure.

32 PUBLICITY ANNOUNCEMENTS

Publicity announcements for the purpose of including subjects in a study must be submitted to the ethics committee for revision and approval. They must also contain the following information:

1. Purpose of the study and a summary of the inclusion criteria,
2. A clear and precise description of the benefits to the participant,
3. The location of the study and the name of the person to be contacted for more information, and
4. Researchers are not to be identified by name in any public announcement.

33 SPECIAL CATEGORIES OF PARTICIPANTS

Special consideration is reserved for protecting the wellbeing of certain categories of study participants, such as children and adolescents, pregnant women, prison inmates, the mentally ill, individuals who are not born native speakers of the language used in the study, or the underprivileged. These constitute vulnerable groups. Certain types of research also require particular attention and the committee may impose additional conditions to protect the wellbeing of the participants in a study.

Participation in studies by the following types of persons requires special attention:

1. Minors,
2. Persons with mental or intellectual handicaps,
3. Inept persons,
4. Dependent persons,
5. Group participants in a study,
6. Pregnant women.

The types of research requiring special attention include:

1. Research involving traditional health systems;
2. Research on emergency care;
3. Innovative therapies or interventions;
4. Research that is ambiguous for the participants.

34 EPIDEMIOLOGICAL RESEARCH

All epidemiological studies must be approved by the ethics committee and carried out in compliance with the established protocol, adhering to the objectives of the research, the documents required and defining the manner in which the data will be collected, used and stored. When the committee analyzes an epidemiological research protocol, it must determine whether:

- The research complies with the laws of Rwanda or the strategies of confidentiality and privacy,
- The researchers have the pre-requisite resources and knowledge in epidemiology to perform the study,

- Access to medical records and other documents will be restricted to qualified researchers,
- There is a scientifically acceptable procedure for distributing the information and the research results, and there are scientifically justifiable reasons if the distribution of information is selective/restricted.

Participants must generally sign an informed consent form before identified or potentially identifiable data is used for each epidemiological study.

35 GENERAL PROCEDURE

In accordance with international standards on bio-ethics, before granting its approval, the ethics committee ensures that the research protocol adheres to the spirit of the following directives:

- The Nuremburg Code (1947)
- The Helsinki Declaration of the World Medical Association (1964, …2000)
- The Oviedo Convention (1997)
- The international ethics directives on biomedical research involving human subject (1993);
- The Council of International Organizations in the Medical Sciences (CIOMS)
- The WHO/OMS directives on Best Clinical Practices (1995)
- The directives on Best Clinical Practices (1996);
- International Conference on Harmonization (ICG GCP);
- The directives on Best Clinical Practices in conducting clinical trials on human subjects in South Africa, 2000

No subject shall be included in a clinical trial before the ethics committee has given its written consent.

No change or modification to the protocol, which increases the risk to the participants and/or significantly affects the conduct of a clinical trial is to be made without the advance written approval of the ethics committee, except for the purpose of eliminating immediate risks to the participants or if the modifications in question only involve logistical and administrative aspects of the trial. The ethics committee must be informed immediately of any new information that could affect the safety of the participants or the conduct of the trial.

35.1 Specific Guidelines on Ethical Considerations for Clinical Trials by the Committee (RNEC)

Description of ethical considerations relating to the trial should include the following issues:

1. Choice of investigators,
2. Monitors and monitoring plan,
3. Indicate how additional staff (monitors, pharmacists, nursing staff, etc.) will maintain patient confidentiality, follow the protocol, and abide by ethical requirements.
4. Insurance and indemnity measures,
5. Patient Information leaflets and Informed Consent forms for any proposed archiving of biological specimens for later research or for genetics research,
6. Treatment and/or management of participants and their disease condition(s) after completion of trial,
7. Institutional Review Board, where applicable, to monitor site of clinical trial(s),
8. Provide an explanation if minimum recommended compensation for a participant is not being provided,
9. Follow-up of trial study participants after the conclusion of the trial,
10. In case of transfer of materials, provide Material Transfer Agreement (MTA) highlighting among other things, the following:
    a. Identification of the provider and recipient,
    b. Identification of the material and the volume of material,
    c. Definition of the trial and how the material will and will not be used,
    d. Maintenance of confidentiality of background or supporting data or information, if any,
    e. Indemnification and warranties (where applicable).
    f. Data Handling and Record Keeping,
    g. Publication Policy if not addressed in a separate agreement.

35.2 The Investigator's Brochure

The investigator's brochure must contain at least the following information in respect to the investigational medicinal product:

1. The physical, chemical and pharmaceutical properties,
2. The pharmacological aspects including its metabolites in all animal species tested,
3. The pharmacokinetics and metabolism including its biological transformation in all animal species tested,

4. Toxicological effects in any animal species tested under a single dose study, a repeated dose study or a special study,
5. Results of clinical pharmacokinetic studies,
6. Information regarding safety, pharmacodynamics, efficacy and dose responses that were obtained from previous clinical trials in humans.

35.3 Requirements concerning Informed Consent

In obtaining and documenting informed consent, the investigator should comply with Committee requirement(s) and must adhere to the ethical principles that have their origin in the Declaration of Helsinki.

Prior to the beginning of the trial, all investigators should obtain Ethical Clearance from approval.

Informed consent to study participants shall be administered in Kinyarwanda and English or French languages and all information to be given to study participants both oral and written must be in Kinyarwanda and English languages. The consent form together with the accompanying information shall be in Kinyarwanda and English languages.

The written informed consent form and any other written information to be provided to participants should be revised whenever important new information becomes available that may be relevant to the participant's consent. Any revised written informed consent form, and written information should receive the Committee approval in advance of use.

The participant or the participant's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the participant's willingness to continue participation in the trial. The communication of this information should be documented.

Neither the investigator, nor the trial staff, should coerce or unduly influence a participant to participate or to continue to participate in a given trial.

None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the participant or the participant's legally acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.

The investigator, or a person designated by the investigator, should fully inform the participant or, if the participant is unable to provide informed consent, the participant's legally acceptable representative, of all pertinent aspects of the trial including the written information and the RNEC approval.

The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the participant or the participant's legally acceptable representative and the impartial witness, where applicable.

Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the participant or the participant's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the participant or the participant's legally acceptable representative.

Prior to participation in the trial, the written informed consent form should be signed and personally dated by the participant or by the participant's legally acceptable representative, and by the person who conducted the informed consent discussion.

If a participant is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to participant, is read and explained to the participant or the participant's legally acceptable representative, and after the participant or the participant's legally acceptable representative has orally consented to participate in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form.

By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant or the participant's legally acceptable representative, and that informed consent was freely given by the participant or the participant's legally acceptable representative.

Both the informed consent discussion and the written informed consent form and any other written information to be provided to participants should include explanations of the following:

1. That the trial involves research.
2. The purpose of the trial.
3. The trial treatment(s) and the probability for random assignment to each treatment.
4. The trial procedures to be followed, including all invasive procedures.
5. The participant's responsibilities.
6. Those aspects of the trial that are experimental.

7. The reasonably foreseeable risks or inconveniences to the participant and, when applicable, to an embryo, fetus, or nursing infant.
8. The reasonably expected benefits. When there is no intended clinical benefit to the participant, the participant should be made aware of this.
9. The alternative procedure(s) or course(s) of treatment that may be available to the participant, and the important potential benefits and risks.
10. The compensation and/or treatment available to the participant in the event of trial-related injury.
11. The anticipated prorated payment, if any, to the participant for participating in the trial.
12. The anticipated expenses, if any, to the participant for participating in the trial.
13. That the participation in the trial is voluntary and that the participant may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the participant is otherwise entitled.
14. That the Committee or Rwanda FDA will be granted direct access to the participant's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the participant, by signing a written informed consent form, the participant or the participant's legally acceptable representative is authorizing such access.
15. That the records identifying the participant will be kept confidential and will not be made publicly available. If the results of the trial are published, the participant's identity will remain confidential.
16. That the participant or the participant's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the participant's willingness to continue participating in the trial.
17. The person(s) to contact for further information regarding the trial and the rights of trial participants, and whom to contact in the event of trial- related injury.
18. The foreseeable circumstances and/or reasons under which the participation in the trial may be terminated.
19. The expected duration of participating in the trial.
20. The approximate number of participants involved in the trial.
21. Prior to participation in the trial, the participant or the participant's legally acceptable representative should receive a copy of the signed and dated written informed consent form and any other written information provided to the participants. During participation in the trial, the participant or the participant's legally acceptable representative should receive a copy of the signed and dated consent

form updates and a copy of any amendments to the written information provided to participants.

22. When a clinical trial includes participants who can only be enrolled in the trial with the consent of the participant's legally acceptable representative (e.g., minors, or patients with a severe mental health condition), the participant should be informed about the trial to the extent compatible with the participant's understanding and, if capable, the participant should sign and personally date the written informed consent.

In emergency situations, when prior consent of the participant is not possible, the consent of the participant's legally acceptable representative, if present, should be requested. When prior consent of the participant is not possible, and the participant's legally acceptable representative is not available, enrolment of the participant should require measures described in the protocol and/or elsewhere, with documented Committee approval to protect the rights, safety and well-being of the participant and to ensure compliance with the Committee requirements. The participant or the participant's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate should be requested.

35.4 Approval of Clinical Trials by Local Institutional Review Boards (IRBs)

The Local Institutional Review Boards (IRBs) are ethical review bodies established by a respective academic or healthcare facility within the facility approved, accredited and recognized by the Committee (RNEC), to ensure that in-house non-clinical research that falls within the powers of the IRB is conducted in an ethical manner.

35.5 Key Roles of Local IRBs in Clinical Trial Research

Local IRBs are tasked to monitor the implementation of clinical trials approved by the Committee. The local IRBs, in particular undertake the following:

1. Ensure that the rights and safety of research participants are respected at the clinical research site,
2. Ensure that documents provided by the sponsor or CRO of a given clinical trial comply with the documents approved by RNEC,
3. identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research;

4. determine that the risks will be minimized to the extent possible;
5. identify the probable benefits to be derived from the research;
6. determine that the risks are reasonable in relation to the benefits to subjects, if any, and the importance of the knowledge to be gained;
7. assure that potential subjects will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits; and
8. determine intervals of periodic review, and, where appropriate, ensure that adequate provisions are in place for monitoring the data collected;
9. monitor site of clinical trial(s) of the academic or healthcare facility research,
10. determine the adequacy of the provisions to protect the privacy of subjects and to maintain the confidentiality of the data,
11. Upon successful accreditation by the Committee, a local IRB may request the Committee for ethical review of clinical trials,
12. where the subjects are likely to be members of a vulnerable population (e.g., mentally disabled, fetus or pregnant women, prisoners, or children), determine that appropriate additional safeguards are in place to protect the rights and welfare of these subjects.
13. Establish internal rules and regulations governing the functioning and code of conduct of the IRB.
14. Regularly provide written reports to the Committee on the progress of the Clinical Trial using the approved format.

35.6 IRB Requirements and guidance for informed consent in clinical research

Informed consent is at the heart of ethical research. Informed consent is a process by which a subject voluntarily confirms willingness to take part in clinical research, after having been informed of all aspects relevant to their decision to participate. It is freely given and each participant should be fully informed, must be obtained from every participant, unless they are incapacitated.

Written and verbal versions of the information will be presented to the subject detailing no less than:

1. the exact nature of the research
2. the implications and constraints of the protocol
3. the known side effects and any risks involved
4. the fact that they are free to withdraw from the trial at any time for any reason without prejudice to future care, and with no obligation to give the reason for withdrawal.

A written participant information sheet must have the approval of a RNEC. Participants must be allowed as much time as needed to consider the information, and to question the investigator, their medical professional(s) or

other independent parties. Consent will be documented on a consent form also approved by the RNEC, which is signed and dated by the participant and the person who presented informed consent. A copy of the signed form will be given to the subject.

Persons taking informed consent must be appropriately trained and authorised to do so by the/principal investigator. The research team should be aware that the participant information sheet should, at all times, reflect the full information available for the research. Any new information should be promptly addressed in an amendment, then submitted to the RNEC, and the Rwanda FDA– where applicable.

35.7 Consent involving Incapacitated Participants

Adult incapacitated participants are allowed for inclusion in clinical trial so long as:

1. consent is given by a legal representative on behalf of the participant;
2. the trial relates directly to the condition from which the participant suffers; and
3. the benefits outweigh the risks, or produce no risk at all.

Inclusion of incapacitated adults in emergency research without consent is permitted under the following circumstances:

1. treatment is required urgently;
2. the nature of the trial is such that urgent action is essential (e.g. clinical trials in emergency care settings);
3. obtaining consent from a legal representative is not reasonably practicable; and
4. The Committee has given approval.

35.8 Joint Roles of RNEC and Rwanda Food and Drug Authority in Clinical Trial Approval process

Apart from where these Guidelines explicitly state the joint roles of regulatory bodies in the management of clinical trials the Rwanda FDA has powers to regulate clinical trials as stated under Law No 003/2018 Of 09/02/2018 Establishing Rwanda Food and Drugs Authority and Determining Its Mission, Organisation Functioning, and the Guidelines.

Dr. Jean Baptiste MAZARATI
Chairperson,
Rwanda National Ethics Committee

36 GLOSSARY OF TERMS AND DEFINITIONS

1. **Active Study Files**
   Supporting and approved documents, records containing communications, and reports that correspond to each active (current) study approved by the Committee.
2. **Advantage/Benefit:**
   An element that has a positive influence on the interests or wellbeing of an individual or group.
3. **Adverse Drug Reaction (ADR)**
   In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase responses to a medicinal product means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.
   Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function.

4. **Adverse Event(AE)**

An untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.

An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product.

5. **Amendment**

Text describing one or more substantial changes to a protocol, signed by the researcher and the promoter, and which must be approved by the Ethics Committee before being implemented. All amendments must be drafted in coordination with the promoter. In multicentric studies, amendments must be applied at all centers.

6. **Amendment protocol package**

A package of the amended parts and related documents of the protocol, previously approved by the IEC/IRB, but later decided to make changes after the study had been carried for some time.

7. **Applicable Regulatory requirement(s)**

Any law(s) and regulation(s) addressing the conduct of clinical trials of investigational products.

8. **Application Assessment Form**

An official record that documents the protocol review process.

9. **Approval (in relation to IRB/EC**

The affirmative decision of the IRB/EC that the clinical trial has been reviewed and may be conducted(at the institution site) within the constraints set forth by the IRB/EC, the institution, Good Clinical Practice (GCP), and the applicable regulatory requirements.

10. **Approval of the addendum**

The secretariat brings the proposal to the meeting to be deliberated at the Committee meeting.

11. **Aptitude**

The ability of an individual or group to make an informed decision in accordance with his/her fundamental values.

12. **Audit**

A systematic and independent examination of research trial related activities and documents to determine whether the review and approval activities were conducted, and the data were recorded, analyzed and accurately reported according to the protocol, SOPs, Good clinical

practice(GCP), Declaration of Helsinki and applicable regulatory requirements.

13. **Autonomy:** The capacity to determine one's own rules.

14. **Autonomy (principle of):** The right to exercise the capacity to determine one's own rules.

15. **Biomedical research**
    Any trial or experiment organized and performed on human beings for the purpose of
    increasing biological or medical knowledge.

16. **Biopsy**
    Removal from a living patient or animal of an organ, tissue or tumor fragment in order to perform a histological examination (microscopic analysis of the appearance of the cells, their chemical and functional properties). Can be performed under local anesthesia.

17. **Case Report Form (CRF)**
    A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject.

18. **Chairperson**
    A member of the Committee presiding over a meeting. He/she is responsible for expedited approvals on behalf of the Committee.

19. **Clinical trial/Study**
    Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.

20. **Compliance**

Correspond to the general attitude of a patient during a trial. Among other things, this consists of strictly adhering to the recommendations on visits and taking medications.

21. Confidentiality

Keeping private information secret. In the field of research, confidentiality requires a mechanism for managing personal information. Prevention of disclosure, to other than authorized individuals, of Committee information and documents.

22. Conflict of interest

Subordination of a person's professional judgment to his/her private or personal interests (e.g. financial gain or backer interest).

A situation in which a person, such as a public official, an employee, or a professional, has a private or personal interest sufficient to appear to influence the objective exercise of his or her official duties. There are three key elements in this definition: financial interest; official duties; professional interest. A conflict of interest occurs when:

1. An individual's private interest differs from his or her professional obligations to the institute.
2. Professional actions or decisions occur that an independent observer might reasonably question.
3. A conflict depends upon situation and not on the character or actions of the individual.

Potential conflicts of interest must be disclosed and managed as per policy. To guarantee that a committee is independent of the researchers or promoters and to avoid any conflict of interest, every committee member having special or particular interests, either direct or indirect, in a proposal must recuse himself from evaluating the proposal if the interests in question risk skewing his impartiality. Committee members must comply with the same interest disclosure requirements as medical and scientific research personnel with regard to their financial interests or anything else that could be interpreted as generating a conflict of interest.

One concrete way to avoid the appearance of conflict of interest is to require the Committee members to make a declaration of potential conflicts of interest. Any member making a declaration of this type must then recuse himself, if the

circumstances clearly require it, either at the member's own discretion or the request of the other members. Before recusing himself, the member in question must be authorized to formulate comments on the protocol or answer questions from other members.

23. Deviation

Any instance in which the current guidelines approved by the Committee cannot be or has not been followed.

24. Document/Documentation

All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records, and scans, X-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken.

25. Double blind

The volunteers participating in a double blind trial are randomly divided into different groups (one group receives the experimental drug, another a placebo or the same experimental drug but at a different dosage, or even a control treatment). Neither the volunteer nor the physician monitoring him during the study knows to which group he has randomly been assigned, but this can be found out by lifting the blind in the event of a problem.

26. Expedited approval

A Committee's approval granted only by the Chairperson of the Committee or designated member for minor changes to current approved research activities and for research, which involves no more risk than minimal risk.

27. Expedited review

A review process by only a few designated Committee members who then report the decision to the full Committee meeting. An expedited review is a speedy review for minor changes to the protocol and for research that pose minimal risk to participants.

28. Final Report

An obligatory review of study activities presented as a written report to the Committee after the last subject has completed all visits and all adverse experiences have been brought to appropriate resolution.

29. GCP (Good Clinical Practice)

A standard concerning the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides

assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

30. Guideline

Advice or information given to perform various tasks.

31. Inactive study files

Supporting and approved documents (protocols, protocol amendments, informed consents, advertisements, investigator and site information), records containing communications and correspondence with the investigator, and reports (including but not limited to Continuing Review Reports, IND Safety Reports, reports of injuries to participants, scientific evaluations) that correspond to each study approved by the RNEC for which a final report has been reviewed and accepted.

32. Independent consultant

An expert who gives advice, comments and suggestion upon review of the study protocols with no affiliation to the institutes or investigators proposing the research protocols.

33. Informed consent

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

34. Inspection

The act by a regulatory authority of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authorities to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organization's (CRO) facilities, Office of Ethics Committees, or at other establishments deemed appropriate by the regulatory authorities.

35. Investigating files

A file keeping research Protocols that are under investigating or on-going study.

36. Investigational Medical Device

A medical device, which, is the object of clinical research to determine its safety or effectiveness.

37. Investigational New Drug

Investigational new drug means a new drug, antibiotic drug, or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms "investigational drug" and "investigational new drug" are deemed to be synonymous for purposes of this part.

38. Medical Device

A medical device is any health care product that does not achieve any of its intended purposes by chemical action or by being metabolized. Medical devices include items such as diagnostic test kids, crutches, electrodes, prescribed beds, pacemakers, arterial grafts, intraocular lenses, and orthopaedic pins. Medical devices also include diagnostic aids such as reagents and test kids for in vitro diagnosis of disease and other conditions, for example, pregnancy.

39. Minutes

The official record of events, activities, and actions taken on agenda items presented to a duly constituted (quorum present) RNEC meeting. The minutes identify fully each protocol and/or activity and record the outcomes of each voting action. RNEC votes separately on each collective set or each item submitted for review: protocol, consent form, investigator, and advertisement(s). The record notes the number for, number against, the number of abstaining votes, and the reason for the abstention(s), without identifying the individual members' names.

40. Monitoring

Overseeing that a clinical study progresses properly, in accordance with the protocol, any amendments there may be, the GCPs and regulatory and legal requirements. This includes in particular:

• Verifying that complete, readable and coherent data is collected, which conforms with the source documents.

• Checking informed consent forms and the researcher's file (all documents relating to the study and retained by the researcher).

• Tracking serious undesirable events (their occurrence, reporting procedures).

41. Monitoring visit

An action that IEC/IRB or its representatives visit study sites to assess how well the selected investigators and the institutes are conducting researches, taking care of subjects, recording data and reporting their observations, especially serious adverse events found during the studies. Normally monitoring visit shall be arranged in advance with the principal investigators.

42. New Study

A study protocol including the informed consent, investigator's qualifications, information on the drug or device and advertisements (if applicable) presented to the Committee for approval for the first time and not previously approved by this RNEC. This includes re-application for those studies denied approval by RNEC.

43. Non-compliance record

A list containing the identity of investigators who are considered by RNEC to be non-compliant with Rwanda FDA regulations or who fail to respond to the Committee's requests and the incident justifying the reasons for the termination of the study.

44. Non-significant Risk Device (NSR)

A non-significant risk device is an investigational device that does not pose a significant risk.

45. Participants' rights

Recognition of the inherent dignity and of the equal and inalienable rights of all members of the human family is the foundation of freedom, justice and peace in the world. It is essential that Human Rights should be protected by the rule of law.

46. Placebo

An inert substance that has no pharmacological action and looks the same as the product to which it is be compared.

47. Prerequisites

Items of information the knowledge of which is deemed critical prior to initiating a study:

analytic data, galenic data, toxicological data, pharmacokinetic data, pharmacological data, pre-clinical and earlier clinical data. These elements may be presented in the form of a confidential summary, i.e. the researcher's brochure.

48. Principle

The opposite of "rule". Rules and principles are standards that are to inspire decision makers.

They also serve to assess, evaluate or correct actions, directives or procedures. Rules

are absolute: They are either followed or violated. When rules come in conflict, it becomes necessary to look to principles which are more general, more fundamental and more easily applied. Resorting to principles is not a mechanical process to be followed blindly, without maturely thought-out and considered judgment. The value or the weight

afforded to a principle in a given situation is important since nothing can replace wisdom when it comes to applying it to conflict situations. However, principles attract attention to certain fundamental questions that must be examined in critical situations.

49. Privacy

Extent, opportunities and circumstances connected to the desire to share one's intimate details (physical, behavioral or intellectual) with others. Privacy constitutes a zone of exclusivity where persons or groups are sheltered from others.

50. Progress Report

An ongoing review of each investigator's study activities presented as a written report to obtain extended approval for the study from the Committee. Generally, these reports are due annually with Secretariat sending a written notification reminding the investigator of this obligation. More frequent reports may be requested at the discretion of the Committee.

51. Project Manager

Individual responsible for coordinating an investigational study.

52. Promoter

A promoter is the individual or legal entity that takes the initiative in a biomedical study on human beings, and who provides management support and ensures that financing for it is in place. The promoter or his legal representative must be based in the European Community. If more than one person takes the initiative in the same biomedical study, then appoint one individual or legal entity to act as the promoter and assume the relevant obligations.

53. Protocol

A document that describes the objectives, concepts, methodology, statistical notes and

other steps of a trial. Protocols ordinarily provide the context and reason for the trial, but this information can be provided in other documents cited in the protocol.

54. Protocol Amendment

A change to the study protocol during the planning or course of the trial. The amendment is a foreseen change to the study plan that requires formal approval by the sponsor.

55. Quality assurance

A program intended to control and evaluate systematically the various aspects of a project, service or installation in order to ensure compliance with quality standards (quality assurance does not constitute research, even it could call upon individuals and, thereby, be subject to these guidelines.

56. Quorum

Attendance at any convened meeting of RNEC where three of the regular (or alternate) members, including at least one physician and one layperson, is maintained throughout the discussions and voting portions of the meeting.

57. Randomization

From the English word "random" and is the equivalent of drawing lots. The purpose of randomization in a trial is to create two groups of subjects, which can be compared to
determine whether the differences observed between these groups of patients are indeed
attributable to the treatments received.

58. Research

A systematic investigation intended to establish the facts, principles and knowledge that can be generalized.

59. Researcher

The individual (or individuals) who direct and supervise the conduct of the study at a
location is called a researcher.
If the promoter for a biomedical study tasks several researchers with conducting the trial,
either at one or several locations in France, he appoints one of them to act as a coordinator.

60. Respect for others

A notion comprising two fundamental aspects:

- respect for the autonomy of individuals who are able to make informed decisions and
  respect for their free choice, and
- protecting individuals with reduced or restricted autonomy, i.e. those who are unfit or
  incapable of making voluntary decisions.

61. Risk

The concept of risk is viewed here as a function of the significance, probability and nature of disadvantages.

62. Rwanda National Ethics Committee

Independent Research Ethics Review Committee established by a legal instrument that reviews the ethical aspects of research involving human participants.

63. Secondary data use

Use of information collected specifically for other purposes.

64. Serious Adverse Event (SAE) or Serious Adverse Drug reaction (Serious ADR)

Any manifestation resulting in one of the following for a participant in a clinical study:

- Death,
- Immediate threat to life (i.e. outside of any possibility of curative or palliative therapeutic intervention undertaken as soon as the threat is identified)
- Hospitalization or prolongation of existing hospitalization,
- Significant or lasting incapacity or disability/incapacity (clinically significant, temporary or permanent),
- Congenital anomaly or deformation, likely to be tied to the research undertaken.

The adverse event is serious and should be reported when the patient outcome is:

Death - Report if the patient's death is suspected as being a direct outcome of the adverse event.

Life- Threatening -Report if the patient was at substantial risk of dying at the time of the adverse event or it is suspected that the use or continued use of the product would result in the patient's death. *Examples: Pacemaker failure; gastrointestinal hemorrhage; bone marrow suppression; infusion pump failure which permits uncontrolled free flow resulting in excessive drug dosing.*

Hospitalization (initial or prolonged) -Report if admission to the hospital or prolongation of a hospital stay results because of the adverse event. *Examples: Anaphylaxis pseudo membranous colitis or bleeding causing or prolonging hospitalization.*

Disability -Report if the adverse event resulted in a significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life. *Examples: Cerebrovascular accident due to drug-induced hypercoagulability; toxicity,. peripheral neuropathy.*

Congenital Anomaly_-Report if there is suspicions that exposure to a medical product prior to conception or during pregnancy resulted in an adverse outcome in the child. *Examples: Vaginal cancer in female off spring from diethylstilbestrol during pregnancy,' malformation in the offspring caused by thalidomide.*

Requires Intervention to Prevent Permanent Impairment or Damage -Report if suspect that the use of a medical product may result in a condition, which required medical or surgical intervention to preclude permanent impairment or damage to a patient. *Examples.. Acetaminophen overdose-induced hepatotoxicity requiring treatment with acetylcysteine to prevent permanent damage, burns from radiation equipment requiring drug therapy, breakage of a screw requiring replacement of hardware to prevent malunion of a fractured long bone.*

65. Significant Risk Device (SR)

A significant risk device is an investigational device that:

(1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of the subject,

(2) is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of the subject,

(3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impingent of human health and presents a potential for serious risk to the health, safety, or welfare of the subject, or

(4) otherwise presents a potential for serious risk to the health, safety, or welfare of the subject.

66. Site Coordinator

The person at the study site who is responsible for managing the study. This person can also be referred to as a Project Manager.

67. Standard Operating Procedure (SOP)

Detailed, written instructions, in a certain format, describe activities and action undertaken by an organization to achieve uniformity of the performance of a specific function.

68. Versus

Latin word meaning “against” or “opposed to” In a trial, this term means that the product is compared either to a control treatment or a placebo.

69. Vulnerable group

Generally, a group that is susceptible to bodily or moral injury. These groups are described here based on their exposure to this type of injury, for example due to their lack of aptitude, the non-voluntary nature of their decisions or imbalance of power.

70. Vulnerable individuals

Persons whose desire to participate in a clinical trial can be unduly influenced by the hope, either justified or not, to receive benefits from their participation or the belief that there will be reprisals from more influential members of a chain of command if they refuse. Let us mention, for example, members of groups that have a hierarchy, such as those who are studying medicine, pharmacology, dentistry and nursing, junior employees at hospitals or laboratories, employees in the pharmaceuticals industry, members of the armed forces, and inmates. Patients suffering incurable diseases, persons living in homeless shelters, the poor or unemployed, patients facing emergency situations, members of ethnic minorities, the homeless, nomads, refugees, minors as well as individual persons incapable of giving their own consent are also vulnerable subjects.

71. Vulnerable Subjects

Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, and patients in

emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

37 REFERENCES

1. Haskins M. Standard Operating Procedures; Pharma-Ethics Independent Research
   Ethics Committee. South Africa, 2005.
2. Standard Operating Procedures for Ethics Review Committee in Eastern Africa. Dares
   Salaam, 2005.
3. European Directive on bio-ethics 2001/20/EC. Official Diary of the European
   Communities. 2001; L 121/34 to L 121/44
4. Recommendations of the French National Consultative Committee on Ethics;
   CPP of Angers and Tours, 2006.
5. Helsinki Declaration of the World Medical Association. Tokyo, 2004
6. Sobel A. Ethics, AIDS and Society Activity report of the National Council on AIDS,
   Vol. III. Paris, 2000.
7. Operational Guidelines for Ethics Committees tasked with Evaluating Biomedical Research of the WHO/OMS. Geneva, 2000.
8. Haskins M. Standard Operating Procedures; Pharma-Ethics Independent Research
   Ethics Committee. South Africa, 2005.

APPENDIX 01: CONFIDENTIALITY/CONFLICT OF INTEREST AGREEMENT

CONFIDENTIALITY

In recognition of the fact that, member's name, and his/her affiliation herein after referred to as the "undersigned" and as a member of the Committee has been asked and appointed to assess research studies involving human subjects, in order to ensure that the studies are conducted in a humane ethical manner, with highest standard of care according to the applied national local regulations, institutional policies and guidelines;

You have been appointed as a member of the Committee as an individual, not as an advocate or representative of your home province/territory/community or as the delegate of any organization or private interest. Your fundamental duty is to independently review both scientific and ethical aspects of research protocols involving human subjects and make a determination and the best possible objective recommendations, based on the merits of the submissions you review.

The Committee aims to meet the highest ethical standards in order to merit the trust and confidence of the communities' protection of rights and well being of human subjects. As a member of the Committee you are expected to meet the same high standards of ethical behaviour as you carry out your mandate.

This Agreement, encompasses any information deemed confidential or proprietary provided to the Undersigned in conjunction with duties as a member of the Committee. Any written information provided to the undersigned that is of a confidential, proprietary or privileged nature shall be identified accordingly.

As such, the undersigned agrees to hold all confidential or proprietary trade secrets ("information") in trust or confidence and agrees that it shall be used only for contemplated purposes; shall not be used for any other purpose or disclosed to any third party. Written confidential information provided for review shall not be copied or retained, and all confidential information (and any copies and notes thereof) shall remain the sole property of the committee.

The undersigned agrees not to disclose or utilize, directly or indirectly, any confidential or proprietary information belonging to a third party in fulfilling this agreement. Furthermore, the undersigned confirms that his/her performance of this agreement is consistent with the institute's policies and any contractual obligations they may have to third parties.

CONFLICT OF INTEREST

It is a policy of the Committee that no member may participate in the review or approval for activities in which that member has a conflict of interest except to provide information as requested by the Committee.

You shall immediately disclose to the Chairperson of the Committee any actual or potential conflicts of interest that you may have in relation to any particular proposal submitted for review by the Committee and to abstain from any participation in discussions or recommendations in respect of such proposals.

If an applicant submitting a protocol believes that an Committee member has a potential conflict, the investigator may request that the member be excluded from the review of the protocol.

The request must be in writing and addressed to the Chairperson. The request must contain evidence that substantiates the claim that a conflict exists with the member(s) in question. The Committee may elect to investigate the applicant's claim of the potential conflict.

When a member has a conflict of interest, the member should notify the Chairperson and shall not participate in the review or approval of a proposal except to provide information if the Committee requests such. Conflict of interest cases include, for examples:

i) A member is involved in a potentially competing research grant.
ii) Access to funding or intellectual information that may provide an unfair competitive advantage.
iii) Personal biases that may interfere with his or her impartial judgment.

A member or members who may have a conflict of interest may not be counted toward a quorum and may not vote.

Confidentiality and non-disclosure

In the course of your activities as a member of the National Ethics Review Committee, you may be provided with confidential information and documentation (referred to as the "Confidential Information"). You agree to take reasonable measures to protect the Confidential Information: subject to applicable legislation, including the Access to Information Act, not to disclose confidential information to any person; not to use confidential information for any purpose outside the committee, and for any purpose outside the Committee's mandate, and in particular, in a manner which would result in a benefit to yourself or any third party, and to return all confidential information (including any minutes or notes you have made as part of your committee duties) to the Chairperson upon termination of your functions as a committee member.

Please sign and date this agreement, if the undersigned agrees with the terms and conditions set forth above. The original shall be kept in file in the custody of the regularly compliance office. A copy shall be provided for your records.

I (name) …… Address……..
……
Have read and accept the aforementioned terms and conditions as explained in this agreement.

…… ……..
Undersigned Signature Date

…… ……

Compliance Officer Date

APPENDIX 02: GENERAL OUTLINE FOR A STUDY PROTOCOL

Study title, principal collaborators and institutions

Summary of study = synopsis

1. Background
2. Aim and objectives
   2.1. Aims
   2.2 Objectives
3. Methods
   3.1.1.Study description
   3.1.2. Study design
   3.1.3. Study site
   3.1.43. Study population
   3.1.5. Proposed intervention if interventions study
   3.1.6. Main exposures and/or confounders and/or outcomes to be measured

4. Selection of study population
   4.1.Inclusion criteria
   4.2.Exclusion criteria
   4.3.Sampling

4.4.Randomization if randomized trial

5. Study procedures
   5.1.Procedures at enrolment
   5.2.Follow-up if cohort study or trial
   5.3.Measurement of exposures and confounders
   5.4.Measurement of outcomes
   5.5.Laboratory methods if the study has a lab component

   5.6.Sample size
   5.7.Data Management
   5.8.Proposed analysis

6. Ethical considerations
   6.1.Confidentiality
   6.2. Informed consent
   6.3. Ethical approval
7. Logistics
   7.1. Distribution of responsibilities
   7.2. Timetable
   7.3 Budget
8. References
9. Appendices

APPENDIX 03: INFORMED CONSENT

Basic Principles of Informed Consent

Four overriding principles which are meant to apply to all consents, unless there are specific exceptions made or allowed elsewhere in the regulations.

These principles are:

1. Human research can proceed only with informed consent

No investigator may involve a human being as a participant in research without legally effective informed consent of the participant or his/her legally authorized representative.

2. Minimize coercion in obtaining consent

An investigator shall seek consent under conditions that provide the prospective participant or his/her representative sufficient opportunity to

consider whether to participate, and that minimize the possibility of coercion or undue influence.

3. Consent must involve understandable language

The information that is given to the prospective participant or his/her representative shall be in language the participant or the representative can understand.

4. Waiver of rights is prohibited in the consent process

No informed consent, whether oral or written, may include any exculpatory language through which the prospective participant or his/her representative is made to waive or appear to waive any of the prospective participant's legal rights, or made to release or appear to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

Required Elements of Informed Consent

1. Purpose and Procedures

You must tell a prospective participant that the study involves research, explain the purpose of the study and the length of time you expect the person to participate, describe the procedures to be followed, and identify any experimental procedures.

2. Risks and/or Discomforts

You must describe any reasonably foreseeable risks or discomforts to the prospective participant.

3. Benefits

You must describe any benefits to the prospective participant or to others which may reasonably be expected from the research.

4. Alternatives

You must disclose any appropriate alternative procedures or courses of treatment that might benefit the prospective participant.

5. Confidentiality

You must tell prospective participants whether their records will be kept confidential and, if so, explain the level of confidentiality.

6. When there is Greater than Minimal Risk[1]

You must tell prospective participants whether they will receive any compensation and/or medical treatments if injury occurs and, if so, what compensation or treatment will consist of, or where to obtain further information.

7. Persons to Contact (Telephone number)

You must tell prospective participants whom to contact if they have questions about the research and their rights as a study participant, and whom to contact if they have an injury that may be related to the research.

8. Voluntary Participation, Refusal, and Withdrawal

You must state that participation is voluntary, that refusal to participate involves no penalty or loss of benefits to which the person is otherwise entitled, and that the person may discontinue participation at any time without penalty.

---

*1 Minimal risk means that the **probability and magnitude** of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. Both factors must be considered in weighing whether a risk is greater than "minimal risk." In deciding if research involves minimal risk, the IRB/IEC is expected to consider risk from study procedures in relation to all persons eligible to participate--not just from the perspective of a person in good health or of someone with health problems matching circumstances of the research.*

Additional Elements of Consent

When appropriate, the following six additional elements of consent should be included:

1. Unforeseeable Risk - You should state that the study treatment or procedures may have risks

for the prospective participant (or to the embryo or foetus, if the participant is or may become

pregnant) that you cannot currently foresee.

2**. Termination of Participation Without Consent**

You should explain anticipated circumstances under which the investigator may terminate the participant's further involvement without regard to the person's consent.

3. Additional Costs / compensation

You should describe any additional costs/ compensation to prospective participants that may result from participation in the study.

4. Consequences and Process of Withdrawal

You should explain how participants can leave the study and what may happen if they choose to withdraw.

5. Impact of Significant New Findings

You should state that participants will be told of any significant new findings developed during the research which may relate to their willingness to continue in the study.

6. Number of Participants

You should tell prospective participants the approximate number of persons involved in the study

Example of PATIENT INFORMATION AND INFORMED CONSENT FORM

Protocol Nr.:……
Protocol Title:……

Dear Participant

You have been invited to take part in a research project with ……

Before joining the project in question, you need to read this information form, since it contains important information to assist you in deciding whether or not signing up to participate is in your best interests. We request that you ask as many questions as you wish in order to make sure that you understand the procedures for the study, the risks and benefits. If you have a question about this document that has not been sufficiently answered or explained, do not hesitate to ask one of the research team members for more information.

The study has been approved by the Ethics Committee and the Council of the National

Medical Association since it complies with medical ethics standards. Additionally, the trial will be conducted in accordance with the Helsinki Declaration and the Guide on Best Clinical Practices.
The study physician will be paid by the sponsor for conducting the clinical trial.
Your participation in this trial is voluntary. You may choose not to participate in the study or to leave it at any time simply by informing the study physician. If you decide not to participate in the study or to retract your consent, you will not lose any advantage that you would be due.

1. Goal of the Study
The goal of this study is to……
The treatment provided in this trial has/has not been approved by the Council of the National
Medical Association or other regulatory authorities.
Approximately……participants will be included in this trial, of which ….. will be in Rwanda.
The period planned for you to participate is……..

2. Context of the Study
During this study, you will be randomized into groups to receive (described the randomization procedure, if necessary)…….. **A placebo is a substance that has no active treatment**
Ingredient. Neither you nor the study physician will know which treatment you have
received. **However, this can be determined in case of emergency.**

3. The Study Procedure
In order to determine whether you are eligible to enter this study, you must meet these
conditions (briefly described the inclusion procedures; **amounts of blood samples to be**
taken must be shown in milliliters)
If you satisfy the inclusion criteria and you agree to participate in this trial, we ask that you follow the procedures below: (give short description of the procedures for each center. Amounts of blood samples to be taken must be shown in milliliters).
In order for this study to be successful, it is important that you cooperate fully with the study physician and follow his/her instructions exactly. Do not take

any other type of treatment (traditional, herbal, etc.) without notifying the study physician in advance.

4. What are the potential risks or inconveniences of being in the study?

Here you must mention the risks from the experimental product, control treatment with a
placebo and any other invasive method. The inconveniences from filling out questionnaires are also to be added.

You must inform the study physician as soon as you notice any negative effect, injury or
complication that may be linked to the treatment in the study.

The state of your health could remain unchanged by participating in this study, or it could be altered. There can also be as yet unknown risks from using experimental treatment. You will be informed of any significant new development that could impact the continuity of this study.

Risks for women of childbearing age

The treatment provided during the trial could affect a fetus or breastfeeding of infants.

Therefore, you are not eligible to participate in the study if you are pregnant, are breastfeeding or expecting to become pregnant. Women of childbearing age must take a pregnancy test. If you are capable of having a child, you must use these birth control methods for the duration of your participation in the study…. (Specify the period) and at the end of the study: Specify the acceptable forms of contraception.

If necessary: If you are a male participant and have a spouse of childbearing age, you and/or your partner must agree to use the birth control measures shown above.

If you become pregnant during the study, you must terminate experimental treatment and
notify the study physician immediately. The study physician will provide you advice suitable to your situation and future medical care for the baby.

5. What are the possible benefits of participating in a clinical trial?

Your state of health could be improved by your participation in the study, however this cannot be guaranteed. If the experimental treatment is not effective of if you have received a placebo, there will not be any benefit to you. The information obtained from this trial could be useful in eventually discovering an effective treatment.

The close medical attention you will receive while participating in the trial will enable you to obtain more information about the state of your health. The experimental treatment, as well as the laboratory exams and other procedures related to the study, such as those described in the protocol, will be administered at no cost to you or your health insurance company.

6. Alternative Treatments

Instead of participating in the study, you may elect to take the normal treatment for your
condition. The researcher will discuss with you the benefits and risks of these standard
treatments. You are not obliged to participate in this clinical trial in order to receive care and treatment for your condition.

7. Compensation in case of an incident/injury from the trial

The sponsor undertakes to pay all reasonable medical expenses if an incident or injury should occur, which directly stems from participating in the trial. It is recommended that the sponsor of the clinical trial, without any other form of proceedings, pay the compensation without your having to prove fault for any injury directly resulting from administering experimental treatment or other procedures performed in accordance with the protocol for this study.

The sponsor will not be liable for any loss, injury and/or damage resulting from:

• Use of any other medication during the study,

• Any injury caused by departing from the study protocol, study requirements and/or any other instruction or indication given by the study physician

• Any injury resulting from an act or omission by a third party to effectively produce an undesirable event or a reaction to the experimental treatment,

• Any injury stemming from negligence on your part.

Your right to claim compensation for injury due to negligence, which you can prove, will not be affected.

8. Confidentiality

All documents that identify you will be held in the strictest confidence and will not be
released to the public. The physician and research team will use **your personal information** to perform the study.

This information may include your name, address, medical history, and data from your medical consultations. However, this information will not be entered into the study data sent to the sponsor or his representatives. You will be

identified by a code number in each report for publication produced based on this study.
In order to ensure that the study data collected about you are correct and truly relate to you, a group of hand-picked individuals who work for the sponsor, as well as representatives of governmental regulatory agencies, and members of the Ethics Committee will have access to your personal information at the research center. These persons will be required to keep this information confidential. By signing this document, you are permitting this access.
The sponsor or his representatives may use the data from the study, which are sent to them, for the following purposes:

- To see if the experimental treatment is working properly
- To compare the experimental treatment with other treatments
- For other activities related to the treatment being studies.
- You have the right to demand that the study physician allow you to view the personal
  data collected on you and make any corrections to it, which may be necessary.

9. Payment, expenses and costs

You will not receive any salary for participating in this study.
The sponsor will pay the costs of the experimental treatment, supplemental examinations and procedures specified in the protocol. Neither you nor your health insurance will pay these expenses.
The sponsor has made provisions to pay for the expense of traveling to a center and other
expenses related to participating in the study. You will receive the amount of …..per
consultation. If your study-related expenses exceed the amount specified above and you have receipts for these expenses, you may discuss this with the study physician.

10. End of participation in the study

Your participation in the study can be terminated for any of the following reasons:

- You do not follow the research physician's instructions,
- You do not take the research treatment as prescribed,
- The research physician decides termination is in your best interests,
- There are insufficient participants in the study or the number of participants planned
  is already reached,

- The sponsor or research center terminates the study for unspecified reasons.
- The sponsor disbands the group you are in for an unspecified reason.

11. Contacts for answers relating to research, your rights in the event of incident

The study:

Injuries related to the study:

Your rights as a participant in the research:

If you have any questions about this trial/study, you will have to discuss it with the research physician at …(telephone number)

If you have a question about your rights as a research volunteer you should contact the Chairperson of the Ethics Committee at …(tel number) or the secretary of the ethics Committee (put names and telephone number).

12. Statement of consent

By signing the above, I acknowledge that:

- I have read the information sheet and consent form, version ..... for this study,
- I had the opportunity to ask questions and the answers were satisfactory for me,
- I took time to discuss this information with others and to decide to take part or not,
- I will receive a dated and signed copy of the consent form,
- I agree to take part in this study.

.....

Name of the subject (in capital letters)

....

Signature of the subject Date

.....

Name of the legal representative (in capital letters)

....

Signature of the legal representative Date

.....

Name of the person requiring the consent (If not the researcher)

....

Name of the researcher (in capital letters) Date

....

Signature of the Researcher Date

.....

Name of the witness (in capital letters)

…… ……

Signature of the witness Date

APPENDIX 04: PARENTAL CONSENT – QUALITATIVE STUDY

SAMPLE OF INFORMED CONSENT FORM (WHO template)

For use with: Participant Observation, Focus Group Discussions (FGD), Interviews, and Surveys

(Language used throughout form should be at the level of a local student of class 6th/ 8th)

Notes to Researchers:

1. Please note that this is a template developed by WHO ERC to assist the Principal Investigator in the design of their informed consent forms (ICF). It is important that Principal Investigators adapt their own ICFs to the outline and requirements of their Particular study. **The logo of the collaborating institution must be used on the ICF and not the WHO logo.**
2. Do not be concerned by the length of this template. It is long only because it contains guidance and explanations which are for you and which you will not include in the informed consent forms that you develop and provide to participants in your research.
3. In this template:
   - Square brackets indicate where specific information is to be inserted
   - Bold lettering indicates sections or wording which should be included
   - Standard lettering is used for explanations to researchers only and must not be included in your consent forms
   - Italics are used to provide examples of phrasing.

These are only examples. Researchers should use wording which provides the best information about their particular research project and which is most appropriate to their research population.

Informed Consent Template for Research Involving Children (Qualitative Studies)

Research Ethics Review Committee (WHO ERC)

[Informed Consent Form for _____]

Name the group of individuals for whom this consent is written. Because research for a single project is often carried out with a number of different groups of individuals - for example healthcare workers, patients, and parents of patients - it is important that you identify which group this particular consent is for.

Example: This informed consent form is for parents of adolescent girls and boys participating in the research titled, "What do we want: Adolescents and health systems."

[Name of Principle Investigator]
[Name of Organization]
[Name of Sponsor]
[Name of Project and Version]

This Informed Consent Form has two parts:

- **Information Sheet (to share information about the study with you)**
- **Certificate of Consent (for signatures if you agree that your child may participate)**

You will be given a copy of the full Informed Consent Form

Part I: Information Sheet

Introduction

Briefly state who you are and explain that you are inviting them to have their child participate in research which you are doing. Inform them that may talk to anyone they feel comfortable talking with about the research and that they can take time to reflect on whether they want their child to participate or not. Assure the parent that if they do not understand some of the words or concepts, that you will take time to explain them as you go along and that they may ask questions now or later.

Example: I am X, and I work at Y organization in _____. I am doing some research which might help your clinic/hospital do more to help teenagers become and stay healthier. In our research we will talk to many teenagers, both girls and boys, and ask them a number of questions.

Whenever researchers study children, we talk to the parents and ask them for their permission.

After you have heard more about the study, and if you agree, then the next thing I will do is ask your daughter/son for their agreement as well. Both of you have to agree independently before I can begin.
You do not have to decide today whether or not you agree to have your child participate in this research. Before you decide, you can talk to anyone you feel comfortable with.
There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me or of another researcher.
[YOUR INSTITUTIONAL LETTERHEAD]
Please do not submit consent forms on the WHO letterhead

Purpose

Explain in lay terms why the research is being done and what is expected from the results.
Explain why you need to conduct the research with children.
Example: It is possible that the clinics and the hospital in this region are not providing some of the services that are important for teenagers. In this study we will talk to teenage girls and boys about what they know about caring for their bodies in a healthy way including sexual and reproductive health. We will invite them to share their knowledge and understanding with us so that we can find ways of meeting their needs at the local clinics and hospital.

Type of Research Intervention

Briefly state the intervention. This will be expanded upon in the procedures section.
Example: A questionnaire OR a focus group OR an interview

Selection of Participants

State clearly why you have chosen their child to participate in this study. Parents may wonder why their children have been chosen for a study and may be fearful, confused or concerned.
Example: We want to talk to many teenagers about their health and what information or services they want for themselves. One part of health that we want to talk to them about is sexuality. We would like to ask your daughter/son to participate because she/he is a teenager and lives in this region.

Voluntary Participation

Indicate clearly that they can choose for their child to participate or not and reassure they will still receive all the services they usually do if they choose not to participate. Also inform them that their child will also have input into the decision. This can be repeated and expanded upon later in the form as well. It is important to state clearly at the beginning of the form that participation is

voluntary so that the other information can be heard in this context. Participants may also be more alert at the beginning.

Example:You do not have to agree that your daughter/son can talk to us. You can choose to say no and any services that you and your family receive at this centre will not change. We know that the decision can be difficult when it involves your children. And, it can be especially hard when the research includes sensitive topics like sexuality. You can ask as many questions as you like and we take the time to answer them. You don't have to decide today. You can think about it and tell me what you decide later.

Protocol

Explain what each of the steps or procedures involves. Indicate when the research will take place and where. If there are surveys, indicate where and how the surveys will be collected and distributed.

1) The following applies only to focus group discussions*:*

Example: Your daughter/son will take part in a discussion with 7-8 other teenagers, or

a mix of teenagers and social service workers from the community. The girls and boys

will be in separate groups. This discussion will be guided by[give name of moderator]

or me.

2) The following applies only to interviews*:*

Example: Your daughter/son will participate in an interview with [name of interviewer] or myself.

3) The following applies only to questionnaire surveys*:*

Example: Your daughter/son will fill out a questionnaire which will be provided by

[name of distributor of blank questionnaires] and collected by [name of collector of

*completed questionnaires].**OR** the questionnaire can be read aloud and she/he can*

give me the answer which she/he wants me to write.

Explain the type of questions that the participants are likely to be asked in the focus group discussion, interview or in the questionnaire. If the questions are sensitive, acknowledge this, try to anticipate parents' concerns and protective responses, and address these. Parents may be concerned that talking about sexuality may encourage sexual behavior. Other concerns may include disbelief that their child is ready to talk about sexuality, or parents may be personally embarrassed.

1) The following applies only to focus group discussions:

Example: The group discussion will start with me, or the focus group guide (use the

local word for group discussion leader), making sure that the participants are

comfortable. We will also answer questions about the research that they might have.

Then we will ask questions about the health system in this community. We will talk

about where they go for information about health, and whether they get the

information and services they need and want. We will encourage them to talk about

sexual and reproductive health as well as other important health topics such as food

and nutrition. These are the types of questions we will ask. We will not ask them to

share personal stories or anything that they are not comfortable sharing.

The discussion will take place in [location of the FGD], and no one else but the people who take part in the discussion and the guide or I will be present during this discussion. The entire discussion will be tape-recorded, but no-one will be identified by name on the tape. The tape will be kept [explain how the tape will be stored]. The information recorded is confidential, and no one else except [name of person(s) with access to the tapes] will be allowed to listen to the tapes. [The tapes will be destroyed after ____period of time.]

2) The following applies only to interviews:

Example: If your daughter does not wish to answer any of the questions during the

interview, she may say so and the interviewer will move on to the next question. The

interview will take place in [location of the interview], and no one else but the

interviewer will be present unless your child asks for someone else to be there. The

information recorded is confidential, and no one else except [name of person(s) with

access to the information] will have access to the information documented during your

interview.) [The tapes will be destroyed after _____period of time.]

3) The following applies only to questionnaires and surveys:

Example: If your daughter/son does not wish to answer some of the questions included

in the questionnaire, she/he may skip them and move on to the next question. The

information recorded is confidential, and no one else except [name of person(s) with

access to the information] will have access to her questionnaire. [The questionnaires

will be destroyed after _____period of time.]

Duration

Include a statement about the time commitments of the study for the child and any time commitments on the part of the parent(s). Include both the duration of the study and follow-up, if relevant.

Example: We are asking your child to participate in an interview which will take about 1 hour of her/his time. We can do this outside of school/work hours. There is also a questionnaire that we will either provide to your child or which we will do together with her/him. This also takes about an hour.

Altogether, we are asking for about 2 hours of your child's time.

Risks and Discomforts

Explain any risks or discomforts including any limits to confidentiality.

Example: There is a slight risk that your son/daughter may share some personal or confidential information by chance or that he/she may feel uncomfortable talking about some of the topics.

However, we do not wish this to happen, and he/she may refuse to answer any question or not take part in a portion of the discussion/interview/questionnaire if he/she feels the question(s) are too personal or if talking about them makes him/her uncomfortable.

Your daughter/son may choose to tell you about the interview and the questionnaire but she does not have to do this. We will not be sharing with you either the questions we ask or the responses given to us by your child.

Benefits

Describe any benefits to their child, to the community, or any benefits which are expected in the future as a result of the research.

Example: There will be no immediate and direct benefit to your child or to you, but your child's participation is likely to help us find out more about the health needs of teenage girls and boys and we hope that these will help the local clinics and hospitals to meet those needs better in the future.

Incentives

State clearly what you will provide the participants with as a result of their participation. WHO does not encourage incentives beyond reimbursements for expenses incurred as a result of participation in research. The expenses may include, for example, travel expenses and reimbursement for time lost. The amount should be determined within the host country context.

Example: Your daughter/son will not be provided with any payment to take part in the research.
However, she/he will be given with [provide a figure, if money is involved] for her/his time, and travel expense (if applicable).

Confidentiality:

Explain how the research team will maintain the confidentiality of data, especially with respect to the information about the participant. Outline any limits there are to confidentiality. Note that with focus groups confidentiality cannot be guaranteed because what is said within the group becomes common knowledge. Participants can be asked not to share outside of the group but this does not guarantee confidentiality.

Example: Because something out of the ordinary is being done through research in your community, it will draw attention. If your daughter/son participates, she and you may be asked questions by other people in the community.
We will not be sharing information about your son or daughter outside of the research team. The information that we collect from this research project will be kept confidential. Information about your child that will be collected from the research will be put away and no-one but the researchers will be able to see it. Any information about your child will have a number on it instead of his/her name. Only the researchers will know what his/her number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except [name who will have access to the information, such as research sponsors, DSMB board, your clinician, etc].

The following applies to focus groups*:*
Example: We will ask your child and others in the group not to talk to people outside the group about what was said in the group. We will, in other words, ask each participant to keep what was said in the group confidential. You should know, however, that we cannot stop or prevent participants who were in the group from sharing things that should be confidential.

Sharing of Research Findings

Include a statement indicating that the research findings will be shared in a timely fashion but that confidential information will remain confidential. If you have a plan and timeline for the sharing of information, include the details. Also inform the parent that the research findings will be shared more broadly, for examples, through publications and conferences.

Example: At the end of the study, we will be sharing what we have learnt with the participants and with the community. We will do this by meeting first with the participants and then with the larger community. A written report will also be given to the participants whom they can share with their families. We will also

publish the results in order that other interested people may learn from our research.

Right to refuse or withdraw

Explain again the voluntary nature of consent. Also explain that their child will be asked to agree - or assent - and that the child's concerns and wishes will be taken very seriously.

Example: You may choose not to have your child participate in this study and your child does not have to take part in this research if she/he does not wish to do so. Choosing to participate or not will not affect either your own or your child's future treatment at the Centre here in any way. You and your child will still have all the benefits that would otherwise be available at this Centre.

Your child may stop participating in the discussion/interview at any time that you or she/he wish without either of you losing any of your rights here.

Who to Contact

Provide the name and contact information of someone who is involved, informed and accessible (a local person who can actually be contacted. State also that the proposal has been approved and how.

Example: If you have any questions you may ask them now or later, even after the study has started.

If you wish to ask questions later, you may contact any of the following: [name, address/telephone number/e-mail]

This proposal has been reviewed and approved by [name of the IRB], which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find about more about the IRB, contact [name, address, and telephone number.]

PART II: Certificate of Consent

Certificate of Consent

This section can be written in the first person. It should include a few brief statements about the research and be followed by a statement similar to the one in bold below. If the participant is illiterate but gives oral consent a witness must sign. A researcher or the person going over the informed consent must sign each consent. Because the certificate is an integral part of the information sheet and not a stand-alone document, the layout or design of the form should reflect this.

Example: I have been asked to give consent for my daughter/son to participate in this research study which will involve her completing one interview and one questionnaire .I understand that she/he will also be asked to give permission and that her/his wishes will be respected. I have been informed that the risks

are minimal and may include only _____. I am aware that there may be no benefit to either my child or me personally and that we will not be compensated beyond travel expenses. I have been provided with the name of a researcher who can be easily contacted using the number I was given for that person.

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily for my child to participate as a participant in this study and understand that I have the right to withdraw her/him from the study at any time without in any way affecting our care at this Centre.

Print Name of Parent or Guardian _____

Signature of Parent of Guardian_____

Date _____

Day/month/year

If illiterate

A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness_____ AND Thumb print of participant

Signature of witness _____

Date _____

Day/month/year

I have accurately read or witnessed the accurate reading of the consent form to the parent/guardian of the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of researcher_____

Signature of researcher _____

Date _____

Day/month/year

A copy of this Informed Consent Form has been provided to the parent or guardian of the participant ____ (initialed by researcher/assistant)

An Informed Assent Form will ____ OR will not ____ be completed.

APPENDIX 05: SAMPLE OF INFORMED ASSENT FORM FOR CHILDREN

An Informed Assent Form does not replace a consent form signed by parents or guardians. The assent is ***in addition to*** the consent and signals the child's willing cooperation in the study.

[Informed Assent Form for _____]

Name the group of individuals for whom this assent is written.
Explanation
Example
[Name of Principle Investigator]
[Name of Organization]
[Name of Sponsor]
[Name of Project and Version]
This Informed Assent Form has two parts:

- **Information Sheet (gives you information about the study)**
- **Certificate of Assent (this is where you sign if you agree to participate)**

You will be given a copy of the full Informed Assent Form
Part I: Information Sheet
Introduction
This is a brief introduction to ensure the child knows who you are and that this is a research study.
Explanation
Example
Purpose: Why are you doing this research?
Explain the purpose of the research in clear simple terms.
Example
Choice of participants: Why are you asking me?
Children, like adults, like to know why they are being invited to be in the research. It is important to address any fears they may have about why they were chosen.
Example
Participation is voluntary: Do I have to do this?

State clearly and in child-friendly language that the choice to participate is theirs. If there is a possibility that their decision not to participate might be over-ridden by parental consent, this should be stated clearly and simply.
Example
I have checked with the children and they understand that participation is voluntary __ (initial)

Information on the Trial Drug [Name of Drug]: What is this drug and what do you know about it?
Include the following section only if the protocol is for a clinical trial:

1) Give the phase of the trial and explain what that means. Explain to the participant why you are comparing or testing the drugs.
2) Provide as much information as is appropriate and understandable about the drug such as its manufacturer or location of manufacture and the reason for its development.
3) Explain the known experience with this drug
4) Explain comprehensively all the known side-effects/toxicity of this drug, as well as the adverse effects of all the other medicines that are being used in the trial
Example
Procedures: What is going to happen to me?
Explain the procedures and any medical terminology in simple language. Focus on what is expected of the child. Describe which part of the research is experimental.
Example
I have checked with the child and they understand the procedures _____ (initial))
Risks: Is this bad or dangerous for me?
Explain any risks using simple, clear language.
Example
Discomforts: Will it hurt?
If there will be any discomforts state these clearly and simply. State that they should tell you and/or their parents if they are sick, experience discomfort or pain. Address what may be some of the child's worries, for example, missing school or extra expense to parents.
Example
I have checked with the child and they understand the risks and discomforts ____(initial)
Benefits: Is there anything good that happens to me?

Describe any benefits to the child.
Example
I have checked with the child and they understand the benefits_____ (initial)
Incentives: Do I get anything for being in the research?
Mention any reimbursements or forms of appreciation that will be provided.
Explanation
Example
Confidentiality: Is everybody going to know about this?
Explain what confidentiality means in simple terms. State any limits to confidentiality. Indicate what their parents will or will not be told.
Example
Compensation: What happens if I get hurt?

Describe to the ability of the child to understand and explain that parents have been given more information.
Example
Sharing the Findings: Will you tell me the results?
Describe to the ability of the child to understand that the research findings will be shared in a timely fashion but that confidential information will remain confidential.
Explanation
Example
Right to Refuse or Withdraw: Can I choose not to be in the research? Can I change my mind?
You may want to re-emphasize that participation is voluntary and any limits to this.
Example
Who to Contact: Who can I talk to or ask questions to?
List and give contact information for those people who the child can contact easily (a local person who can actually be contacted). Tell the child that they can also talk to anyone they want to about this (their own doctor, a family friend, a teacher).
Example
If you choose to be part of this research I will also give you a copy of this paper to keep for yourself. You can ask your parents to look after it if you want.

PART 2: Certificate of Assent

This section can be written in the first person. It should include a few brief statements about the research and be followed by a statement similar to the one identified as 'suggested wording' below. If the child is illiterate but gives oral assent, a witness must sign instead. A researcher or the person going over the informed assent with the child must sign all assents.

Example

I know that I can choose to be in the research study or choose not to be in the research study [include any limits to child's assent]. I know that I can stop whenever I want.

I have read this information (or had the information read to me) and I understand it.

I have had my questions answered and know that I can ask questions later if I have them.

I understand any changes to this will be discussed with me.

I agree to take part in the research.

OR

I do not wish to take part in the research and I have <u>not</u> signed the assent below._____ (initialled by child/minor)

<u>Only if child assents:</u>

Print name of child _____

Signature of child: _____

Date: _____

Day/month/year

If illiterate:

A literate witness must sign (if possible, this person should be selected by the participant, not be a parent, and should have no connection to the research team). Children who are illiterate should include their thumb print as well.

I have witnessed the accurate reading of the assent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given assent freely.

Print name of witness (not a parent) _____ AND Thumb print of child/ minor

Signature of witness _____

Date _____

Day/month/year

I have accurately read or witnessed the accurate reading of the assent form to the potential participant, and the individual has had the

opportunity to ask questions. I confirm that the individual has given assent freely.
Print name of researcher_____
Signature of researcher_____
Date_____
Day/month/year
Copy provided to the participant _____ (initialled by researcher/assistant)
Parent/Guardian has signed an informed consent ___Yes ___No _____(initialled by researcher/assistant)

APPENDEX 06: SAMPLE OF INFORMED CONSENT FORM for CLINICAL STUDIES

(Language used throughout form should be at the level of a local student of class 6th/ 8th)
Notes to Researchers:
1. Please note that this is a template developed by WHO ERC to assist the Principal
Investigator in the design of their informed consent forms (ICF). It is important that
Principal Investigators adapt their own ICFs to the outline and requirements of their
particular study. **The logo of the collaborating institution must be used on the ICF**
2. Do not be concerned by the length of this template. It is long only because it contains
guidance and explanations which are for you and which you will not include in the
informed consent forms that you develop and provide to participants in your research.
2. in this template:
• Square brackets indicate where specific information is to be inserted
• Bold lettering indicates sections or wording which should be included
• Standard lettering is used for explanations to researchers only and must not be
Included in your consent forms

• Italics are used to provide examples of phrasing. **These are only examples. Researchers should use wording which provides the best information about**
their particular research project and which is most appropriate to their research population.

Research Ethics Review Committee (WHO ERC)
Informed Consent Template for Clinical Studies
[Name of Principle Investigator]
[Informed Consent Form for _____]
Name the group of individuals for whom this consent is written. Because research for a single project is often carried out with a number of different groups of individuals - for example healthcare workers, patients, and parents of patients - it is important that you identify which group this particular consent is for.
Example: This Informed Consent Form is for men and women who attend clinic Z, and who we are inviting to participate in research X.
[Name of Principal Investigator]
[Name of Organization]
[Name of Sponsor]
[Name of Proposal and version]
This Informed Consent Form has two parts:
• Information Sheet (to share information about the research with you)
• Certificate of Consent (for signatures if you agree to take part)
You will be given a copy of the full Informed Consent Form
PART I: Information Sheet
Introduction
Briefly state who you are and explain that you are inviting them to participate in the research you are doing. Inform them that they may talk to anyone they feel comfortable talking with about the research and that they can take time to reflect on whether they want to participate or not. Assure the participant that if they do not understand some of the words or concepts, that you will take time to explain them as you go along and that they can ask questions now or later.
Example: I am X, working for the Y Research Institute. We are doing research on Z disease, which is very common in this country. I am going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, the study doctor or the staff.

Purpose

Explain in lay terms why you are doing the research. The language used should clarify rather than confuse. Use local and simplified terms for a disease, e.g. local name of disease instead of malaria, mosquito instead of anopheles, "mosquitoes help in spreading the disease" rather than "mosquitoes are the vectors". Avoid using terms like pathogenesis, indicators, determinants, equitable etc. There are guides on the internet to help you find substitutes for words which are overly scientific or are professional jargon.

Example: Malaria is one of the most common and dangerous diseases in this region. The drugs that are currently used to help people with malaria are not as good as we would like them to be. In fact, only 40 out of every 100 people given the malaria drug
XYZ are completely cured. There is a new drug which may work better. The reason we are doing this research is to find out if the new drug ABX is better than drug XYZ which is currently being used.

Type of Research Intervention

Briefly state the type of intervention that will be undertaken. This will be expanded upon in the procedures section but it may be helpful and less confusing to the participant if they know from the very beginning whether, for example, the research involves a vaccine, an interview, a biopsy or a series of finger pricks.

Example: This research will involve a single injection in your arm as well as four follow-up visits to the clinic.

Participant selection

State why this participant has been chosen for this research. People wonder why they have been chosen to participate and may be fearful, confused or concerned.

Example: We are inviting all adults with malaria who attend clinic Z to participate in the research on the new malaria drug.

Voluntary Participation

Indicate clearly that they can choose to participate or not. State, only if it is applicable, that they will still receive all the services they usually do whether they choose to participate or not. This can be repeated and expanded upon later in the form as well. It is important to state clearly at the beginning of the form that participation is voluntary so that the other information can be heard in this context.

Example: Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. You may change your mind later and stop participating even if you agreed earlier.

Include the following section only if the protocol is for a clinical trial:

Information on the Trial Drug [Name of Drug]

1) Give the phase of the trial and explain what that means. Explain to the participant why you are comparing or testing the drugs.

2) Provide as much information as is appropriate and understandable about the drug such as its manufacturer or location of manufacture and the reason for its development.

3) Explain the known experience with this drug

4) Explain comprehensively all the known side-effects/toxicity of this drug, as well as the adverse effects of all the other medicines that are being used in the trial

Example: The drug we are testing in this research is called ABX. It has been tested before with people who do not have malaria but who live in areas where malaria is common. We now want to test the drug on people who have malaria. This second research is called a "phase 2" trial.

The drug ABX is made by Company C. You should know that it has a few side effects. One of the side effects, or problems, is that you may feel tired for the first day after being given the drug. Also, 20% of the people who tried the drug in previous research experienced temporary swelling where the injection entered the skin. We know of no other problem or risks.

Some participants in the research will not be given the drug which we are testing. Instead, they will be given the drug XYZ, the drug which is most commonly used in this region to treat malaria. There is no risk associated with that drug and no known problems. It does not, however, cure malaria as often as we would like.

Procedures and Protocol

Describe or explain the exact procedures that will be followed on a step-by-step basis, the tests that will be done, and any drugs that will be given. Explain from the outset what some of the more unfamiliar procedures involve (placebo, randomization, biopsy, etc.) Indicate which procedure is routine and which is experimental or research. Participants should know what to expect and what is expected of them.

Use active, rather than conditional, language. Write "we will ask you to…." instead of "we would like to ask you to….".

In this template, this section has been divided into two: firstly, an explanation of unfamiliar procedures and, secondly, a description of process.

A. Unfamiliar Procedures

This section should be included if there may be procedures which are not familiar to the participant.

If the protocol is for a clinical trial:

1) Involving randomization or blinding, the participants should be told what that means

and what chance they have of getting which drug (i.e. one in four chances of getting

the test drug).

Example Unfamiliar Procedures: randomization or blinding:

Example: Because we do not know if the new malaria drug is better than the currently available drug for treating malaria, we need to compare the two. To do this, we will put people taking part in this research into two groups. The groups are selected by chance, as if by tossing a coin.

Participants in one group will be given the test drug while participants in the other group will be given the drug that is currently being used for malaria. It is important that neither you nor we know which of the two drugs you are given. This information will be in our files, but we will not look at these files until after the research is finished. This is the best way we have for testing without being influenced by what we think or hope might happen. We will then compare which of the two has the best results.

The healthcare workers will be looking after you and the other participants very carefully during the study. If we are concerned about what the drug is doing, we will find out which drug you are getting and make changes. If there is anything you are concerned about or that is bothering you about the research please talk to me or one of the other researchers

2) Involving an inactive drug or placebo, it is important to ensure that the participants

understand what is meant by a placebo or inactive drug.

Example: A placebo or inactive medicine looks like real medicine but it is not. It is a dummy or pretend medicine. It has no effect on a person because it has no real medicine in it. Sometimes when we want to know whether a new medicine is good, we give some people the new medicine and some people the pretend or dummy medicine. For the research to be good, it is important that you do not know whether you have been given the real medicine or the pretend or dummy medicine. This is one of the best ways we have for knowing what the medicine we are testing really does.

3) Which may necessitate a rescue medicine, and then provide information about the rescue medicine or treatment such as what it is and the criterion for its use. For example, in pain trials, if the test drug does not control pain, then intravenous morphine may be used as a rescue medicine.

Example: If we find that the medicine that is being used does not have the desired effect, or not to the extent that we wish it to have, we will use what is called a "rescue medicine." The medicine that we will use is called QRS and it has been proven to control pain. If you find that the drug we are testing does not stop your pain and it is very uncomfortable for you, we can use the rescue medicine to make you more comfortable.

If the protocol is for clinical research:

Firstly, explain that there are standards/guidelines that will be followed for the treatment of their condition. Secondly, if as part of the research a biopsy will be taken, then explain whether it will be under local anesthesia, sedation or general anesthesia, and what sort of symptoms and side effects the participant should expect under each category.

Example: You will receive the treatment of your condition according to national guidelines. This means that you will be (explain the treatment). To confirm the cause of your swelling, a small sample of your skin will be taken. The guidelines say that the sample must be taken using a local anesthesia which means that we will give you an injection close to the area where we will take the sample from. This will make the area numb so that you will not feel any pain when we take the sample.

For any clinical study (if relevant):

If blood samples are to be taken explain how many times and how much in a language that the person understands. It may, for example, be inappropriate to tell a tribal villager that blood equal to a wine-glass full will be taken but it may be very appropriate to use pictures or other props to illustrate the procedure if it is unfamiliar.

If the samples are to be used only for this research, then explicitly mention here that the biological samples obtained during this research procedure will be used only for this research, and will be destroyed after ____ years, when the research is completed. If the tissues/blood samples or any other human biological material will be stored for a duration longer than the research purpose, or is likely to be used for a purpose other than mentioned in the research proposal, then provide information about this and obtain consent specifically for such storage and use in addition to consent for participation in the study - (see last section)

Example: We will take blood from your arm using a syringe needle. Each time we will take about this much blood (show a spoon, vial or other small container with

a small amount of water in it. At the end of the research, in 1 year, your blood sample will be destroyed.

B. Description of the Process

Describe to the participant what will happen on a step-by-step basis. It may be helpful to the participant if you use drawings or props to better illustrate the procedures. A small vial or container with a little water in it is one way of showing how much blood will be withdrawn.

Example: During the research you make five visits to the clinic.

• In the first visit, a small amount of blood, equal to about a teaspoon, will be taken from your arm with a syringe. This blood will be tested for the presence of substances that help your body to fight infections. We will also ask you a few questions about your general health and measure how tall you are and how much you weigh.

• At the next visit, which will be two weeks later, you will again be asked some questions about your health and then you will be given either the test drug or the drug that is currently used for malaria. As explained before, neither you nor we will know whether you have received the test or the dummy/pretend drug.

• After one week, you will come back to the clinic for a blood test. This will involve….

Duration

Include a statement about the time commitments of the research for the participant including both the duration of the research and follow-up, if relevant.

Example: The research takes place over ___ (number of) days/ or ___ (number of) months in total. During that time, it will be necessary for you to come to the clinic/hospital/health facility _____(number of) days , for ____ (number of) hours each day.

We would like to meet with you three months after your last clinic visit for a final check-up.

In total, you will be asked to come 5 times to the clinic in 6 months. At the end of six months, the research will be finished.

Side Effects

Potential participants should be told if there are any known or anticipated side effects and what will happen in the event of a side effect or an unexpected event.

Example: As already mentioned, this drug can have some unwanted effects. It can make you tired and it can cause some temporary swelling around the place where the injection goes into your arm. It is possible that it may also cause some problems that we are not aware of. However, we will follow you closely and keep track of any unwanted effects or any problems. We may use some other

medicines to decrease the symptoms of the side effects or reactions. Or we may stop the use of one or more drugs.
If this is necessary we will discuss it together with you and you will always be consulted before we move to the next step.

Risks

Explain and describe any possible or anticipated risks. Describe the level of care that will be available in the event that harm does occur, who will provide it, and who will pay for it. A risk can be thought of as being the possibility that harm may occur. Provide enough information about the risks that the participant can make an informed decision.

Example: By participating in this research it is possible that you will be at greater risk than you would otherwise be. There is, for example, a risk that your disease will not get better and that the new medicine doesn't work even as well as the old one. If, however, the medicine is not working and your fever does not go down in 48 hours we will give you quinine injections which will bring your fever down and make you more comfortable.
While the possibility of this happening is very low, you should still be aware of the possibility. We will try to decrease the chances of this event occurring, but if something unexpected happens, we will provide you with_____.

Discomforts

Explain and describe the type and source of any anticipated discomforts that are in addition to the side effects and risks discussed above.

Example: By participating in this research it is possible that you may experience some discomfort such as the discomfort of repeated blood pressure readings or venepuncture.

Benefits

Mention only those activities that will be actual benefits and not those to which they are entitled regardless of participation. Benefits may be divided into benefits to the individual, benefits to the community in which the individual resides, and benefits to society as a whole as a result of finding an answer to the research question.

Example: If you participate in this research, you will have the following benefits: any interim illnesses will be treated at no charge to you. If your child falls sick during this period he/she will be treated free of charge. There may not be any benefit for you but your participation is likely to help us find the answer to the research question. There may not be any benefit to the society at this stage of the research, but future generations are likely to benefit.

Incentives

State clearly what you will provide the participants with as a result of their participation. WHO does not encourage incentives? However, it recommends

that reimbursements for expenses incurred as a result of participation in the research be provided. These may include, for example, travel costs and money for wages lost due to visits to health facilities. The amount should be determined within the host country context.

Example: We will give you [amount of money] to pay for your travel to the clinic/parking and we will give you [amount] for lost work time. You will not be given any other money or gifts to take part in this research.

Confidentiality

Explain how the research team will maintain the confidentiality of data, especially with respect to the information about the participant which would otherwise be known only to the physician but would now be available to the entire research team. Note that because something out of the ordinary is being done through research, any individual taking part in the research is likely to be more easily identified by members of the community and is therefore more likely to be stigmatized.

Example: With this research, something out of the ordinary is being done in your community. It is possible that if others in the community are aware that you are participating, they may ask you questions. We will not be sharing the identity of those participating in the research.

The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except [name who will have access to the information, such as research sponsors, DSMB board, your clinician, etc].

Sharing the Results

Where it is relevant, your plan for sharing the information with the participants should be provided. If you have a plan and a timeline for the sharing of information, include the details. You should also inform the participant that the research findings will be shared more broadly, for example, through publications and conferences.

Example: The knowledge that we get from doing this research will be shared with you before it is made widely available to the public. Confidential information will not be shared. There will be small meetings in the community and these will be announced.

After these meetings, we will publish the results in order that other interested people may learn from our research.

Right to Refuse or Withdraw

This is a reconfirmation that participation is voluntary and includes the right to withdraw. Tailor this section to ensure that it fits for the group for whom you are seeking consent. The example used here is for a patient at a clinic.

Example: You do not have to take part in this research if you do not wish to do so and refusing to participate will not affect your treatment at this clinic in any way. You will still have all the benefits that you would otherwise have at this clinic. You may stop participating in the research at any time that you wish without losing any of your rights as a patient here. Your treatment at this clinic will not be affected in any way.

OR You do not have to take part in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected.

Alternatives to Participating

Include this section only if the study involves administration of investigational drugs or use of new therapeutic procedures. It is important to explain and describe the established standard treatment.

Example: If you do not wish to take part in the research, you will be provided with the established standard treatment available at the centre/institute/hospital. People who have malaria are given.…

Who to Contact

Provide the name and contact information of someone who is involved, informed and accessible (a local person who can actually be contacted. State also that the proposal has been approved and how.

Example: If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following: [name, address/telephone number/e-mail]

This proposal has been reviewed and approved by [name of the local IRB], which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find about more about the IRB, contact [name, address, and telephone number.)

PART II: Certificate of Consent

This section can be written in the first person. It should include a few brief statements about the research and be followed by a statement similar to the one in bold below. If the participant is illiterate but gives oral consent, a witness must sign. A researcher or the person going over the informed consent must sign each consent. Because the certificate is an integral part of the informed consent and not a stand-alone document, the layout or design of the form should reflect this.

Example: I have been invited to participate in research of a new malaria drug. I understand that it will involve receiving an injection and five follow-up visits. I have been informed that the risks are minimal and may include only _____. I am aware that there may be no benefit to me personally and that I will not be compensated beyond travel expenses. I have been provided with the name of a researcher who can be easily contacted using the number and address I was given for that person.

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research and understand that I have the right to withdraw from the research at any time without in any way affecting my medical care.

Print Name of Participant_____
Signature of Participant _____
Date _____
Day/month/year

If illiterate

A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb-print as well.

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness_____ AND Thumb print of participant
Signature of witness _____
Date _____
Day/month/year

I have accurately read or witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print Name of Researcher_____
Signature of Researcher _____
Date _____
Day/month/year

A copy of this Informed Consent Form has been provided to participant _____ (initialed by the researcher/assistant)

APPENDIX 07: MATERIAL TRANSFER AGREEMENT

This is an agreement made in order to protect material obtained from: Name of Institution between the

RECIPIENT INSTITUTION NAME (hereafter "**RECIPIENT**"), represented by PRINTED NAME

RECIPIENT SCIENTISTS:

1. Printed name
2. Printed name

And the
PROVIDER INSTITUTION NAME (hereafter "**PROVIDER**"), represented by

PROVIDER SCIENTISTS:

1. Printed name
2. Printed name.

"Original Material":
"Material": The Original Material as described, as well as all unmodified or modified derivatives.

Both parties agree as follows:

1. The Original Material is the sole property of the PROVIDER and is made available as a service to the research community. The RECIPIENT shall have no right in the Original Material other than as provided in this agreement. Ownership of modifications and direct/indirect derivates of material, and income arising from commercializing the direct/indirect derivates of material shall be negotiated in good faith by the parties hereto depending upon (a) their relative contribution to the creation of said modifications and derivates, and (b) applicable laws and regulations relating to the inventor ship.

2. The Material will be used for research purposes only and will not be used for commercial purposes or sublicensed to any third party unless another license is obtained from the PROVIDER.
3. The Recipient agrees to provide the PROVIDER with a copy of any publication, which contains experimental results obtained from the use of the Material. The RECIPIENT guaranties that the PROVIDER will be part of the publication team. The RECIPIENT shall acknowledge the PROVIDER as the source of the material in all publications containing any data or information about the Material, unless the PROVIDER indicates otherwise.

Accepted by:

Provider Scientists

Signature…….

Printed Name:

Institution:

Recipient Scientists:

Signature…….

Printed Name:

Institution

Provider Institution Approval

Approval

Signature …….

Date: …….

Recipient Institution

Signature…….

Date: …….

APPENDIX 08: PROGRESS REPORT FORM

The Rwanda National Ethics Committee (RNEC) would like to know how your study has progressed so far, and if any difficulties have been experienced. Please compete the questionnaire below and return, within two weeks,

To:

The office of Rwanda National Ethics Committee
P.O. Box 84,
Kigali-Rwanda

1. Name of Principle Investigator:
2. Title of study:

3. RNEC reference number:
4. Date of RNEC approval:

5. Briefly describe the purpose of the study (2-3 sentences in non- technical language):

6. Has the study started? Yes/No Starting Date of Study:

7. Number of local research sites recruited: Proposed: Actual:

8. Number of participants recruited into study: **Male** **Female** **Age range**

Proposed
Actual

9. Number of participants completing study: Actual:

10. Number of withdrawals: Actual:
Reasons for withdrawal

11. Have there been any difficulties in recruiting participants to the study? Yes /No

If yes, please give details

12. Have there been any adverse events? Yes/No

If yes, have these been notified to the committee? Yes/ No
Please give details

13. Have there been any amendments to the study? Yes/No
If yes, have these been notified to the committee? Yes/ No
Please give details

14. Has the study been completed? Yes/No Date of completion:
If no, what is the expected completion date?

If the study will not be completed, please give reason(s)

15. Results- please include details of outcomes and conclusions so far (attach a separate page if necessary)

16. Have the findings been disseminated? Yes/No
If yes, how?

Please give details of any publications and send copies when available

17. Any complaints about the research?

Signature of Principal Investigator:……

Print name:……

Postal Address:……Tel. No.:……E-mail:……

Date of submission:……

<u>APPENDIX 09</u>: APPLICATION FOR A NEW TRIAL

Documents to be submitted to RNEC:

- A copy of the request letter and the application form,
- A copy of the protocol and summary,
- A copy of the patient informed consent and the patient information sheet in
  English or French and Kinyarwanda,
- A copy of the financial agreements with the researchers,

- A copy of the previous decisions from other ethics committees or regulatory
  Authorities, where applicable,

- A copy of a placebo usage justification, where applicable,

- Copies of the researcher's brochure (Phase I, II & III),

- One copy of each researcher's CV (1 copy of each document),

- A copy of the insurance policy covering the possible medical consequences of the trial during and after the trial,

- To bound the protocols (each copy of the protocol should be bounded with each copy of the above-mentioned documents).

- All documents are submitted as an electronic copy, above mentioned information must be e-mailed to the Ethics Committee secretariat including the Protocol and summary, Researcher's Brochure Patient Information Sheet.

- A proof of payment of the ethics review fees under the names of the Rwanda Ethics Committee, must be enclosed with the file submitted. The submission fees are paid to the following account number: Rwanda National Ethics Committee 130 -10 53 298 in COGEBANQUE.

Appendix 10: World Medical Association adopted the Declaration of Helsinki

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principle to provide guidance to physicians and other participants in medical research involving human study participants. Medical research involving human study participants includes research on identifiable human material or identifiable data.
2. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.
3. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares

that, " A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."

4. Medical progress is based on research which ultimately must rest in part on experimentation involving human study participants.
5. In medical research on human study participants, considerations related to the well-being of the human study participant should take precedence over the interests of science and society.
6. The primary purpose of medical research involving human study participants is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.
7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.
8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research population is vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be study participant to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.

7. Research investigators should be aware of the ethical, legal and regulatory requirements for research on human study participants in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirements should be allowed to reduce or eliminate any of the protections for human study participants set forth in this Declaration.

B. Basic Principles for all Medical Research

1. It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human study participant.
2. Medical research involving human study participants must conform to general accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.
3. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animal used for research must be respected.
4. The design and performance of each experimental procedure involving human study participants should be clearly formulated in an

experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for study participants.

5. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.
6. Medical human research involving study participants should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human study participant must always rest with a medically qualified person and never rest on the study participant of the research, even though the study participant has given consent.
7. Every medical research project involving human study participant should be preceded by careful assessment of predictable risk and burdens in comparison with foreseeable benefits to the study participant or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.
8. Physicians should abstain from engaging in research project involving human study participants unless they are confident that the risk involved has been adequately assessed and can be satisfactorily managed. Physicians should cease any investigations if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.
9. Medical research involving human study participants should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the study participant. This is especially important when the human study participants are healthy volunteers.
10. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the result of the research.
11. The study participants must be volunteers and informed participants in the research project.
12. The right of research study participants to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the study participant, the confidentiality of every patient's information and to minimize the impact of the study on the study

participant's physical and mental integrity and on the personality of the study participant.

13. In research of human beings, each potential study participant must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The study participant should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the study participant has understood the information, the physician should then obtain the study participant's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.
14. When obtaining informed consent for the research project the physician should be particularly cautious if the study participant is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.
15. For a research study participant who is legally incompetent, physically or mental incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.
16. When a study participant deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.
17. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reason for involving research study participants with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from individual or a legally authorized surrogate.
18. Both authors and publishers have ethical obligation. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicity available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in

accordance with the principle laid down in this Declaration should no be acceptable for publication.

Dr. Jean Baptiste MAZARATI
Chairperson,
Rwanda National Ethics Committee