FOOD, MEDICINE AND HEALTHCARE ADMINISTRATION AND CONTROL AUTHORITY OF ETHIOPIA

CLINICAL TRIAL AUTHORIZATION GUIDELINE

Second Edition

Addis Ababa, Ethiopia

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ACRONYMS

AE	Adverse Events
CPP	Certificate of Pharmaceutical Product
CRF	Case Report Form
CRO	Contract Research Organization
DSMB	Data and Safety Monitoring Board
eCRF	Electronic Case Report Form
EFMHACA	Ethiopian Food, Medicine and Health Care Administration and Control Authority
GCP	Good Clinical Practice
GMP	Good Manufacturing Practices
ICH	International Council for Harmonization
IEC	Independent Ethical committee
IRB	Institutional Review Board
NRA	National Regulatory Authority
NRERC	National Research Ethical Review Committee
PQM	Promoting the Quality of Medicines Program
QA	Quality Assurance
PI	Principal Investigator
SOP	Standard Operation Procedure
SAE	Serious adverse event
USAID	United States Agency for International Development
USP	U. S. Pharmacopeial Convention
WHO	World Health Organization

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The Authority would also like to give special acknowledgement to the Leadership Group, Technical Working Group members, all participants of guideline enrichment workshop and other experts for their unreserved effort to bring this document to reality.

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FORWARD

Clinical research is necessary to establish relatively safe and effective medical products and healthcare practices. What is known today about the risk and benefits of specific products and treatments are the result of randomized controlled clinical trials. However, there are concern about the safety and effectiveness of drugs and clinical research processes among members of medical profession, scientific community, regulatory authorities and the public. For this reason, establishing effective systems at national level to evaluate and authorize clinical trials is important

Recognizing this, The Food, Medicine and Healthcare Administration and Control Proclamation No. 661/2009 article 4, sub-article 11 provides the mandate to the authority to authorize the clinical trials, monitor the process, ensure ethical procedures, evaluate the results and authorize the use of the results of the trial with in the Ethiopian territory.

I have no doubt that with the unwavering government leadership, the commitment of the scientific community to comply with regulatory requirements for clinical trial authorization, the firm commitment of our staffs for our people, and the support of our development partners, we will prevail to meet the implementation of the guideline.

Finally, I would like to take this opportunity to acknowledge and express my appreciation to the United States Agency for International Development (USAID) and the U. S. Pharmacopeial Convention Promoting the Quality of Medicines Program (USP/PQM) for the financial and technical support; and to all those experts who have directly or indirectly extended their helping hands in the preparation of this guideline.

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1. INTRODUCTION

Clinical research is necessary to establish the relative safety and effectiveness of specific health and pharmaceutical products and healthcare practices. Much of what is known today about the risk and benefits of specific products and treatments has come from randomized controlled clinical trials that are designed to answer important scientific and health care questions. However, early 1960, there were widespread concern about the safety and control of investigational drugs and the clinical research process developed among members of medical profession, scientific community, regulatory authorities, and the public. This concern and subsequent international meeting serves a base for the development of Good Clinical Practice (GCP) at an international level, later developed by International Council for Harmonization (ICH).

According to article 4, sub article 11 of the Food, Medicine and Healthcare Administration and Control Proclamation No. 661/2009, a national executive authority is responsible to authorize the conduct of clinical trials, monitor the process as to its conduct in accordance with good medical procedure as well as GCP, evaluate the results and authorize the use of or to publish the results in such a way that it benefits the public; or suspend or otherwise withdraw approval for the conduct of a clinical trial where necessary. Article 15 of this Proclamation provides further detail on the requirements for clinical trials.

To implement the Proclamation No. 661/2009, Ethiopian Food, Medicines and Healthcare Administration and Control Authority was established by Council of Ministers Regulation No. 189/2010. Similarly, articles 22, 24 - 28 of Food, Medicine and Healthcare Administration and Control Council of Ministers Regulation No. 299/2013 provides a detailed description of responsibilities and activities of the Authority, investigators and/or sponsors.

This Guideline supersedes the previous guideline developed based on the Proclamation No. 176/99. The previous guideline was unable to answer the current scientific developments. Hence, this requires the need for revision of this Guideline.

Accordingly, all clinical trials carried out in the territory of the Federal Democratic Republic of Ethiopia must be reviewed by the Authority for use of the investigational product or intervention in human subjects and to ensure that the research is appropriately designed to meet its stated objectives as stated in the Proclamation No.661/2009 and Regulation No. 299/2013.

This Guideline outlines the documents required to be submitted to the Authority in connection with applications to conduct clinical trials in Ethiopia. After approval by the Authority, investigator (s) can initiate ~~a~~ clinical trial under the responsibility of the sponsor as stated in the approved protocol.

Amendments to the approved clinical trial protocols or other changes may be required. In this case, sponsor(s) and/or investigator (s) must apply to the authority in writing for approval of these proposed amendments in accordance with "application for clinical trial amendments" section of the Guideline. The application for amendments distinguishes between those classified as minor and major. For major amendments, prior approval is required before implementation. However, for minor amendments the investigator/sponsor can implement the proposed amendments; immediately after proper categorization of the proposed amendments is confirmed in writing by the Authority to the applicant(s).

To facilitate the application and review process, this Guideline contains ten annexes. Applicants are advised to read and understand the contents of this Guideline before submitting applications for the conduct of clinical trial(s) in Ethiopia. Although the requirements set out in each section of the Guideline are general, applications must be considered and assessed individually. Hence, this Guideline makes reference to the terms ‘‘when applicable", "where appropriate", "where relevant" only to reflect this principle.

Consequently, all users of this guideline are strongly invited to forward their comments and suggestions to the Food, Medicine and Healthcare Administration and Control Authority of Ethiopia, P.O. Box 5681, Tel. 251-11 552 41 22, email: efmhacapharmacovigilance@gmail.com, Addis Ababa, Ethiopia

2. SCOPE

This Guideline applies to the submission of documents for the conduct of clinical trials on human beings in Ethiopia. It is applicable for all clinical trials involving investigational products including new drugs, or new combinations of drugs, vaccines, new therapeutic regimens, food supplements, herbal products and other biological products as well as invasive diagnostic procedures. This Guideline also applies for conduct of bioequivalence/bioavailability studies.

The term 'product' includes pharmaceutical products where the pharmacological, immunological, or metabolic action of the product is still uncertain and being explored; advanced therapy medicinal products or medicinal products derived from human blood or human plasma; interventional clinical trials with medicinal products for the paediatric population and interventional clinical trials with medicinal products manufactured or reconstituted in a (hospital) pharmacy and intended to be supplied directly to the clinical trials participants. It does not include non-invasive medical devices, cosmetics or food.

Veterinary clinical trials (conducted in Ethiopia) is out of the scope of this guideline.

This Guideline is directed towards all those involved in clinical trials whether for academic purposes or for the generation of data intended for inclusion in the regulatory submissions for medicines/products.

3. OBJECTIVES

The objectives of this Guideline are:

- To guide sponsor and/or investigator (s) on the documents and process requirements for the conduct of clinical trials in Ethiopia.
- To provide sponsor and/or investigator (s) information on requirements for amendments of protocols or other clinical trial related documents that are made after approval.
- To guide the period and the content of the (progress & final) report and adverse events reporting in relation to clinical trials conducted in Ethiopia.

4. DEFINITION

The following definitions are provided to facilitate interpretation of the Guideline; they apply only to the words and phrases used in this Guideline. Although every effort has been made to use standard definitions used by ICH, the words and phrases used in this Guideline may have different meanings in other contexts and other documents.

Adverse event(AE)

Any 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 (AE) 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, whether or not related to the medicinal (investigational) product.

Authority

Ethiopian Food, Medicines and Healthcare Administration and Control Authority

Case report form (CRF)

A printed, optical, or electronic document designed to record all the information to be reported to the sponsor on each trial participant.

Clinical Trial (CT)

Any investigation in human participants intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or 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 objective of ascertaining its safety and/or efficacy. It also includes investigation in human participants with invasive diagnostic procedures.

Contract Research Organization (CRO)

A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

Food Supplement

A type of food that supplement the normal diet and which is a concentrated source of vitamin, mineral or other substance with a nutritional or physiological effect alone or in combination, designed to be taken in measured small quantities and is prepared in capsule, pill, powder, liquid, drops or any other similar forms.

Good Clinical Practice (GCP)

A standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials that provides assurance that the data are credible and accurate, and that the rights, integrity and confidentiality of trial participants are protected. Any reference to GCP in this Guideline should be understood as a reference to the current WHO/ICH GCP guidelines.

Good Laboratory Practice (GLP)

A quality system concerned with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.

Good Manufacturing Practice (GMP)

The part of pharmaceutical quality assurance which ensures that products are consistently produced and controlled in conformity with quality standards appropriate for their intended use and as required by the product specification. Any reference to GMP in this Guideline should be understood as a reference to the current ICH GMP guideline.

Investigator (I)

A person responsible for the conduct of the clinical trial at a right site and for the rights, health and welfare of the participants in the trial. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator. The investigator should have qualifications and competence which could be evidenced by an up-to date curriculum vitae and other credentials. The medical/dental care and decisions must always be the responsibility of a clinically competent person legally allowed and registered to practice health care in Ethiopia.

Investigators Brochure(IB)

A collection of data consisting of all the information known prior to the clinical trial concerning the clinical and non-clinical data on the investigational product(s). There should be adequate data to justify the nature, scale and duration of the proposed trial.

Investigational labeling (IL)

Labeling developed specifically for products involved in a clinical trial.

Investigational Product (IP)

A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial including a product with a marketing authorization when used or assembled in a way different from the approved form, or when used for an unapproved indication or when used to gain further information about an approved use.

Major amendments (MA)

Amendments to the trial are regarded as "major" where they are likely to have a significant impact on the safety or physical or mental integrity of the participants; the scientific value of the trial; the conduct or management of the trial; or the quality or safety of any investigational product used in the trial. Examples include changes in the purpose or design of a trial, substantive changes in procedures used, changes to the trial population such as estimated numbers, age range, inclusion/exclusion criteria, a change of the principal investigator, and changes to trial documentation, such as participant information sheets or consent forms.

Minor Amendment

Amendment to the trial are regarded as "minor" where they do not involve a more than minimum risk for participants or the conduct of the trial and do not have significant impact on the scientific value of the trial; the conduct or management of the trial or safety of investigational product used in the trial. Example minor changes to the protocol or other study documentation (e.g. correcting errors, updating contact points, minor clarifications; updates of the investigator's brochure (unless there is a change to the risk/benefit assessment for the trial); changes to the investigator's such as (change of sole investigator at a trial site or any other investigator, other than principal investigators, at a trial site); changes in funding arrangements; changes in the documentation used

by the research team for recording study data; changes in the logistical arrangements for storing or transporting samples. extension of the study period beyond indicated in the application form.

Monitor (M)

A person appointed by the sponsor or Contract Research Organization (CRO), and responsible to the sponsor or CRO, for the monitoring and reporting of progress of the trial and for verification of data.

National Research Ethical Review Committee (NRERC)

Ethical review committee at the national level established to safeguard the dignity, rights, safety, and welfare of all actual or potential research participants and/or communities under Ministry of Science and Technology of Ethiopia.

Principal Investigator (PI)

A person responsible for the conduct of the clinical trial at a trial site who is a medical practitioner, or dentist or other qualified person, resident in the country. If a trial is conducted by a team of investigators at a trial site, the principal investigator is the responsible leader of the team named as such in the protocol.

Proclamation

Food, Medicine and Healthcare Administration and Control Proclamation No. 661/2009

Sponsor

An individual, a company, an institution or an organization which takes responsibility for the initiation, conduct, management and/or financing of a clinical trial. When an investigator independently initiates and takes full responsibility for a trial, the investigator then also assumes the role of the sponsor.

Serious adverse event (SAE)

Any event that is associated with death, admission to hospital, prolongation of hospital stay, persistent or significant disability or incapacity, congenital abnormal/birth defect or is otherwise life threatening or important medical event in connection with a clinical trial.

Study: Is used as a synonym for trial

5. GENERAL GUIDANCE FOR PREPARATION OF DOCUMENTS FOR CLINICAL TRIAL APPLICATIONS

Clear, complete, accurate, organized and structured documents will facilitate the evaluation process and decrease the risk of delay in review by the Authority. Poor quality applications and documents may lead to unnecessary loss of time, for the investigator (s) or sponsor and the Authority. Therefore, documents should have unambiguous contents: title, nature, and their purpose should be clearly stated. They should be submitted in duplicate paper format to make easy for the Authority to check.

Guidance on the compilation document for clinical trial authorization is summarized below:

1. Paper size is A4; top, bottom, header, and footer margins are 12.5 mm; left and right margins are 25mm, with all page numbered sequentially and with the title of the trial
2. Single-spaced paragraphs
3. Times New Roman font, font size 12- point; line space 1.5, letter space 0%.
4. The weight of the font should be legible when copied.
5. The application must include a cover with, labeled with the title of the clinical trial and clinical trial site(s)
6. The attached data and documents should appear in the English language.
7. Any abbreviations should be clearly defined.
8. The compilation of the document should be outlined according to the flow of this Guideline and should be indexed or annotated as described in this Guideline.
9. Applications submitted for clinical trial authorization will be reviewed chronologically by the date of submission to the Authority, and the investigator (s) or sponsor will be notified of the evaluation results within two weeks of its submission to the Authority.
10. Information that is confidential and that the sponsor requests the Authority not to publish must be clearly labeled as confidential.

6. APPLICATION REQUIREMENTS FOR SUBMISSION OF CLINICAL TRIAL AUTHORAZATION

6.1. APPLICATION FORM

Complete the application form as indicated in Annex I in two identical (duplicate) copies. One copy of the application is to be returned to the applicant after evaluation of the application by the Authority.

6.2. SERVICE FEE

The applicant shall pay the required payment in accordance with the Rate of Service Fees for Food, Medicine, Health Professions and Health Institutions Registration and Licensing Council of Ministers Regulation No. 370/2015. The Authority shall not consider applications unless applicable fees have been paid in full.

6.3. AGREEMENT BETWEEN SPONSOR, MONITOR AND INVESTIGATORS

Prior to the commencement of the trial, the investigator(s) and the sponsor must establish written agreement on the protocol, the monitoring, the auditing and on standard operating procedures (SOP), and the allocation of trial-related responsibilities. The logistics and premises of the trial site should comply with requirements for the safe and efficient conduct of the trial. An agreement made on the basis of this principle between the investigator(s) and the sponsor as Annex II and a joint declaration by the sponsor and principal investigator concerning sufficient funds to complete a study should be submitted as Annex III. Declarations of investigator(s) and monitor are included in Annex IV and Annex V respectively

6.4. SPONSOR AND MONITOR

The sponsor is generally responsible for ensuring that the applicable regulatory review is performed by the Authority and to obtain any authorizations that may be required by the Authority for the conduct of the clinical trial before the commencement of the clinical trial. Details of the sponsor including the name and complete addresses should be provided.

Information on the selection of trial site (s) and the selection of properly qualified, trained, and experienced investigators and study personnel should be provided.

The sponsor is also responsible for the quality of investigational product(s) including handling of the investigational products during shipment and updating supporting data on investigational products. Hence such information should be provided in the respective section of this Guideline i.e. as indicated under sections 7 and 8 of this Guideline.

Monitors are responsible for protecting the rights and well-being of human participants, confirming the reported trial data are accurate, complete, and verifiable from source documents, the conduct of the trial in compliance with currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirement(s).

The monitor acts as the main line of communication between the sponsor and the investigator.

Monitor should be appointed by the sponsor. Monitors should be appropriately trained, and should have the scientific and/or clinical knowledge and professional qualifications needed to monitor the trial adequately. A monitor's qualifications should be documented and checked by sponsors.

6.5. CLINICAL TRIAL PROTOCOL

The investigators/sponsor should provide two identical (duplicate) copies of the protocol during submission for approval of the clinical trial of which one of the final approved versions of the copy will have the stamp of the Authority and returned to the applicant (investigator/sponsor).

The protocol should be identified by the title, a sponsor's protocol code number specific for all versions of it, a number and date of version that will be updated when it is amended, and by any short title or name assigned to it. It should be signed by the sponsor and principal investigator (or coordinating investigators for multi-center trials of the sponsor). The version submitted should include all currently authorized amendments and a definition of the end of the trial.

The contents of a clinical trial protocol should generally include the following topics. However, site specific information may be provided on separate protocol page(s), or addressed in a separate agreement, and some of the information listed below may be contained in other protocol referenced documents, such as an Investigator's Brochure.

6.5.1. General Information

- Protocol title, protocol identifying number, and date. Any amendment(s) should also bear the amendment number(s) and date(s).
- Name and address of the sponsor and monitor (if other than the sponsor).

- Name and title of the person(s) authorized to sign the protocol and the protocol amendment(s) for the sponsor.
- Name, title, address, and telephone number(s) of the sponsor's medical expert (or dentist when appropriate) for the trial.
- Name and title of the investigator(s) who is (are) responsible for conducting the clinical trial, and the address and telephone number(s) of the trial site(s).
- Name, title, address, and telephone number(s) of the qualified physician (or dentist, if applicable) who is responsible for all trial-site related medical (or dental) decisions (if other than investigator).
- Name(s) and address(es) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the trial.

6.5.2. Background Information

- Name and description of the investigational product(s).
- A summary of findings from nonclinical studies that potentially have clinical significance and from clinical trials those are relevant to the trial.
- Summary of the known and potential risks and benefits, if any, to human participants.
- Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s).
- A statement that the trial will be conducted in compliance with the protocol, GCP, and the applicable regulatory requirement(s).
- Description of the population to be studied.
- References to literature and data that are relevant to the trial, and that provide background for the trial.

6.5.3. Trial Objectives and Purpose

A detailed description of the objectives and the purpose of the trial.

6.5.4. Clinical Trial Design

The scientific integrity of the trial and the credibility of the data from the clinical trial depend substantially on the clinical trial design. A description of the clinical trial design should include:

- A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.
- A description of the type/design of clinical trial to be conducted (e.g., double-blind, placebo-controlled, parallel design, cross over design) and a schematic diagram of trial design, procedures, and stages.
- A description of the measures taken to minimize/avoid bias, including:
  - Randomization.
  - Blinding.
- A description of the clinical trial treatment(s) and the dosage and dosage regimen of the investigational product(s). Also include a description of the dosage form, packaging, and labeling of the investigational product(s).
- The expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.
- A description of the "stopping rules" or "discontinuation criteria" for individual participants, parts of trial, and entire trial.
- Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.
- Maintenance of trial treatment randomization codes and procedures for breaking codes.
- The identification of any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data), and to be considered source data.

6.5.5. Selection and Withdrawal of clinical trial participants

- Clinical trial participant inclusion criteria.
- Clinical trial participant exclusion criteria.
- Clinical trial participant withdrawal criteria (i.e., terminating investigational product treatment/trial treatment) and procedures specifying:
  - When and how to withdraw subjects from the trial/ investigational product treatment.
  - The type and timing of the data to be collected for withdrawn subjects.
  - Whether and how subjects are to be replaced.
  - The follow-up for subjects withdrawn from investigational product treatment/trial treatment.

6.5.6. Treatment of participants

- The treatment(s) to be administered, including the name(s) of all the product(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s), including the follow-up period(s) for subjects for each investigational product treatment/trial treatment group/arm of the trial.
- Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.
- Procedures for monitoring research participant compliance.

6.5.7. Assessment of Efficacy

- Specification of the efficacy parameters.
- Methods and timing for assessing, recording, and analyzing efficacy parameters.

6.5.8. Assessment of Safety

- Specification of safety parameters.
- The methods and timing for assessing, recording, and analyzing safety parameters.
- Procedures for eliciting reports of and for recording and reporting adverse event and intercurrent illnesses.
- The type and duration of the follow-up of trial participants after adverse events.

6.5.9. Statistics

- A description of the statistical methods to be employed, including timing of any planned interim analysis(es).
- The number of research participants planned to be enrolled. In multicenter trials, the number of enrolled subjects projected for each trial site should be specified. Reason for choice of sample size, including reflections on (or calculations of) the power of the trial and clinical justification.
- The level of significance to be used.
- Criteria for the termination of the trial.
- Procedure for accounting for missing, unused, and spurious data.
- Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in the protocol and/or in the final report, as appropriate).

- The selection of clinical trial participants to be included in the analyses (e.g., all randomized participants, all dosed participants, all eligible participants, evaluateable participants).

6.5.10. Direct Access to Source Data/Documents

The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspection(s) by providing direct access to source data/documents.

6.5.11. Quality Control and Quality Assurance

The sponsor should ensure quality assurance (QA) system throughout the clinical trial period. The description of quality control and quality assurance system including systematic, independent audits that existing quality control systems (e.g., study monitoring; monitoring the trial; data management systems; managing trial data) should be indicated. The protocol should indicate the quality assurance audits may be performed during course of the clinical trial and/or upon trial completion.

6.5.12. Ethics

Description of ethical considerations relating to the clinical trial.

6.5.13. Data Handling and Recordkeeping

Description of handling of data and record keeping related to the clinical trial.

6.5.14. Financing and Insurance

Financing and insurance, if not addressed in a separate document or agreement. Provision for no-fault compensation/treatment in the case of injury or death of a participant if attributable to their participation in the clinical trial, and any insurance or indemnity to cover the liability of the investigator(s) and sponsor.

6.5.15. Publication Policy

Publication policy, if not addressed in a separate agreement.

6.5.16. Supplements

Since the protocol and the clinical trial report are closely related, further relevant information can be found in the ICH Guidance for Structure and Content of Clinical Study Reports.

6.6. ETHICAL COMMITTEE REVIEW AND APPROVAL OF THE PROTOCOL

Clinical trial studies must be reviewed and receive prior written approval from National Research Ethical Committee of the Federal Democratic Republic of Ethiopia (NRERC) and Institutional Review Board of the Federal Democratic Republic of Ethiopia (IRB) prior to enrolment of study participants. Such approval may be conditional or unconditional and sponsor shall strictly adhere to any conditions prior to the enrolment of study participants.

The investigator generally assumes responsibility for obtaining IRB and NRERC review of the study protocol. Copies of any approval are then provided to the sponsor.

The approval letter of the NRERC and of the IRB [level A] are required for all clinical trials. Hence, such approval letter(s) with copy of the approved protocol should be provided for review by the Authority.

6.7. TRIAL SITE(S) AND INVESTIGATOR (S)

The complete address of the clinical site(s) showing the activities performed at the site(s) should be described. Where, the study involves analysis of analyte(s) from biological fluid, the complete address of a bio-analytical site should be included.

There should be adequate number of qualified investigators to conduct the proposed clinical trial. The investigator's curriculum vitae or other statement of education, training and experience may provide initial information about the investigator's qualifications to provide medical care and to conduct clinical research. Such information should be provided using the format indicated in Annex VI.

6.8. SUPPORTING DATA FOR THE INVESTIGATIONAL PRODUCT

Sufficient safety and efficacy data from non-clinical studies and/or clinical trials should be available to support human exposure by the route, at the dosages, for the duration, and in the trial population to be studied.

The sponsor should update the Investigator's Brochure as significant new information becomes available

The information on the investigational product should at least contain:

- Product Description
  - Name, strength, dosage form, doses to be administered, route of administration and the source of the drug
  - Name and address of the manufacturer
  - Complete composition of the product(s)
- Certificate of pharmaceutical product (CPP) if applicable and GMP certificate
- Information about manufacturing procedures
- Tests performed on the actual product to establish that the product is of suitable quality for the intended investigational use (Attach Certificate of Analysis).
- Information on safety and efficacy collected in previous and ongoing clinical trials elsewhere with the investigational product
- For chemical or biological methods to control disease vectors state clearly any potential risks involved to both human populations and other environmental components. Indicate the measures planned to evaluate and mitigate possible environmental changes.
- Manufacturing, Packaging, Labelling, and Coding Investigational Product(s)
- The sponsor should ensure that the investigational product(s) (including active comparator(s) and placebo, if applicable) is characterized as appropriate to the stage of development of the product(s), is manufactured in accordance with any applicable GMP, and is coded and labelled in a manner that protects the blinding, if applicable. In addition, the labelling should comply with applicable regulatory requirement(s).
- The sponsor should determine, for the investigational product(s), acceptable storage temperatures, storage conditions (e.g. protection from light), storage times, reconstitution fluids and procedures, and devices for product infusion, if any. The sponsor should inform all involved parties (e.g. monitors, investigators, pharmacists, storage managers) of these determinations.
- The investigational product(s) should be packaged to prevent contamination and unacceptable deterioration during transport and storage.

- In blinded trials, the coding system for the investigational product(s) should include a mechanism that permits rapid identification of the product(s) in case of a medical emergency, but does not permit undetectable breaks of the blinding.
- If significant formulation changes are made in the investigational or comparator product(s) during the course of clinical development, the results of any additional studies of the formulated product(s) (e.g. stability, dissolution rate, bioavailability) needed to assess whether these changes would significantly alter the pharmacokinetic profile of the product should be available prior to the use of the new formulation in clinical trials.

6.9. THE INVESTIGATIONAL PRODUCT (S): QUALITY, HANDLING AND ACCOUNTING

Quality of the investigational product is ensured by compliance with Good Manufacturing Practices (GMPs) and by handling and storing the product according to the manufacturing specifications and the study protocol. GCP requires that sponsors control access to the investigational product and document the quantity(ies) produced, to whom the product is shipped, and the appropriate management (for example, return or destruction in accordance with the protocol or with the instructions of the Authority) of any unused supplies.

GCP also requires investigators to control receipt, administration, and disposition of the investigational product. After approval of the clinical trial by the Authority, investigator/sponsor can request order permit to import investigational product(s) and comparator product (if applicable) using the requirements indicated on Annex VII.

Procedure for receiving, handling and storing, issuing and investigational products and comparator product (if applicable) should be provided by the sponsor.

6.10. ENROLLMENT OF PARTICIPANTS INTO THE STUDY: RECRUITMENT, ELIGIBILITY, AND INFORMED CONSENT

The clinical investigator has primary responsibility for recruiting clinical trial participants, ensuring that only eligible subjects are enrolled in the study, and obtaining and documenting the informed consent of each participant. Freely given, written, informed consent should be obtained from every clinical trial participant prior to clinical trial study participation. When a subject is not capable of giving informed consent, the prior written informed consent from a legally authorized

representative (such as mother, father or guardian) must be obtained in accordance with regulation No. 299/2013. When children aged between12 to 18 years are to be enrolled in the study, investigators need to sought prior written informed assent from the children, in addition to consent given by parents or guardian.

A description of participants' enrolment and/or recruitment procedure, inclusion and exclusion criteria and a procedure for obtaining and documenting the informed consent of each participant should be provided in the protocol. Copy(ies) of the informed consent form should be provided for review during application for authorization of the clinical trial. When the consent form is other than the local language of the study subjects, translation into the local language must be made available.

6.11. TRIAL DATA ACQUISITION: CONDUCTING THE TRIAL

Research should be conducted according to the approved protocol and applicable regulatory requirements. Study records documenting each trial - related activity provide critical verification that the study has been carried out in compliance with the protocol.

Case report forms (CRFs) for each scheduled study visit to capture all the necessary data collected from and reported for each participant should be developed and a copy of this CRF/eCRF should be provided for review during application of clinical trial authorization.

6.12. SAFETY MANAGEMENT AND REPORTING

The sponsor has primary responsibility for reporting of study safety data to EFMHACA and other investigators and for the ongoing global safety assessment of the investigational product. A data and safety monitoring board (DSMB) may be constituted by the sponsor to assist the overall safety management. Even though reporting of study safety data is the primary responsibility of the sponsor, the principal investigator must report serious adverse event and the measures taken to manage the AE to the Authority, in writing, within 48 hours of occurrence of the event, even if the AE is considered not to be related to the research procedures with the format indicated in **ANNEX VII**. Summary of other non-serious adverse events should be reported every six months together with the progress in tabulated form as annexed in ANNEX IX.

6.13. MONITORING THE TRIAL

Sponsors generally perform site monitoring of a clinical trial to ensure high quality trial conduct. The sponsor may perform such monitoring directly, or may utilize the services of an outside individual or organization (e.g., contract research organization [CRO]). The sponsor determines the appropriate extent and nature of monitoring based on the objective, purpose, design, complexity, size, blinding, and end points of the trial, and the risks posed by the investigational product.

The monitor should be independent of the clinical trial scientific working team and a full address of the monitor should be provided.

6.14. MANAGING TRIAL DATA

Within GCP, managing clinical trial data appropriately ensures that the data are complete, reliable and processed correctly, and that data integrity is preserved. Data management includes all processes and procedures for collecting, handling, manipulating, analyzing, and storing/archiving of data from study start to completion.

The sponsor bears primary responsibility for developing appropriate data management systems. The sponsor and the investigator share responsibility for implementing such systems to ensure that the integrity of trial data is preserved.

Data management systems should address (but not limited and as applicable):

- data acquisition;
- confidentiality of data/data privacy;
- electronic data capture (if applicable);
- data management training for investigators and staff;
- completion of CRFs and other trial - related documents, and procedures for correcting errors in such documents;
- coding/terminology for adverse events, medication, medical histories;
- safety data recording, management and reporting;
- data entry and data processing (including laboratory and external data);
- database closure;
- database validation;

- secure, efficient, and accessible data storage;
- data quality measurement (i.e., how reliable are the data) and quality assurance;
- management of vendors (e.g., CROs, pharmacies, laboratories, software suppliers, off- site storage) that participate directly or indirectly in managing trial data.

6.15. QUALITY ASSURANCE OF THE TRIAL PERFORMANCE AND DATA

Quality assurance (QA) verifies through systematic, independent audits that existing quality control systems (e.g., study monitoring). Quality assurance audits may be performed during the course of the clinical trial and/or upon trial completion. Sponsors bear primary responsibility for establishing quality systems and conducting quality assurance audits.

Quality assurance procedures should be described during submission for authorization of clinical trial conducted in the country.

6.16. REPORTING AND END OF THE TRIAL

a. Periodic Update and Final Report

Formats for biannual progress reports of the clinical trial study should be provided. The final report of the clinical trial should be as per ICH E3 "Structure and Content of Clinical Study Reports" guidelines.

Where permitted, abbreviated or less detailed reports may be acceptable for uncontrolled or aborted studies.

Format for periodic report should consider points such as:

- Protocol deviation
- Protocol amendment
- SAE report (in multi-center study overall safety report (if applicable)
- Recruitment status
- A discussion of any interim analyses

b. End/Termination of Trials

The Authority should be informed with an official letter of the sponsor when discontinuation/termination of the clinical trial occurs either prematurely, or upon suspension or upon the end including completion of the objectives of the clinical trial. The investigator/sponsor

should provide written commitment letter indicating that the Authority will be informed when any such discontinuation/termination of the trial occurs and also upon completion of the trial, to provide the findings of the study (for review) before dissemination. This commitment letter must be submitted during application for clinical trial authorization. The official letter of the sponsor must be provided to the Authority within 90 days of the end of a clinical trial by the sponsor.

The definition of the end of the trial should be provided in the protocol by the sponsor. An earlier end of the clinical trial which is not based on grounds of safety, but on other grounds, such as faster recruitment than anticipated, is not considered as 'early termination'.

In the case of early termination of any clinical trial, the sponsor must notify the end of the trial to the Authority immediately and at the latest within 15 days after the trial is halted, with clear reasons and justification, and describe follow- up measures, if any, taken for safety reasons.

7. CLINICAL TRIAL SUMMARY REPORT

A clinical trial summary report is part of the end of trial notification, even if usually submitted only subsequently to the end of trial notification. The sponsor should provide this summary report to the Authority within one year of the end of the complete trial for non-paediatric clinical trials and six months for paediatric clinical trials.

If the trial is prematurely ended or terminated or suspended for any reason, the investigator should promptly inform the trial participants, should ensure appropriate therapy and follow-up for the participants.

Sponsor/investigator should notify and obtain prior written approval from the Authority before dissemination of the results of the research in accordance with article 24 of Regulation No. 299/2013. Hence, publication and dissemination of results of the research should be conducted after submission of the final clinical report and written approval from the Authority.

8. APPLICATION FOR CLINICAL TRIAL AMENDMENTS

Amendments to be made to the conduct of a clinical trial after its commencement may be allowed. Amendments must be notified to the Authority and where relevant, the NRERC and the IRB. In addition, when a sponsor and/or investigator must take urgent safety measures to protect the trial participants from immediate hazard allows them to do so before notifying the Authority, but they must notify the participants in writing as soon as possible.

Major amendments to the conduct of the clinical trial which may arise from changes to the protocol or from new information relating to the scientific documents in support of the trial should be submitted for approval. However, investigator/sponsor can implement minor amendments immediately after submission and proper categorization of amendments are confirmed in writing by the Authority.

The sponsor or sponsor representative (principal investigator in some case, if appointed by the sponsor) are responsible for the submission of major amendments to the Authority prior to the implementation of such amendments in the conduct of the clinical trial.

The application should include the application form set out in Annex IX and the proposed version of the clinical trial protocol and/or other documents affected by the proposed change, with an explanatory cover letter of the sponsor to the Authority. The applicant must submit the original wording, revised wording, and rationale for the change including a copy of a complete protocol incorporating all amendments.

9. ACTION OF THE AUTHORITY

Where the Authority has objective grounds for considering that the sponsor or the investigator or any other person involved in the conduct of the clinical trial no longer meets the obligations laid down in this Guideline, it shall forthwith inform him thereof, indicating the course of action which s/he must take to remedy this state of affairs. The Authority shall inform the NRERC and the IRB, and other competent authorities of this course of action.'

The 'course of action' of the Authority should include a timetable for its implementation and a date when the sponsor should report back to the Authority on the progress and completion of its implementation.

The sponsor should ensure that the 'course of action' set by the Authority is immediately implemented and report to the Authority on the progress and completion of its implementation in accordance with the timetable set by the Authority.

10. PENALTIES

Any investigators or sponsor conducting a clinical trial in violation of this Guideline shall be penalized in accordance with national laws and regulations.

11. INAPPLICABLE GUIDELINES

Any customary practice or previous guidelines which is inconsistent with this guideline shall not be applicable with respect to those matters provided in this guideline.

12. EFFECTIVE DATE

This guideline is effective starting from the date of 08 July 2017. All clinical trials conducted in Ethiopia shall comply with the requirements of this guideline.

ANNEXES

ANNEX I: APPLICATION FORM FOR APPROVAL OF CLINICAL TRIAL CONDUCTED IN ETHIOPIA

Food, Medicine and Health Care Administration and Control Authority of Ethiopia

A. Trial Identification:

1. Name of scientific working group ……
   ……..
2. Title of clinical trial……...
   ……
   ……
3. Phase of the clinical trial……
4. State the objective of the trial and the reasons thereof……
   ……
   ……
5. Duration of (time period for) the trials…….

B. Sponsor Identification

1. The name of the sponsor of the trial……
2. Full address of the sponsor……
   ……

C. Details of investigator (s)

State the name(s), telephone number(s) and qualification of the person (s) who will conduct the trial

Name	Qualification	Address & telephone number	Email address

D. Details of CRO and/or Clinical trial sites

1. State the name(s), physical address and telephone number of the institution (s) or places where the trial will be conducted. Detail name and address of CRO, Clinical sites, bio analytical site (if required), statistical analysis sites etc. should be provided
   ……
   ……
2. Statement on the capacity of the institutions /trial site to carry out the clinical trial……
   ……
   …….

E. Information on the Investigational product(s), comparator and other concomitantly used medicines/products

1. State the name of the investigational product, its chemical composition, and empirical formulae: ----------
   ----

   ----
2. Therapeutic effect of investigation products
   ……
   ……
   ……
   ……..
3. Administration route, dosage, dosage interval and duration for investigational product and drug being used as a
   control……
   ……
   …….
4. State the name and address of the manufacturing site……
5. Product used as comparator (placebo/other therapy)……...
6. State whether any other medicines/product will be given concomitantly, Yes/No
   If yes, please indicate the name of the medicine/product…….
   ……
   ……

F. Population of the trial participant

1. Description of the participants (e.g. age group of the subjects, type of study participant, sex)……
   ……..……..
2. Number of participants expected to take part and Justification thereof (based on statistical consideration)…….
   ……..……
   ……

G. Ethical committee

1. Is this clinical trial protocol approved by National Research Ethics Review Committee (NRERC)? Yes/No
   If No, Please provide the reasons thereof…….
   ……
   ……
2. Is this clinical trial protocol approved (has got favorable opinion) by Institutional Review Board (IRB), Level A? Yes/No
   If No, Please provide the reasons thereof…….
   ……
   …….
3. If any, Please specify the name and address of other Ethical clearance certificate related to this clinical trial. ……
   …….

H. Insurance

1. Description of the name and address of the company who will insure all the subjects in the proposed trial…….
   ……
   …….
2. State the amount of insurance in respect of each participant…….
   ……..……

Signature of principal investigator Signature of sponsor

…… ……..

Name and address of principal investigator Name and address of the sponsor

Date…….

Date:…….

Stamps

FOR OFFICIAL USE ONLY

Date of Approval……

Signature of the person to sign on the behalf of the Authority

Name……

Position……..

Signature ……..

Date of Rejection and the reasons (if)……..

……

Trial information documents attached:

- Clinical trial protocol
- investigator's brochure
- investigational supplies accountability forms
- signature logs
- case report forms (CRFs)
- informed consent documents
- adverse event or safety reporting forms;
- administrative forms to track research funds and expenses;
- forms to disclose information about the investigator's financial, property, or other interests in the product under study

- formats for reports of monitoring visits;
- Insurance certificate
- Formats for progress reports, annual reports, and final study reports etc.

ANNEX II: AGREEMENT MADE PRIOR TO COMMENCEMENT OF CLINICAL TRIAL

Name of scientific working group (study team):

1. The Sponsor: ……..

2. The Investigator(s): ……

3. Other (if any):……

4. Name of the clinical trial (project):……..

We hereby agree, in the capacity of principal investigator, the sponsor, and the site of the clinical trial in the above-named project to conduct the investigation in accordance with the statements and procedures stipulated in the clinical investigation protocol agreed up on by the Food, Medicine and Health Care Administration and Control Authority of Ethiopia and ourselves.

We also agree to submit a copy of our findings to the Authority prior to its being published elsewhere in any manner or form.

Signature of principal investigator Date:_____

Signature of the sponsor Date: _____

ANNEX III: JOINT DECLARATION BY SPONSOR AND PRINCIPAL INVESTIGATOR CONCERNING SUFFICIENT FUNDS TO COMPLETE STUDY

Title:……
…….

Protocol No:…….

I, <full name>, representing <sponsor >

And

I, <full name>, Principal Investigator

Hereby declare that sufficient funds have been made available to complete the above- identified clinical trial study.

Signed Date

SPONSOR

Name

Address

Contact details

Signed Date

PRINCIPAL INVESTIGATOR

Name

Address

Contact details

ANNEX IV: DECLARATION BY INVESTIGATOR(s)

Name:

Title of Trial:

Protocol:

Site:

I/We, the undersigned have submitted all requested and required documentation, and have disclosed all information which may influence the approval of this application.

I/We, the undersigned, hereby declare that all information contained in, or referenced by, this application is complete and accurate and is not false or misleading.

I/we am (are) familiar with internationally accepted standards of Good Clinical Practice (GCP) and understand the responsibilities and obligations of the Principle Investigator within the context of this study.

I/we have thoroughly read, understood, and critically analyzed the protocol and all applicable accompanying documentation, including the investigator's brochure, patient information leaflet(s) and informed consent form(s).

To the best of my/our knowledge, I/we have the potential at the site(s) I/we am (are) responsible for, to recruit the required number of suitable participants within the stipulated time period.

I/we will not commence with the trial before written authorizations from the relevant Research Ethics Committee(s) as well as the Authority have been obtained.

I/we will obtain informed consent from all participants or if they are not legally competent, from their legal representatives.

I/we will ensure that every participant (or other involved persons), shall at all times be treated in a dignified manner and with respect.

Using the broad definition of conflict of interest below, I declare that I have no financial or personal relationship(s) which may inappropriately influence me in carrying out this clinical trial.

[Conflict of interest exists when an investigator (or the investigator's institution), has financial or personal associations with other persons or organizations that may inappropriately influence (bias) his or her actions.]

I/we have / have not (delete as applicable) previously been the principal investigator at a site which has been closed due to failure to comply with Good Clinical Practice.

I/we have / have not (delete as applicable) previously been involved in a trial which has been closed as a result of unethical practices.

I/We, the undersigned, agree to ensure that if the above-said clinical trial is approved, it will be conducted according to the submitted protocol and all applicable legal, ethical, regulatory requirements and in accordance with GCP.

Signature of principal investigator: Date: _____

Name:

Signature of co-investigator: Date: _____

Name

ANNEX V: RECOMMENDED FORMAT FOR CVS OF INVESTIGATORS IN CLINICAL TRIALS

1. Study Title:
2. Protocol Number:
3. Designation:
4. Personal Details
    - Name:
    - Work Address:
    - Telephone Number:
    - Fax Number:
    - Cell-phone Number:
    - e-mail address:
5. Academic and Professional Qualifications
6. Professional registration status
7. Relevant related work experience (brief) and current position
8. Participation in clinical trials research in the last five years

   [Study title, protocol number, designation. If multiple trials, only list those with relevance to this application, or in the last year]
9. Peer-reviewed publications in the past five years
10. Date of last GCP training

    [As a participant or presenter]
11. Any additional relevant information supporting abilities to participate in conducting this trial

    [Briefly]

Signature:……

Date:……..

ANNEX VI: REQUIRED DOCUMENTATION FOR AUTHORIZING THE IMPORTATION OF THE INVESTIGATIONAL AND COMPARATOR PRODUCTS

Investigational product (s): Name/code of the products

IMPORTATION AND RELEASE OF INVESTIGATIONAL MEDICINAL PRODUCTS			
Checklist of required documentation			
Are the following documents attached and correct, as indicated:			
S. No.	Description	Yes	No.
1	Copy of the letter of approval of clinical trial by the Authority		
2	Certificate(s) of Analysis (CoA) of • investigational product (s) • comparator product (if applicable)		
3	Copy of valid GMP certificate of Manufacturer issued by the competent NRA in the country of manufacture.		
4	CPP issued by competent NRA in the country of manufacture-if applicable		
5	Device/Proof of maintenance of cold chain (if applicable)		
6	Sample of actual labeling materials and/or color print (Outer packaging & immediate container): Should show-the following information		
	Product name or unique code (if blinded)		
	That the product is clinical trial material e.g. “For use in clinical trial only”.		

	Does this concur with the information on the Cover Sheet		
	Storage temperature		
	Batch number		
	Date of Manufacture and expiry date		
	Sponsor contact details		

ANNEX VII: SERIOUS ADVERSE EVENT REPORTING FORM

PROTOCOL AND EVENT TYPE	
Study title	
Protocol No.	
FMHACA Ref. No.	
Date of this report	
Seriousness of adverse event (choose one)	Death Life-threatening Initial or Prolonged hospitalization Disability Congenital Anomaly Required intervention to prevent permanent impairment Other medically important condition
Severity of the event	Minimum Moderate Sever Life-threatening Fatal
Was this event expected in terms of its severity?	Yes No
Was this event expected in terms of its specificity?	Yes No
Relationship of event to gene transfer product	Unrelated Unlikely Possible Probable Definite
Attribution of AE	Concomitant medication Product Intervention Underlying disease Route of administration Other suspected cause (describe)
DEMOGRAPHICS	

PI Name	
Name of Clinical Trial site/Organization	
PI Telephone No.	
PI E-mail Address	
Reporter Name	
Reporter Telephone No.	
Reporter E-mail Address	
Research Participant's study identification number	
Research Participant's gender	
Research Participant's date of birth	
Research participant's date of death (if any)	
Research Participant's weight in kg	
Research participant's height in cm	
Which arm/cohort/treatment group was the participant assigned to?	
Which arm/cohort/treatment group was the subject assigned to?	
Was the participant dosed?	Yes No Information not available
What study product was received	Investigation product Placebo Comparator product
Were there any protocol deviations/violations/Exceptions for this participant?	Yes: (if yes, indicate in detail) …… …… …… No
DETAILED ADVERSE EVENT INFORMATION	
Adverse event date	

Description of events	
Relevant tests (e.g. X-rays) and results	
Treatment (s) of adverse events (include medications used to treat this event)	
Name of Concomitant Medications (Do not include medications used to treat this event)	
Pre-existing conditions/relevant clinical history (if this is an oncology trial, please designate primary disease, e.g. Ovarian Cancer)	
Date(s) of treatment(s) of the adverse event	
Was autopsy performed?	Yes No
Date of autopsy, if yes for 3.7	
Outcome of event	Recovered/Resolved Recovering/Resolving Not recovered/not resolved Recovered/resolved with sequelae Fatal Unknown
Documentation accompanying the report (e.g. H & P, Progress notes, discharge summary, lab or autopsy reports, other, etc)	
PRODUCT AND DOSING INFORMATION	
Name of investigational product	
Generic name	
Batch/Lot Number	
Manufactured date	
Expiry date	
Name and address of the manufacturing site	
Route of administration	

Site of administration	
Did the participant receive the dose specified in the protocol	
If not for 4.9, what dose was given?	
Date of first exposure of the product	
Date of most recent exposure of the product	
Total dose received prior to the event	
Total dose quantity administered to the participant to date	
Unit of measure of a single dose	
Dose quantity in a single administration	
If course used, how many were given prior to this event?	
How many doses on the last course were given?	
Was the administration of this product stopped because of this adverse event?	
Name of other treatment (s) (medications, radiation, surgery) received by research participant as required by the protocol	

ANNEX VIII: NOTIFICATION FOR MAJOR AMENDMENT TO CLINICAL TRIAL CONDUCTED IN ETHIOPIA

DATE OF APPLICATION: _____

IDENTIFICATION OF TRIAL

- Title of clinical trial:

  _____

  _____

  _____

  _____
- Previous Approval number and date of approval: _____, _____
- Previous protocol No.: _____
- Principal Investigator: _____
- Sponsor:_____

  _____

MAJOR AMENDMENT IDENTIFICATION:

- Amendment to information in the CT application form yes ☐ No ☐
- Amendment to the protocol yes ☐ No ☐
- Amendment to other documents appended to the initial application form yes☐ No☐
- Amendment to other documents or information: yes☐ No☐
- This amendment concerns mainly urgent safety measures already implemented yes☐ No ☐
- This amendment is to notify a temporary halt of the trial yes ☐ No ☐
- This amendment is to request the restart of the trial yes ☐ No ☐
- If Other please specify_____

  _____

  _____

  _____

BRIEF DESCRIPTION OF THE CHANGE:

_____

_____

_____

_____

_____

_____

REASONS FOR THEMAJOR AMENDMENTS:

- Changes in safety or integrity of trial participants yes ☐No ☐
- Changes in interpretation of scientific documents/value of the trial yes ☐No ☐
- Changes in quality of investigational product(s) yes ☐No ☐
- Changes in conduct or management of the trial yes ☐ No☐
- Change or addition of principal investigator(s), co-coordinating investigator yes☐ no ☐
- Change of sponsor yes ☐ No ☐
- Change/addition of site(s) yes ☐ No ☐
- Change in transfer of major trial-related duties yes ☐ No ☐
- If other changes_____

  _____

  _____

  _____

OTHER REASONS FOR MAJOR AMENDMENT:

_____

_____

_____

_____

_____

_____

_____

I/We, the undersigned, agree to conduct / manage the above-mentioned trial under the conditions as stated in this application.

(The person(s) undertaking legal responsibility to sign this form).

Signature of principal Investigator:_____ Date_____

Name:_____

Signature of Sponsor:_____ Date_____

Name & Position_____

ANNEX IX: CLINICAL TRIAL ADVERSE EVENT (AE) REPORTING FORMAT

Reporting Date:……

Clinical Trial:……

Clinical Trial site:……

Principal Investigators…… Signature…… Date……

S. No	*Participant ID*	*Age*	*Sex*	*Treatment type**	*Date of AE*	*Description of AE*	*Severity grading **	*Causality results*** *	*Outcome#*	*Measures taken*	*Remark*
1											
2											
3											

*investigational product or placebo or comparator product

**Severity grading: Grade 1= mild, Grade 2=moderate, Grade 3= Severe and Grade 4= Life treating

***Causality results can be certain, Probable/likely, possible, unlikely, conditional, unclassified etc.

Outcome in the form of Fatal, Not resolved, Resolved, Resolved with sequelae, Resolving and Unknown

REFERENCE

1. Detailed guidance on the application format and documentation to be submitted in an application for an Ethics Committee opinion on the clinical trial on medicinal products for human use, Revision 1, Enterprise and Industry Directorate-General, Consumer goods, Pharmaceuticals European Commission, February 2006.
2. Detailed guidance for the request for authorization of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial, Revision 2, European commission Enterprise Directorate-general, Brussels, October 2005.
3. Guideline for Good Clinical Practice, E6(R1), Current Step 4 version, dated 10 June 1996, ICH Harmonized Tripartite Guideline.
4. Guideline for Good Clinical Practice, E6(R2), Current step 4 version, dated 09 November, 2016, ICH Harmonized Tripartite Guideline.
5. Guidance for Industry, E6 Good Clinical Practice: Consolidated Guidance, Center for Drug Evaluation and Research (CDER) Available at http://www.fda.gov/cder/guidance/index.htm
6. Guidelines for Good Clinical Trial Practice in Zimbabwe, 2012, Medicine Control Authority of Zimbabwe.
7. Handbook for good clinical research practice (GCP): Guidance for implementation, 2002, World Health Organization, Geneva, Switzerland.
8. Kalberg, Johan Petter, Einar (2010), Reviewing Clinical Trials: A guide for the ethical committee, Hong Kong, PR China.
9. National Research Ethics Review guideline, Fifth Edition, 2014, FDRE Ministry of Science & Technology, Addis Ababa, Ethiopia.
10. Standard Operating Procedure for Clinical Trial Authorization, SOP for CTA-Version1, 28-June-06, Clinical Trials office, London and Leiden

WORKSHOP PARTICIPANTS

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