ETHIOPIAN FOOD AND DRUG AUTHORITY

GUIDELINE FOR CLINICAL TRIAL AUTHORIZATION

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Document History

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001	New version	Dec 2009
002	To separate the CT authorization guideline and CT inspection to harmonize with international standards and practice	June 2017
003	To revise and update the existing version	April 2023
004	To incorporate recommendations of stakeholders	Aug 2024
005	To align with QMS document control SOP formatting; to align the timeline for non-routine application review and further review for non-routine; to incorporate an evaluation timeline for safety report and CT application form and omit CT evaluation checklist.	May 2025

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Signature:

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The Authority would also like to give special acknowledgement to 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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ACRONYMS

AE	Adverse Events
ADRs	Adverse Drug Reactions
CPP	Certificate of Pharmaceutical Product
CRF	Case Report Form
CRO	Contract Research Organization
DSMB	Data and Safety Monitoring Board
eCRF	Electronic Case Report Form
EFDA	Ethiopian Food and Drug 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
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
IB	Investigator's Brochure
IP	Investigational Product

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 and Medicine Administration Proclamation No. 1112/2019 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 and order the clinical trial to be suspended or stopped 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 staff 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 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. I also call upon interested parties to continue their support by forwarding their comments and suggestions to the EFDA P.O.Box 5681 Addis Ababa, Ethiopia., Tel.251-115524122, e-mail: contactefda@efda.gov.et.

Heran Gerba Director General, EFDA

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 serve a base for the development of Good Clinical Practice (GCP) at an international level, later developed by the International Council for Harmonization (ICH).

According to article 4 sub article 11 of the Food and Medicine Administration Proclamation No. 1112/2019, a national executive authority is responsible to authorize the conduct of clinical trials, monitor the process as to its conduct in accordance with 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 27 of this Proclamation provides further detail on the requirements for clinical trials.

To implement the Proclamation No. 1112/2019, Ethiopian Food and Drug Administration was established by Council of Ministers Regulation. The current Food and Drug Administration council of Ministers regulation provides a detailed description of responsibilities and activities of the Authority, investigators and/or sponsors.

This Guideline supersedes the previous guideline developed based on Proclamation No. 661/2009. The previous guideline was unable to answer the current scientific developments and international regulatory requirements. Hence, this requires the need for revision and updating of the 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.1112/2019, current regulation and directive No.964/2023.

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

Amendments to the authorized 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 twelve 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.

2. SCOPE

This guideline applies to the application, review, authorization, and good clinical practice of clinical trials conducted on investigational Products or new combinations of medicines, biological products including vaccines, new therapeutic regimens, diagnostic procedures, bioequivalence or bioavailability studies and medical procedures.

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 sponsors or applicants on the documents and process requirements for the conduct of clinical trials in Ethiopia.
- To guide the Sponsors or applicants regarding the requirements, review process and timelines for clinical trial authorization.
- To guide the period and the content of the (progress & final) report and adverse events

reporting in relation to clinical trials conducted in Ethiopia.

- To guide Sponsors or applicants on contents and steps for applications submission to be handled by non-routine clinical trial procedures.
- To describe the roles and responsibilities of key stakeholders in Clinical trial regarding compliance of Good clinical Practice.

4. DEFINITIONS

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

Any untoward medical occurrence that may be present during treatment with a medicine but does not necessarily have a causal relationship with this treatment, that is, an adverse outcome that occurs while the patient is taking the medicine but is not, or not necessarily, attributable to it.

Amendment

A written description of a change(s) to or formal clarification of a protocol

Assent

The agreement to participate in research by people who are 12-17 years and too young to give informed consent but who are old enough to understand the proposed research.

Authority

Ethiopian Food and Drug Authority

Bioavailability Study

A pharmacokinetic study that demonstrates the rate and extent to which the active ingredient is absorbed from a drug product and becomes available at the site of action.

Bioequivalence Study

A special study where two drugs or two sets of formulations of the same drug are compared to show that they have nearly equal bioavailability and Pharmacokinetic/Pharmacodynamics parameters.

Biological Products

Diverse group of medicines which includes products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues and recombinant therapeutic proteins.

Case Report Form

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

Clinical Trial

Any systematic study on medicines, biological products including vaccines or medical procedures in volunteer human participants in order to discover or verify the effects of, and/or identify any adverse reaction to the products, and or to study its absorption, distribution, metabolism, and excretion with the object of ascertaining their efficacy and safety.

Clinical Trial Report

A written description of a detailed report of an authorized clinical trial conducted on human subjects, in which the clinical description, presentations, and analyses are fully integrated into a single report.

Compassionate Use

A way to provide investigational therapy to a patient who is not eligible to receive that therapy in a clinical trial, but who has a serious or life-threatening illness for which other treatments are not available.

Contract Research Organization

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.

Consent

A process by which a participant 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 participant's decision to participate.

Data Safety Monitoring Board

An independent data-monitoring committee that maybe established by the sponsor to assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints and to recommend to the sponsor whether to continue, modify, or stop a trial.

Expedited Review

Reviewing and approving clinical trials following a fast-track or non-routine procedure during public health emergencies, addressing public health interest, or where access to new therapies needs to be made faster than the routine timelines to save or dramatically improve patients' lives are necessary.

Good Clinical Practice

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

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

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.

Independent Ethics Committee

An independent body (a review board or a committee, institutional, regional, national, or supranational), constituted of medical professionals and non-medical members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial and 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 participants.

Investigator's Brochure

A collection of data consisting of all the information known before the trial concerning the clinical and non-clinical data on the investigational product

Investigational Labeling

Labeling developed specifically for products involved in a clinical trial.

Investigational Product

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.

Principal Investigator

A medical practitioner, dentist, or other qualified person who is a resident of the country and is responsible for conducting the clinical trial at a trial site.

Sub-investigator/Co-investigator

Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions.

Monitor

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.

Multi-center Trial

A clinical trial conducted according to a single protocol but at more than one site, and therefore by more than one investigator.

Placebo

An inactive treatment, be it in a pill or tablet form or it may be in any pharmaceutical dosage form and often looks like and tastes an investigational product that is being studied except with no effect on the disease the new investigational product is intended to treat.

Proclamation

The Food and Medicine Administration Proclamation No. 1112/2019.

Protocol

A document that describes the objective, design, methodology, statistical considerations, and organization of the trial, giving background and rationale of the trial.

Essential Document

Documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. and demonstrating the compliance of investigator's, sponsor's and monitor's with the standards of GCP and all applicable regulatory requirements.

Source Document

Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, participants' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, photographic negatives, microfilm or magnetic media, x- rays, subject files, and records kept at the pharmacy and laboratories involved in clinical trials).

Source Data

All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial are necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).

Protocol Deviation

Accidental or unintentional changes to, or non-compliance with the research protocol that does not increase risk or decrease benefit or does not have a significant effect on the subject's rights, safety or welfare; and/or on the integrity of the data.

Protocol Violation

Accidental or unintentional change to, or non-compliance with the IRB approved protocol without prior sponsor and IRB approval. Violations generally increased risk or decrease benefit, affect the participant's rights, safety, or welfare, or the integrity of the data.

Serious Adverse Event

Any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

Sponsor

An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.

Study Participant

An individual who participates in a clinical trial, either as a recipient of the investigational product(s) or as a control.

Randomization

The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

Blinding/Masking

A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the participant(s) being unaware and double- blinding usually refers to the participant(s), investigator(s) and monitor being unaware and triple blind participant(s), investigator(s) and data analyst(s) being unaware of the treatment assignment(s).

Developmental Safety Update Report

It is a per-marketing periodic report which covers safety information of new drugs, marketed drugs under study and biological products including vaccines under development.

Suspected Unexpected Serious Adverse Event

An adverse event that occurs in a clinical trial subject, which is assessed by the sponsor and or study investigator as being unexpected, serious and as having a reasonable possibility of a causal relationship with the study drug.

Study: Is used as a synonym for trial

5. GENERAL GUIDANCE FOR PREPARATION OF DOCUMENTS FOR CLINICALTRIAL 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 content: title, nature, and their purpose should be clearly stated. They should be submitted in duplicate paper format to make it 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 pages 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 as per the specified period described in clinical trial directive 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. REQUIREMENTS FOR SUBMISSION OF CLINICAL TRIAL APPLICATIONS AND REVIEW PROCESS

6.1. SUBMISSION REQUIREMENTS

APPLICATION FORM

During the initial application, the Sponsor/Applicant completes the application form as indicated in Annex-I and submits one hard copy and one soft copy of the protocol and related documents. Once the application is received, the authority will begin screening the application to determine if it is a clinical trial or not and a decision on screening will be made within seven working days for routine clinical trial application and within four working days for non-routine trial applications. If the application is really a clinical trial, a comprehensive protocol evaluation should be performed, and the applicant is required to provide two final hard copies of the protocol and accompanying documents after incorporating all relevant authority comments and one copy with the authority's stamp shall be returned to the applicant.

SERVICE FEE

The applicant shall pay the required payment in accordance with the current Rate of Service Fees regulation of Food and Drug Administration. The Authority shall not consider applications unless applicable fees have been paid in full.

AGREEMENTS AND DECLARATIONS

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) are included in Annex IV.

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.

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 who is responsible for all trial-site related medical 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.

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 are relevant to the trial requirement for submission and evaluation of non-clinical data including formats for submission and checklist for evaluation.
- 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.

Trial Objectives and Purpose

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

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.

Phase of Clinical Trial

The phase of the clinical trial should be clearly indicated in the specified protocol based on the trial objective. Clinical trials are generally classified into four phases. A brief description of the individual phases, based on their purposes as related to clinical development of medicinal products, is given below:

Phase I - These are the first trials of a new active ingredient or new formulations in man, often carried out in 20 to 100 healthy volunteers or people with the disease. Their purpose is to establish a preliminary evaluation of safety, and a first outline of the pharmacokinetic and, where possible, a pharmacodynamic profile of the active ingredient in humans.

Phase II - These trials are performed in a limited number of study participants (up to several hundred people with the disease/ condition). Their purpose is to demonstrate therapeutic activity and to assess short-term safety of the active ingredients in patients suffering from a disease or condition for which the active ingredient is intended. This phase also aims at the determination of appropriate dose ranges or regimens and (if possible) clarification of dose response relationships in order to provide an optimal background for the design of extensive therapeutic trials.

Phase III - Thousands of volunteer trial participants with the disease of interest are normally required for this phase to be conducted in Ethiopia. Trials in larger (and possibly varied) patient groups with the purpose of determining the short and long-term safety/efficacy balance of formulation(s) of the active ingredient, and of assessing its overall and relative therapeutic value. The pattern and profile of any frequent adverse reactions must be investigated, and special features of the product must be explored (e.g. clinically relevant drug interactions, factors leading to differences in effect such as age). These trials should preferably be of a randomized double-blind design, but other designs may be acceptable, e.g. long-term safety studies. Generally, the conditions under which these trials are carried out should be as close as possible to normal conditions of use.

Phase IV - Studies performed after marketing of the medicinal product. Trials in phase IV are carried out on the basis of the product characteristics on which the marketing authorization was granted and are normally in the form of post marketing surveillance, or assessment of therapeutic value or treatment strategies. Although methods may differ, these studies should use the same scientific and ethical standards as applied in premarketing studies. After a product has been placed on the market, clinical trials designed to explore new indications, new methods of administration or new combinations, etc. are normally considered as trials for new medicinal products.

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.

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.

Assessment of Efficacy

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

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.

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, evaluate able participants).

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.

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 the course of the clinical trial and/or upon trial completion.

Ethics

Description of ethical considerations relating to the clinical trial.

Data Handling and Record keeping

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

Insurance and compensation

Research participants should not bear any financial cost to rectify harms that occur as a result of trial participation. It is thus essential that provision is made for comprehensive insurance against trial related injury. In Ethiopia, it is mandatory to have adequate comprehensive insurance cover for clinical trials participants. The following points should be taken into consideration:

- Sponsors adopt the morally right convention of paying for insurance cover for medical treatment in the event of trial-related injuries, including death.
- The insurer pays the medical costs of necessary treatment to restore the participant to his/her previous position, if possible. Payment of medical expenses by the insurer is triggered when bodily or other injury is attributable to trial participation.
- The provision of insurance cover and payment of medical expenses does not mean that an injured participant may not pursue legal action against the Sponsor to claim compensation based for negligence in an Ethiopian court for loss or harm not covered by the insurance.
- The insurance cover usually does not extend to situations where an IP fails to demonstrate its intended effect or to provide any other benefit to the participant
- The amount to be paid or the adequacy/sufficiency of payment will be determined by the seriousness of the case. Compensation disputes will be resolved by the legal court, and the Authority may be asked to provide technical reports/information.
- Any trial-related compensation claim should be provided in the participant information sheet (what they can claim, how to claim, and what level of coverage they have).

Publication Policy

Publication and result dissemination shall be clearly stated on the protocol according to the CT Directive.

ETHICAL COMMITTEE REVIEW AND APPROVAL OF THE PROTOCOL

There should be an independent Ethics Committee that reviews, approves a clinical application, and monitors the conduct of clinical trials that comply with ethical principles such as protecting the rights, welfare, and privacy of trial participants. The independent ethics committee's composition shall have members with professional competency, research ethics training, and experience balanced regarding relevant expertise, gender, age, and community representation and the committee should be independent of the investigator, the sponsor, or any other kind of undue influence.

An Independent National Ethics Committee shall review clinical trials under the following conditions:

- In the absence of a recognized Independent Ethics Committee within the institution where the trial is conducted
- Where the Independent Ethics Committee is unable to perform the ethical review activities according to the standards
- The clinical trial is conducted in more than one site or multi-center trial.

The investigator generally assumes responsibility for obtaining the Institutional Review Board (IRB) and/or National Research Ethics Review Board (NRERB) of the study protocol. Copies of any approval are then provided to the sponsor. The approval letter of the NRERB and/or of the IRB 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.

TRIAL SITE(S) AND INVESTIGATOR (S)

The full address of the clinical site(s) as well as the activities carried out at the site(s) should be described. Furthermore, if the study involves the analysis of analyte(s) from biological fluid, the full address of a bio-analytical site should be included. Adequate number of qualified investigators to conduct the proposed clinical trial should be available at the study site and the following information gives the Authority about investigator (s) qualification to provide appropriate medical care during the conduct of clinical trials,

1. Current workload of Investigator(s):
    - Number of studies currently undertaken by the investigator
    - The total number of patients represented by these studies.
    - Time-commitments of researchers(s) in relation to clinical trial work and non-trial work.
2. The investigator's curriculum vitae or other statements 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 V.

6.2. REVIEW PROCESS

Clinical trial protocol and essential documents submitted to the authority shall be reviewed by two or more experts. The authority may use the external assessors and advisory committee to review the clinical trial application and related documents.

A clinical trial application review may be conducted by a joint review with other countries' regulatory authorities and regional or international organizations based on agreements or collaborative initiatives. The Authority may recognize, receive and use the relevant clinical trial decisions, reports or information from other national regulatory authorities, regional and international bodies like WHO, AVAREF, EMA and USFDA.

The time of routine review at the authority shall be 45 working days to handle a duly completed application (including service fee) for first feedback; however, the review for a clinical trial with high

risk may be extended up to 90 calendar days whereas the review time for non-routine application will be 22 working days.

The applicant should submit the response within six months of receiving the authority's feedback. If it is not possible to respond in six months, the applicant shall notify the Authority before the elapse of the six months. When there is no sufficient justification for the delay, the authority shall reject responses made after six months and notify the applicant to make a new application to proceed with the trial

The application shall be rejected when the applicant cannot provide the requested information and make adequate changes to the protocol after feedback is provided in the form of a further request for three consecutive times. The time of routine and high-risk review for further replies should be within 20 working days whereas for non-routine should be10 working days.

7. THE INVESTIGATIONAL PRODUCT (S)

7.1. Quality, Handling and Accountability

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 authorization 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 VI.

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

7.2. Labeling and Dispensing of Investigational Products

Investigational, comparator and /or placebo products used in a clinical trial must be properly labelled and should contain the following information:

- A statement indicating that the medicine is an investigational product to be used only by a qualified investigator
- The name, number or identifying mark of the IP

- The expiration date of the IP
- The recommended storage conditions for the IP
- Lot number of the IP
- The name and address of the sponsor
- The protocol code or identification
- The name and address of the premises where the clinical trial is to be carried out.
- Registered products that are incorporated in the trial must also be labelled in the same information.

Trial medications must be stored in a secure place and dispensed by the pharmacy or the pharmaceutical department at the trial site in accordance with good dispensing practices. The general principle is that investigational products used in clinical trials should be handled in the same way as registered medicines.

7.3. Chemistry and Manufacturing and Control

Investigational medicinal products must be manufactured in accordance with the cGMP as the marketed medicinal products. Depending on the level of risks of the IP, IP manufacturing lines (that the manufacture of the investigational product) may be subject to audit/inspection in the same way as in the case of marketed medicinal products. Certificates of analysis (COAs) must be provided for all investigational and comparator products.

The manufacturing information provided in the clinical trial application should be presented in a concise manner. If the pharmaceutical or chemical properties of the investigational product have been altered compared to those in use during animal testing or previous clinical trials, such alterations must be described and justified. This, for instance, applies to impurities and degradation products.

Pharmaceutical and/or chemical alterations in an investigational product that is used in an ongoing clinical trial, and that may affect the quality, safety and/or efficacy of the medicinal product must immediately be reported to the Regulatory Authority. If the composition of the medicinal product is altered, additional bioavailability or bioequivalence studies may be required. In cases where an extension of the shelf life for the finished medicinal product is desired, an application for this must be submitted to the Regulatory Authority. In such cases stability data or certificates of analysis (COAs) from reanalysis of the relevant batches must be submitted.

The re-labelling of any remaining packages from previously manufactured batches must be performed in accordance with Good Manufacturing Practices (GMP). The comparator product for bioequivalence study should be obtained from the country of origin. Furthermore, for clinical trials involving a placebo comparator, a detailed description of the manufacturing process is required.

7.4. Importation of IP

Investigational products should not be imported unless the clinical trial is authorized and import permit is obtained from the authority. Authorization for the importation and use of the investigational product shall apply only to the Premises specified in the application and to the types of medicinal products and pharmaceutical forms and quantity specified in that application.

7.5. Disposal and destruction of investigational product(s)

Investigational Product Returns by Study Participants to the trial site(s):

- Dispensed IP to study participants and then returned by a study participant should be maintained at pharmacy unit in separate areas before returned to the sponsor or held for monitoring.
- IP returned in an unsatisfactory condition (eg, loose tablets, soiled bottles / product) should be reconciled and the record maintained at pharmacy. The inability to reconcile and reason can be documented on the drug accountability record.
- Returned IP from study participants should be counted and documented solely on the drug accountability record.

IP returns to study Sponsors, Intact/Unused containers of investigational drugs shall be returned to the study sponsor at the termination of a study or destroyed at the sponsor's request by the medicine waste management and disposal directive of the authority. Certificate of destruction indicating quantity of destructed shall be attached as part of the report.

Note: IP disposal or waste management should be clearly stated on the protocol.

7.6. Reconciliation

The Periodic Reconciliation report of IP should be reported to the authority every six months, and the complete reconciliation report should be submitted at the end of the trial.

Compassionate Use and Disposal of Investigational Product.

The authority may authorize the investigational product not used or left from the clinical trial site/s for compassionate use. Unless the authority authorizes for compassionate use, the IP shall be disposed by

following medicinal waste management and disposal directive of the authority, and a certificate of destruction or disposal shall be submitted with the study report.

8. 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 Directive No. 964/2023. When children aged between 12 to 17 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.

9. 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/e-CRF should be provided for review during application of clinical trial authorization.

10.SAFETY MANAGEMENT AND REPORTING

The sponsor has primary responsibility for reporting of study safety data, development safety update report (DSUR) and suspected unexpected serious adverse reactions (SUSAR) to EFDA and other investigators and for the ongoing global safety assessment of the investigational product. Reporting of study safety data is the primary responsibility of the sponsor. The Principal Investigator (PI) shall

submit a written report to the Authority within 48 hours of any serious adverse event (SAE), including a description of the event and measures taken for its management. This requirement applies regardless of whether the SAE is deemed related to the research procedures and must follow the format outlined in Annex VII. The Sponsor/PI is responsible for conducting the causality assessment of all SAEs. A preliminary review of SAE reports will be conducted by Clinical Trial (CT) experts, and any decisions, queries, or recommendations will be communicated to the Sponsor/PI and relevant stakeholders within 7 calendar days of report submission.

A monthly summary of non-serious adverse events must be reported in a tabulated format as specified in Annex IX. CT experts will carry out a preliminary review of the monthly reports. The outcomes, including any decisions, queries, or recommendations, will be shared with the Sponsor/PI and relevant stakeholders within 14 calendar days of receipt.

If the Authority determines that review by the National Clinical Trial Advisory Committee (NCTAC) is necessary, the safety report and the preliminary review will be forwarded accordingly. NCTAC's queries and/or recommendations will then be communicated to the Sponsor/PI and relevant stakeholders within 14 calendar days of NCTAC receiving the report.

11.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., CRO, pharmacies, laboratories, software suppliers, off-site storage) that participate directly or indirectly in managing trial data.

12.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.

13.REPORTING AND END OF THE TRIAL

13.1. Periodic Update, Progress and Final Report

Progress reports and final results of clinical trials must be communicated to the Authority. The sponsor or the applicant must provide a periodic, progress, and final report of the clinical trial according to the specified timelines in the approved protocol and in this guideline. In the case of trials lasting for more than 12 months, the progress report shall be submitted at 6 months' intervals and final report should be within 3 months after completion of the trial. For those trials with a study period of less than one year, the final report shall be submitted at the end of the period.

The progress report should include the number of patients so far treated, number and type of Serious Adverse Events (SAEs) reported, number of discontinued patients and the reasons for discontinuation (see progress report template- Annex-X). Progress or safety reports submitted by the sponsor or the applicant need to be reviewed by the Authority and decisions must be made.

The sponsor or applicant should provide clinical Trial summary report to the Authority within one year of the end of the complete trial for non-pediatric clinical trials and six months for pediatric clinical

trials. The format for the summary report should be as per Annex-XI and the applicant should provide the format for the progress report. All progress and summary reports must be stored in an electronic system or database at the Authority. 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

13.2. 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 Sponsor/applicant should provide a 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 but for early terminated trials the final report should be submitted within 3 months of discontinuation.

14.DISSEMINATION OF RESULTS

The sponsor or applicant should notify and obtain prior written approval from the Authority before dissemination of the results of the Clinical Trial. The time to review the Trial results by the regulatory

authority shall be within 15 days and hence publication and dissemination of results should be conducted after submission of the final clinical trial report and written approval from the Authority.

15.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 NRERB and the IRB. In addition, when a sponsor and/or investigator must take urgent safety measures to protect the trial participants from immediate hazard, it allows them to do so before notifying the Authority, but they must notify the participants in writing as soon as possible. During the implementation of amendments, which may have a direct impact on the participants' safety and well-being. The participants must be provided with detailed information regarding the amendment, and they should give re-consent.

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 authorization. However, investigator/sponsor can implement minor amendments immediately after submission and proper categorization and authorization of amendments are confirmed in writing by the Authority.

Amendments to the trial are regarded as "major" when 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. Major changes include but are not limited to the following points:

- Changes in the purpose or design of a trial,
- Changes in procedures used,
- Changes to the trial population such as estimated numbers, age range, inclusion/exclusion criteria,
- Change of the principal investigator, and changes to trial related documents, such as participant information sheets or consent forms
- Changes that affect participant selection and monitoring
- Changes that affect participant discontinuation
- Changes that affect clinical efficacy and safety requirements (e.g. Dosage adjustments, study procedures, etc).

- Changes that result to chemistry and manufacturing information may affect drug safety and quality (for example: specifications for the drug where the limits of the test are relaxed or deleted; where a new impurity or degradation product has been identified; and, the addition of new raw materials, solvents, reagents, catalysts or any other material used in the manufacture of the drug substance.).
- Changes that result in the extension of the duration of the clinical trial.
- Addition/deletion of an investigation site.
- Change of sponsor,
- Ip shelf life
- Manufacturing site change
- Change in insurance arrangement
- Change to the risk/benefit assessment for the ip in the ib.
- Changes in the logistical arrangements for storing or transporting samples,
- Change in laboratory analysis center
- Change in data analysis method/ statistical method

Amendment to the trial is regarded as “minor” when 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.

Minor changes include but are not limited to the following points:

- 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 investigators such as (change of any other investigator other than principal investigators at a trial site).
- Changes in research procedures have a minor impact on risks of harm, such as changes in the amount and frequency of blood draws (which remain within the expedited criteria), the addition of a clinic visit that involves no new procedures, or addition of a questionnaire that does not introduce new subject matter.
- An increase in the number of study visits for the purpose of increased safety monitoring

The sponsor or sponsor representative (principal investigator in some case, if delegated by the sponsor) are responsible for the submission of 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-VIII 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. Any amendments should also bear the amendment number(s), date and change history.

Application for amendment(s) to a previously authorized clinical trial shall be made in forms (Annex-VIII) and should be accompanied with amendment fees as prescribed in the current rate of service fees Regulation of the Authority. The Authority shall review and give feedback for amendment applications within 15 working days.

16.NON-ROUTINE PROCESSING OF CLINICAL TRIAL APPLICATIONS

A clinical trial shall qualify for expedited review where one of the following criteria is present after consideration of risks and benefits associated with the clinical trial.

1. Conducting clinical trials for life- threatening conditions may be possible to determine whether the condition is serious and the IP can be used for survival and day-to-day functioning but will progress to a more serious if left untreated.
2. Available data on the investigational product demonstrates the potential to address an unmet medical need, especially during a national epidemic, a global pandemic, or other similar emergencies.
3. Risks associated with the clinical trial are reasonable in relation to expected clinical benefits.

Expedite review process.

- The authority may initiate the expedited review process with its initiation or based on the applicant’s request.
- The process includes pre-review of the submitted application on priority basis and fast-track review of the application by one or two assigned reviewers instead of convened review in order to shorten the timelines.

- The applicant shall submit an application following Annex-XII when applying or requesting clinical trials for non-routine clinical trial procedures in addition to the documents required to be submitted.
- The applicant must meet the qualifications and requirements as applicant for routine clinical trial procedure.
- The evaluation fee is based on the current rate of service fee regulation of the Authority.
- The expedited review procedures.
    - The submitted application for expedited review will be assessed for eligibility.
    - Screening of the application for full submission of required documents and information, if not more information will be requested.
    - The authority will decide the application for expedited review or routine review and communicate with the applicant.

17.ROLES AND RESPONSIBILITIES OF CLINICAL TRIAL STAKEHOLDERS

17.1. Sponsor

The Sponsor is required to register the clinical trial, for which the sponsor is responsible for, in the Ethiopian and an internationally recognized Clinical Trials Registry before initiating patient screening and recruitment.

The Sponsor should implement a quality management system to manage quality throughout the design, conduct, recording, evaluation, reporting and archiving of clinical trials. The Sponsor is responsible for implementing and maintaining quality assurance systems to ensure that the clinical trial is conducted and data generated, documented, and reported in compliance with the protocol, GCP and the regulatory authority requirements. Methods used to ensure and control trial quality should be proportionate to the risks inherent in the trial and the importance of the information collected.

The sponsor is primarily responsible for the following trial related activities:

- Designing the clinical trial,
- Developing the study protocol, investigator's brochure and related materials to describe the procedures that will be followed, study endpoints, data collection tools and other study requirements,
- Ensuring that the protocol complies with applicable national and local laws and regulations

- When safety is a concern establish an independent data safety monitoring board with its charter and adequate members with appropriate qualifications and notify the authority.

The sponsor is responsible for securing agreement from all involved parties to ensure direct access to all trial related sites, source data/documents and reports for the purpose of monitoring and auditing by the sponsor and inspection by regulatory authority. Agreements made by the sponsor with the investigator/institution, monitor and any other parties involved with the clinical trial should be in written agreement.

The investigator and the sponsor required to establish written agreement on the protocol, the monitoring, the auditing, and on standard operating procedures, and the allocation of adequate budget and trial-related responsibilities before the commencement of the trial.

The sponsor may delegate any or all the trial-related functions to another person. However, in such cases, the sponsor should remain responsible for ensuring that the conduct of the trials and the final data generated by those trials comply with the approved protocol and relevant clinical trial law of the country.

The sponsor is required to ensure that the trial site team is adequately trained and qualified, a quality management system is in place, a monitor is assigned, and insurance is available for the conduct of the trial.

The sponsor is responsible for providing a periodic, interim, and final report of the clinical trial according to the specified timelines in the approved protocol and the respective trial directive. A progress report should be submitted biannually for clinical trials with a study period of more than one year and the final report should be submitted within three months of the trial's completion. In the event of trials lasting less than a year, the progress report should be submitted quarterly, and the final report should be submitted at the end of the trial. If a study is discontinued prematurely for whatever reason, the sponsor should notify the authority and submit a summary report within three months after the termination.

The sponsor is responsible for the ongoing safety evaluation of the investigational medicinal product(s). The sponsor should promptly notify other investigator(s) participating in the trial, the authority and relevant Ethics Review Committee when severe adverse reactions occur in the trial and are associated with any investigation product used in the trial and a severe adverse event that occurs in another trial.

The Sponsor should provide insurance for all trial participants. In addition, they should indemnify (legal and financial coverage) the Investigator/Institution against claims arising from the trial, except for claims that arise from professional malpractice and/or negligence.

The sponsor should ensure that the investigational product(s) is:

- Characterized as appropriate to the stage of development of the product(s),
- Justifiable quantities of IPs that should be imported relative to the timeline in the CT protocol. IPs imported into Ethiopia only after approval of the protocol by EFDA.
- Manufactured following current good manufacturing practice (cGMP),
- Reconciliation and destruction/disposal are performed appropriately.

The Sponsor should ensure that written procedures include instructions and relevant documents for the Investigator to follow for handling and storage of IP for the trial. The procedures address adequate and safe receipt, handling, storage, dispensing, retrieval of unused product from participants and return of unused to the Sponsor or alternative disposition if authorized by the Sponsor and in compliance with Ethiopian regulations. Ensure timely delivery and maintain records that document shipment, receipt, disposition, return and destruction of the IP.

The sponsor should ensure that the product label on outer packaging of IPs or, where there is no outer packaging, on the immediate packaging, contains standard, internationally accepted information in English.

The sponsor should ensure laboratories used for generating data for clinical trials should be compliant with Good Laboratory Practices (GLP).

The sponsor should be responsible for submitting amendments/variations to the authority prior to implementing such amendments/variations in the conduct of the clinical trial

The sponsor is responsible for establishing a recording system and ensure the trial subjects' confidentiality. The Sponsor also requires retaining essential documents until at least five years after the formal discontinuation of clinical development of the investigational product.

The Sponsor should provide insurance for all trial participants. In addition, they should indemnify (legal and financial coverage) the Investigator/Institution against claims arising from the trial, except for claims that arise from professional malpractice and/or negligence.

The Sponsor is responsible for developing a monitoring plan tailored to specific human participant protection and data integrity risks of the trial.

The Sponsor may establish an independent Data Safety Monitoring Board (DSMB) to assess the progress of a clinical trial, including safety data and critical efficacy endpoints at intervals, and to recommend to the Sponsor whether to continue, modify or stop a trial.

Sponsors ensure only select investigator(s) who are qualified by education, experience and training and have adequate resources to conduct the proposed clinical trial. When necessary, Sponsor will report the DSMB's request to involve EFDA for final decision on specific areas reviewed under the scope of DSMB.

Sponsor is responsible for submitting the material transfer agreement to the regulatory Authority for biological samples intended to be analyzed outside of Ethiopia.

17.2. Investigator

In most cases, clinical trials are conducted by an Investigator who has entered into an agreement with a Sponsor to conduct a clinical trial. In the case of a multi-center trial, each site must have a local PI and at least one sub-investigator who are registered Health Professionals in Ethiopia. The PI Should be an Ethiopian based clinician and other qualified professionals who are qualified, trained and experienced and have actively participated in clinical trials as a sub-investigator. Sub-investigator should be an Ethiopian based member of the clinical team designated and supervised by the PI at a trial site to perform critical trial related procedures and/or to make important trial-related decisions.

For multi-center studies in Ethiopia, a National Principal Investigator (NPI), with expertise and experience in the relevant field, may be appointed to take overall responsibility for the conduct of a trial. The NPI must meet all requirements to be a PI, require signing a declaration letter accepting responsibility and co-ordinate concerns of investigators regarding conduct of trial and communicate these to the Sponsor, Ethics committee and EFDA as necessary. It is recommended that the NPI should be involved as an investigator at one of the trial sites. If the PI and/or sub-investigator withdraw(s) for any reason (including death) before completion of the study, a suitably qualified successor should be appointed by the Sponsor and approved by EFDA and the relevant Ethics committee.

The investigator is responsible for:

- Ensure that a qualified pharmacist maintains appropriate records of the product's delivery to the trial site, the inventory at the site, the use by each trial subject, and the return to the sponsor or alternative disposition of unused product(s).
- Keep a record of all documents, including records that show subjects were provided the doses specified by the protocol and reconciliation of all investigational products.

- Ensure the confidentiality of all records related to the clinical trial activity.
- Maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties
- Permit monitoring and auditing by the sponsor and inspection by the authority.
- Carry out its responsibility in Pharmacovigilance throughout the conduct of the clinical trial through the recording of all adverse events (AE), including abnormal laboratory results, as instructed in the protocol; reporting to the sponsor all serious adverse events (SAE); providing follow-up reports of SAEs, and any other information requested, within the time frame identified in the protocol.
- Submit written summaries of the progress report of the trial status to the authority bi-annually or more frequently, if requested.
- Document all refusals and withdrawals and ensure that no data for the clinical trial is collected from subjects that refuse to participate in or have withdrawn from the clinical trial.

The investigator should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current investigator's brochure, product information and other sources provided by the sponsor. Only the investigator is responsible for unblinding a subject's treatment allocation during a clinical trial if unblinding is relevant to the subject's safety.

The investigator is responsible for giving adequate information to the study participant in respect of the clinical trial in accordance with EFDA GCP guideline. The investigator should have adequate resources and facilities for the foreseen duration of the trial to conduct the trial to these standards.

The investigator should ensure that adequate free medical care is provided to the study subject if there is a trial-related injury until such time as the study subject is completely recovered from the effects of such injury.

During the conduct of a clinical trial, no person, other than a holder of approval, or a designated principal investigator approved by EFDA, or any person assisting him in a clinical trial should treat a study participant or administer any test material to such study participant.

The investigator required them to know and comply with good clinical practice and applicable regulatory requirements.

17.3. Contract Research Organization

A Sponsor may transfer any or all of the Sponsor's trial-related duties and functions to a CRO, but ultimate responsibility for quality and integrity of trial data always remains with the Sponsor. Although

the CRO must implement quality assurance and quality control, the Sponsor is responsible specifically for:

- Ensuring oversight of any trial-related duties and functions carried out on its behalf and ensuring that the relevant CRO has the required skills, experience and competencies to conduct clinical trials.
- Any trial-related duty and function that is transferred to and assumed by a CRO should be specified in written agreement. In addition, the Sponsor must approve of writing any further sub-contracting of trial-related duties and functions by the CRO.
- Any trial-related duty and function not specifically transferred to and assumed by a CRO remains with the Sponsor.

Note: All references to Sponsor in this guideline apply to a CRO to the extent that the CRO has assumed the trial-related duties and functions of the Sponsor.

17.4. Clinical Trial Monitor

A monitor is appointed by the sponsor, appropriately trained and has adequate scientific and/or clinical knowledge to monitor the trial and act as the main line of communication between sponsor and investigator. The monitor is responsible:

- To protect the rights and well-being of human subjects.
- To ensure the reported trial data are accurate, complete, and verifiable from source documents.
- To ensure the conduct of the trial complies with the currently approved protocol and amendment, with good clinical practice, and with the applicable regulatory requirements.
- To verify that the Investigator has adequate qualifications and adequate resources throughout the trial period and that facilities are adequate to safely and properly conduct the trial and remain adequate throughout the trial period.
- To verify that the storage times and conditions, the availability of IP suppliers throughout the trial, the correct administration of protocol-specified IP doses only to eligible participants, the necessary instructions provided to participants on properly using, handling, storing, and returning IP as well as the receipt, use, and return of IP at the trial sites are adequately controlled and documented and the disposal of unused IP at the trial sites complies with regulatory requirements.

A monitor responsible for verifying that the Investigator follows the approved protocol and all approved amendments, written informed consent was obtained before the commencement of each trial, the Investigator receives the current IB, all documents and all trial supplies needed to conduct the trial properly and safely.

A monitor should be thoroughly familiar with the investigational product(s), the protocol, the written informed consent form, and any other written information to be provided to subjects, the sponsor's SOPs, GCP and the applicable regulatory requirement(s).

The extent and nature of monitoring should be determined by the sponsor and stated in the protocol.

Verify that the Investigator and the Investigator's staff are performing specified trial functions in accordance with the protocol and any other written agreement between the Sponsor and the Investigator and that functions have not been delegated to unauthorized individuals.

Verify that the Investigator enrolls only eligible participants and ensure that source documents and other trial records are accurate, complete, kept up-to-date and maintained. And also verify that the Investigator provides all required reports, notifications, applications and submissions and that these documents are accurate, complete, timely, legible and dated.

Inform the Investigator of any CRF entry error, omission or illegibility. The Monitor must ensure that appropriate corrections, additions or deletions are made, dated, explained (if necessary) and initialed by the Investigator or by an authorized member

Determine whether adverse events are appropriately reported within time periods required by GCP, the protocol, the Ethics Committee, the sponsor and EFDA. communicate deviations from the protocol, SOPs, GCP and EFDA requirements to the investigator and take appropriate action designed to prevent recurrence of the detected deviations.

The monitor is responsible for submitting a written monitoring report to the Sponsor and the Investigator after each site visit or trial-related communication in a timely manner for review and follow up as indicated.

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

17.5. Data and Safety Monitoring Board

The Drug Safety and monitoring Board (DSMB) is established by the Sponsor and is responsible:

1. To adhere to the DSMB charter requirements and approve any changes to the DSMB charter with sign-off by the DSMB Chairman.

2. To provide recommendations to the Executive Committee and sponsor the surrounding study conduct matters that affect safety and review the safety data at the planned safety reviews and identify if significant safety concerns arise during the study.
3. To request an ad hoc analysis for safety whenever it feels one is warranted and review any other data that may affect subject continuation. Making recommendations to the sponsor whether to continue, modify, or stop a trial.
4. To abide by rules of conduct (e.g, terms of reference describing frequency of meetings, how data will be analyzed, how records of proceedings will be generated).
5. To implement systems and procedures for assessment of safety in clinical trials and conduct objective and independent review of the safety data and efficacy endpoints of the drug in the clinical trials.
6. To communicate concerns with the Sponsor in a timely manner and maintain accurate records of all reviews.
7. For trials that will involve Data and Safety Monitoring Board to monitor clinical trials, the following issues related to DSMB should be submitted:
    - A broad statement of the aims and objectives of the DSMB
    - Terms of Reference
    - Composition of the DSMB\
    - Qualifications of the DSMB members
    - The role of statistical stopping rules\
    - Relationship with the principal investigators and trial management team
    - Clarification of the decision-making powers
    - How DSMB meetings will be organize.
    - Whether the DSMB will be blinded to treatment
    - What options DSMB can recommend
    - In what form and to whom decisions shall be conveyed
    - Who the DSMB will report to
    - The role of the DSMB in the publication of results
    - Disclosure of competing interests of DSMB members

17.6. Clinical Trial Ethics Review Committee Supervisory Body

The clinical trial ethics review committee supervisory body have the following roles and responsibilities:

- Monitor, supervise the activity, and provide guidance for independent ethics committees at all levels,
- Recognize the independent ethics committee established at an institutional, regional, or national level that reviews clinical trials conducted on human subjects
- Ensure the availability of an independent ethics committee at all levels. The supervisory body is responsible for ensuring the absence of conflict of interest, including verifying the source of funding, competency, independence and composition of an independent ethics committee.

17.7. Independent Ethics Committee

There should be an independent Ethics Committee that reviews, approves clinical trial applications and monitors the conduct of clinical trials that comply with ethical principles such as protecting the rights, welfare and privacy of trial participants.

The independent ethics committee's composition required members with professional competency, research ethics training and experience balanced regarding relevant expertise, gender, age, and community representation.

The committee should be independent of the investigator, the sponsor, or any other kind of undue influence.

The committee required to have the following roles and responsibilities:

- Approve or modify the application of clinical trial in perspective to ethical compliance.
- Monitor the conduct of the clinical trial to ensure that it complies with the ethical requirement; or
- Notify measures taken on noncompliance with the authority and may withdraw its approval.
- An Independent National Ethics Committee required to review clinical trials under the following conditions:
- In the absence of a recognized Independent Ethics Committee within the institution where the trial is conducted

- Where the Independent Ethics Committee is unable to perform the ethical review activities according to the standards
- The clinical trial is conducted in more than one site or multi-center trial.

17.8. National Clinical Trial Advisory Committee

The NCTAC will be responsible for reviewing clinical trial applications, with particular emphasis on early phase trials and other phases deemed to be necessary. The assessment and recommendation process includes safety and progress reports from the authorized clinical trials, as requested by the EFDA. Generally, the National CT advisory committee is responsible for:

- Regularly attend the committee meetings.
- Provide inputs to the legal documents and important procedures on authorization, GCP inspection and system establishment.
- Take assignments from the committee and submit a report accordingly.
- Respect and comply with all decisions made by the committee.
- Share relevant scientific updates and scale up promising best practices in the area.
- Assist EFDA periodically to assess and analyze activities, CT oversight related initiatives, training needs, research needs, and to come up with appropriate recommendations and directions.
- Follow up the implementation of activities as per the terms of reference (TOR).
- Create awareness for the newly joined committee members.
- Ensure that all members should express their commitment to the activities of the committee and participate actively.
- Committee members should be required to submit a completed and signed confidentiality agreement and declare conflict of interest before any involvement in the activities.

18.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 NRERB 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.

19.INAPPLICABLE GUIDELINES

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

20.EFFECTIVE DATE

This guideline is effective starting from the date of May 2025. All clinical trials conducted in Ethiopia shall comply with the requirements of this guideline.

21.ANNEXES

21.1. Annex I: Routine Clinical Trial Application Form

A. Trial Identification:

☐

Is the application for non-routine clinical trial procedure? Yes No ☐
If yes, Specify the conditions for non-routine procedures

_____

Name of scientific working group .....
.....

Title of clinical trial (Include trials short title if available)
.....
.....

Protocol Number, Date and Version ___

Phase of the clinical trial (Phase I, II, III, IV), Bioequivalence, Other specify
.....

State the objective of the trial and the reasons there of.....

.....
Duration of (time period for) the trials.....

B. Sponsor Identification

The name of the sponsor of the trial.....
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……

……

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

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

---

4. Therapeutic effect of investigation products

……

5. Administration route, dosage, dosage interval and duration for investigational product and drug being used asa control……
6. State the name and address of the manufacturing site……

7. Product used as comparator (placebo/other therapy) ……...

8. State whether any other medicines/product will be given concomitantly, Yes/No

If yes, please indicate the name of the medicine/product…….

E. Population of the trial participant

9. Description of the participants (e.g. age group of the subjects, type of study participant, sex)

……

10. Number of participants expected to take part and Justification there of (based on statistical consideration) …….

F. Ethical committee

11. Is this clinical trial protocol approved by National Research Ethics Review Board (NRERB)? Yes/No

If no, please provide the reasons thereof…….

……

12. Is this clinical trial protocol approved (has got favorable opinion) by Institutional Review Board (IRB)? Yes/No

If no, please provide the reasons thereof…….

……

13. If any, please specify the name and address of other Ethical clearance certificate related to this clinical trial.

……

…….

G. Insurance

14. Description of the name and address of the company who will insure all the subjects in the Proposed trial……

15. State the amount of insurance in respect of each participant……

H. Regulatory Details

1. Name other regulatory Authorities of Ethics committees to which this application has been submitted, and/ or approved?_____

2. If Applicable, explain why the Trials are not going to be conducted in the host country of the Applicant/ sponsor? _____

3. If applicable, name other regulatory Authorities or Ethics committees that have rejected this trial and explain the reason. _____

4. If Applicable, provide details and explain why this trial was halted at any stage by other regulatory Authorities.

_____

Applicant Identification: who is submitting the Application?

☐ Sponsor ☐ Sponsor's legal representative person/ Organization Authorized by the person to submit the Application

Applicant Name:_____Address: _____

Signature_____

Name and address of principal investigator …….

Signature of principal investigator……

Name and address of the sponsor……

Signature of sponsor……..

Date…… Stamps

FOR OFFICIAL USE ONLY

Date of Application Receipt ……

Name of the person who received the application ……

Position……..

Signature ……

21.2. 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 and Drug 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:.....

21.3. 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

21.4. Annex IV: Declaration by Investigator(S)

Name:…….

Title of Trial:……

Protocol No:……

Site Name:……..

I/We, the undersigned have submitted all requested and required documentation and have disclosed all the 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 people), 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:……

21.5. 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:…….

21.6. Annex VI: Required Documentation for Authorizing the Importation of 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		
7.	Product name or unique code (if blinded)		
8.	That product is clinical trial material e.g. “For use in clinical trial only”.		
9.	Does this concur with the information on the Cover Sheet		
10.	Storage temperature		
11.	Batch number		
12.	Date of Manufacture and expiry date		
13.	Sponsor contact details		

21.7. Annex VII: Serious Adverse Event Reporting Form

PROTOCOL AND EVENT TYPE	
Study title	
Protocol No.	
EFDA Ref. No.	
Date of this report	
Seriousness of adverse events (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	

21.8. 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 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: _____

21.9. 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

21.10. Annex X: Clinical Trial Progress Report Format

Clinical Trial Study Progress Report Template

1. General Information

1.1 Protocol number:

1.2 Study title:

1.3 Principal investigator:

Name: _____ Job title: _____ Place of work: _____

_____ Address: _____Telephone: _____

E-mail: _____

2: Study Details

2.1 Summary: _____

_____

_____

2.2 Study dates:

(a) Date of original Ethics Review Board approval: _____

(b) When did the study begin? _____

(c) Anticipated completion date: _____

2.3 Study phase (select all that apply):

☐ Inactive / on hold / not started ☐ Pilot study / initial scoping

☐ Active enrolment of participants ☐ Ongoing study and analysis

☐ Final data analysis and manuscript/report preparation

2.4 Study progress:

(a) Provide a summary of the study progress and results achieved.

(b) Have there been any challenges or delays in carrying out this study? ☐ Yes–please explain: ☐ No

2.5 Participant recruitment and sample analysis (if applicable):

(a) If the study involves recruitment of human participants: _____

Number of participants enrolled to date: _____

Number of additional participants required: _____

Number of participants who have withdrawn: (specify reason)

Number of participants who have completed the study and with whom no further contact for study purposes is planned:__

(b) If the study involves sample analysis (e.g., human biological materials):

Number of samples received to date: _____ Number of samples analyzed to date: _____

_____ Number of additional samples to come: _

_____

3: Administrative Information

3.1 Funding status:

☐ Funded–funding end date (if applicable): _____

☐ Unfunded

If the project funding has changed since the last review, please explain:_____

3.2 Amendments:

Have all modifications to the Protocol been submitted for approval?

☐ Yes ☐ No complete and submit an Amendment Request

☐ N/A (no modifications have been made to the study)

3.3 Adverse events:

Have all adverse events experienced by participants been reported?

☐ Yes ☐ No complete and submit an Adverse Event Report Form

☐ N/A (no adverse events have occurred)

3.4 Privacy and confidentiality:

Has there been a change in persons with access to study data, the location of stored data, security arrangements, or the duration of the data conservation period?

☐ Yes - Please explain ☐ No

☐ N/A

3.5 Conflicts: Does the principal investigator or any member of the study team have a new (i.e., previously undeclared) real, apparent or potential conflict of interest? ☐ Yes - Please explain ☐ No ☐ N/A
4: Signature
4.1 Attestation of principal investigator: I certify that all the information provided herein is accurate and complete, and that I will inform the Authority immediately if any changes are made to the protocol or if any errors are discovered in this progress report. **Principal investigator:** Signature: _____ Date: _

21.11. ANNEX XI: Clinical Trial Summary Report Format

Clinical Trial Summary Report Format
Title page
Synopsis
Ethics and regulatory approval ➢ Independent ethics committee approval ➢ Ethical conduct of the study ➢ Patient information and consent ➢ Regulatory approval
Investigators and study administrative structure
Introduction ➢ Therapeutic area ➢ Rationale for the study
Study objectives

Investigational plan ➢ Overall study design and plan ➢ Discussion of study design ➢ Selection of study population ➢ Treatments ➢ Efficacy and safety variables ➢ Data quality assurance ➢ Statistical methods planned in the protocol & determination of sample size ➢ Changes in the conduct of the study or planned analyses
Study population
➢ Results ➢ Data sets analysed ➢ Demographic and other baseline characteristics ➢ Measurements of treatment compliance ➢ Study duration ➢ Immunogenicity results and tabulations of patient data
Safety evaluation
Discussion and overall conclusions
Tables, figures and graphs
References
Appendices

21.12. Annex XII: Format for contents of non-routine clinical trial applications

Title	Format for contents of non-routine clinical trial applications	
	Basic Information	
	Title of the Study	

	Sponsor of the trial	
	Principal Investigators	
	Site of Clinical Trial	
Indication		
	Disease or condition going to be studied	
	Existing Therapy/Treatment for the condition if any	
	The Condition(s) for non-Routine Procedure	
	Detail Explanation on proposed areas to be exempted as non-routine procedure	
Investigational Products		
	Name of product	
	Proposed Therapeutic Indication	
	Detail Justification/analysis of Risk and Benefit in relation to the proposed condition and available treatments if any for non- routine CT authorization procedure	
	Detail explanation of on areas of exemption in relation to investigational product	
Other Relevant Administrative Documents		
	Sponsor declaration that the trial is	

	candidate for non- routine procedures	
	Document proposed for exemption if any for non-routine procedure	
	Signature of Sponsor: Date:	Signature of PI: Date:
	For authority use only	
	Screened by Name:	Comment/Statement:
	Approved By Name:	Comment/Statement:

22.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