RWANDA FDA
Rwanda Food and Drugs Authority

GUIDELINES FOR CLINICAL TRIAL APPLICATION IN RWANDA

APRIL, 2023

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DOCUMENT REVISION HISTORY

Date of revision	Revision number	Changes made and/or reasons for revision
05/02/2021	00	First issue
18/06/2021	01	1. Provisions for expedited review of Clinical Trial Application (CTA) were included; 2. Provisions for application, review, and approval of clinical Trial during health emergencies; 3. Provisions for reliance pathway approval as the non-routine procedure for clinical trial authorization in Rwanda were incorporated; 4. Requirements for renewal of clinical trial Authorizations were included; 5. The flowchart for the clinical trial was revised and included; 6. The table revision history was included; 7. Necessary editorial changes and formatting were made.
01/04/2023	02	1. The reference number was changed from DIS/GDL/033 to FDISM/PVSM/GDL/005 Rev_2 as per the current SOP on document control 2. Provisions for expedited review of CTA were moved to the Guidelines for Review and Approval of CTAs; 3. Provisions for the application, review, and approval of clinical trials during health, emergencies were moved to the Guidelines for Review and Approval of CTA; 4. Provisions for reliance pathway approval as the non-routine procedure for clinical trial authorization in Rwanda were moved to the Guidelines for Review and Approval of CTAs; 5. Criteria to be followed for accepting evidence of GMP compliance for imported IMPs were included; 6. Section 1.3 regarding the review process was moved to the guidelines for the Review and Approval of CTA; 7. Critical requirements for acceptance of CTA were included; 8. Format and content of the CTA updated; 9. Requirements for amendments were included; 10. Requirements for renewal were included; 11. Included necessary editorial changes in line with SOP on Document control.

FOREWORD

Rwanda Food and Drugs Authority (Rwanda FDA) is a regulatory body established by Law N° 003/2018 of 09/02/2018, specifically in article 8, paragraphs 7 and 12 to regulate and inspect clinical trials. In reference to the provisions of the technical regulation N° FDISM/PVSM/TRG/001 Rev_2 governing the conduct of clinical trials, the Authority Issues *Guidelines N°* FDISM/PVSM/GDL/005 Rev_2 on clinical trial application in Rwanda.

These guidelines have been developed to provide guidance to the applicants and the Authority in preparation and managing applications for clinical trials. These guidelines were developed in reference to the existing guidelines the of World Health Organization (WHO) and the International Conference on Harmonization of Technical Requirements for Good Clinical Practices (ICH E6) and other available literature.

The Authority acknowledges all the efforts of key stakeholders who participated in the development, review and validation of these guidelines.

Digitally signed by Rwanda FDA (Director General) Date: 2023.04.06 10:37:35 +02'00'

Dr. Emile BIENVENU
Director General

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ACRONYMS AND ABBREVIATIONS

AE	Adverse Event
API	Active Pharmaceutical Product
AVAREF	African Vaccine Regulatory Forum
CIOMS	Council of International Organization for Medical Science
CRO	Contract Research Organization
CRF	Case report form
CTA	Clinical Trial Application
CTA-A	Clinical Trial Application for Amendment
DSMB	Data Safety and Monitoring Board
EUAL	Emergency Use Assessment and Listing Procedure
FPP	Finished pharmaceutical Product
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
IB	Investigator's Brochure
ICH	International Conference on Harmonization
ICFs	Informed Consent Forms
IRB	Institutional Review Board
IP	Investigational Product
MTA	Material Transfer Agreement
NDA	New Drug Application
QOS	Quality Overall Summary
PI	Principal Investigator
RNEC	Rwanda National Research Ethics Committee
Rwanda FDA	Rwanda Food and Drugs Authority
SAEs	Serious Adverse Events
SmPC	Summary of product characteristics
SUSARs	Suspected Unexpected Serious Adverse
WHO:	World Health Organisation

GLOSSARY

In these guidelines, unless the context otherwise states:

''Applicant'' means the Sponsor or Principal Investigator or any other authorized person to apply for clinical trial and issued a Clinical Trial Certificate. The applicant shall therefore be responsible for signing the application form.

"Authority" Means Rwanda Food and Drugs Authority or its acronym "Rwanda FDA", established under the article 2 of the Law Nº 003/2018 of 09/02/2018.

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

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

"Assent" A process by which a child, who is capable of understanding 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 child's decision to participate. Assent is documented by means of a written, signed and dated assent form from the child. As part of the assent process, parents and guardians must give informed consent.

"Audit" A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analyzed and accurately reported according to the protocol and applicable standard operating procedures (SOPs), the Authority and ICH-GCP requirement(s).

"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), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

"Case Report Form" A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each study participant.

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

"Clinical Trial Report" A written description of a trial/ study of any therapeutic, prophylactic or diagnostic agent conducted in human study participants in which the clinical and statistical description, presentations and analyses are fully integrated into a single report.

"Contract" A written, dated and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract.

"Data and Safety Monitoring Board" An independent data monitoring committee that may be 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.

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

"Essential Documents" Documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.

"Ethical Clearance" An authorization to conduct a clinical trial issued by the Rwanda National Research Ethics Committee (RNEC) based on ethical issues related to trials involving human participants in Rwanda.

"Good Clinical Practice" A standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials that provide assurance that the data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial/study participants are protected.

"Good Manufacturing Practice (GMP)" The part of pharmaceutical quality assurance which ensures that products are consistently produced and controlled to quality standards appropriate to their intended use and as required by the marketing authorization.

"Impartial witness" A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the participant or the participant's legally acceptable representative cannot read, and who reads the Informed Consent Form and any other written information supplied to the participant.

"Informed Consent" A process by which a study 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 study participant's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.

"Inspection" The act of conducting an official review of documents, facilities, records, and any other resources that are deemed by the Authority to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or CRO's facilities or at other establishments deemed appropriate by the Authority.

''Investigational Product" A pharmaceutical product in 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 (formulated or packaged) 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. These include but are not limited to pharmaceutical products, biologicals (e. vaccines), medical devices.

"Investigator" A physician, dentist, or another qualified person who conducts a clinical trial at a trial site. See also Sub-investigator.

"Investigator's Brochure" A compilation of the clinical and non-clinical data on the investigational product(s), which is relevant to the study of the investigational product(s) in human study participants.
"Legal representative" The name given to describe the executor, administrator or the person who looks after another person's affairs.

"Materials Transfer Agreement" An MTA is a written contract that governs the transfer of tangible research materials or biological samples between parties.

"Multi-centre Trial" A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.

''Notifications" means changes to the details of a trial that have no significant implications for the study participants, conduct, management, and scientific value of the research

"Phase I trials" These are the first trials of a new active ingredient or new formulations in man, often carried out in healthy volunteers. Their purpose is to establish a preliminary evaluation of safety and a first outline of the pharmacokinetic and, where possible, pharmacodynamics profile of the active ingredient.

"Phase II trials" These trials are performed with a limited number of study participants and are often, at a later stage, of a comparative (e.g. placebo-controlled) design. Their purpose is to demonstrate therapeutic activity and to assess the short-term safety of the active ingredient 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 trials" 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 investigation product 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" Studies performed after marketing of the pharmaceutical 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 pre-marketing 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 pharmaceutical products.

"***Pharmaceutical product*****"** any substance capable of preventing, treating human or animal diseases and any other substance intended for administration to a human being or an animal in order to diagnose diseases, restore, correct or carry out modification of organic or mental functions.

"Placebo" An inactive substance or sham form of a therapy administered as a control in testing experimentally or clinically the efficacy of a biologically active preparation or procedure.

"Pre-clinical Studies" Biomedical studies not performed on human study participants.

"Principal Investigator" A person responsible for the conduct of the clinical trial at a trial site who is a physician, dentist or other qualified person, resident in Rwanda and a member of good standing of a professional body. If a trial is conducted by a team of individuals at a trial site, the principle investigator is the responsible leader of the team. See also Sub-investigator.

"Protocol" A document that describes the objective(s), design, methodology, statistical considerations and organization of a trial. The protocol usually also gives the background and rationale for the trial but these could be provided in other protocol referenced documents.

"Protocol Amendment" A written description of change(s) to or formal clarification of a protocol.

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

"Reliance" is the act whereby the regulatory Authority in one jurisdiction may take into account and give significant weight to regulatory work performed by another regulatory or trusted institution for purposes of reaching its own regulatory decisions.

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

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

"Sponsor-Investigator" An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a study participant. The term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.

"Standard Operating Procedures (SOP)" Detailed written instructions to achieve uniformity of the performance of a specific function.

"***Substantial amendment***": means change to the terms of the protocol or any other trial supporting documentation that is likely to have significant impact and affect the safety and integrity of trial participants, the scientific value of the research, the conduct or management of the research, and the quality or safety of any investigational medicinal product used in research.

"The law" means Law No. 003/2018 of 09/02/2018 establish Rwanda Food and Drugs Authority and Determining its Mission, Organization and Function.

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

"Trial Site" The location(s) where trial-related activities are actually conducted.

1. INTRODUCTION

Clinical trials are planned scientific investigations conducted in humans and animals to gather information on the safety and efficacy of medical products and health technologies. Such experiments involve the administration of investigational products in patients, healthy volunteers or animal species to generate data which can later on be used for marketing authorization of a product. The regulatory authority mandated to regulate the conduct of clinical trials in Rwanda is Rwanda Food and Drugs Authority.

These guidelines highlight requirements that need to be followed by Investigators and Sponsors when submitting their applications for approval to conduct clinical trials in Rwanda. Good Clinical Practice (GCP) principles and other ethical considerations are also detailed with the aim of ensuring that trial participants are protected and safeguarded against any harm that might arise as a result of participating in clinical trials.

The guidelines are arranged in a modular format as adopted from the ICH guidelines to allow consistent and uniform documentation of submissions. These will in-turn pave-a-way for speedy assessment of applications by the Authority and ultimately decisions on approval/non-approval based on clear and transparent criteria.

These guidelines have been developed and updated to assist applicants to compile clinical trial application dossier for authorization to conduct clinical trials in Rwanda. The clinical trial application dossier is divided into three different modules as follows:

a) **Module I**: administrative and protocol-related information about the trial;
b) **Module II:** Information related to the Quality (Chemistry, Manufacturing, and Control) summaries about the investigational products to be used in the proposed trial;
c) **Module III:** Other Supporting Information.

Applicants should submit their applications as per the Modules. The information in these Modules should be presented in relevant sections and should not be modified.

1.1 Scope of these Guidelines

The scope of these guidelines applies to the regulatory requirements for clinical trial applications including bioequivalence studies to the Authority for Authorization prior to initiation. They are addressed to investigators, the pharmaceutical industry, Clinical Research Organizations (CROs) and sponsors of clinical trials, whether for academic purposes or for the generation of data, intended for inclusion in the regulatory submissions for investigational products.

A new application for clinical trial conduct in Rwanda is required for the following categories of products/ circumstances:

1. New Medicines, Vaccines and other biological products, herbal medicines, cosmetics, medical devices and diagnostics for which safety/efficacy profile has not been determined;
2. A clinical investigation of a non-CE-marked (Certificate of European) medical device in the following circumstances:
3. The introduction of a completely new concept of device into clinical practice where components features and/or methods of action, are previously unknown;
    a) Where a device incorporates materials previously untested in humans, coming into contact with the human body or where existing materials are applied to a new location in the human body, in which case compatibility and biological safety will need to be considered;
    b) Where a device, either CE-marked or non-CE-marked, is proposed for a new purpose or function;
    c) Where in vitro and/or animal testing of the device cannot mimic the clinical situation
4. Registered medicines, vaccines and other biological products, herbal medicines, cosmetics, medical devices and diagnostics where the proposed clinical trials are outside the conditions of approval. These may include changes to:
    a) Indications and clinical use
    b) Target patient or animal population(s) e.g. age group and race.
    c) Routes of administration
    d) New dosage scheme/regimen.
    e) The intended use of a device(s)
    f) New combination drug products
    g) New drug delivery/release system
5. Academic clinical trials: clinical trial not funded by pharmaceutical or Biotechnology Company for commercial ends but by public-good agencies (usually universities or medical trusts) to advance medicine.

1.2 General Information

All applications and supporting documents shall be in one of the official languages used in Rwanda. Data shall be presented in A4 papers either hard copy or electronic format using New Times, font 12. The clinical trial application documents shall be submitted in modules I, II, and III in hard or soft copies in searchable PDF. Extension sheets, tables, diagrams and other supporting documents shall as far as possible be of the same size, well annotated, numbered and appropriately cross-referenced. The information/data must be compiled in accordance with these guidelines. In case the information is required in the application forms its location shall be cross-referenced in the submission.

2. CLINICAL TRIAL APPLICATION PROCESS AND REQUIREMENTS

2.1 Requirements for Pre-Submission Meeting Application

An application for a pre-submission consultation meeting is optional and shall be made by the sponsor or Principal investigator who submit to the Authority following documents:

a) The cover letter requesting the pre-submission meeting;
b) A brief synopsis of the proposed trial protocol as per **ANNEX-VI**
c) A list of preliminary questions to be discussed in the meeting;

The Authority will acknowledge the receipt of the application and will confirm the meeting date, venue and time of meeting within fifteen (15) calendar days after the receipt of meeting request.

After the meeting, the sponsor should prepare and send to the Authority a written record of the discussions and conclusions of the meeting within 14 calendar days.

2.2 Clinical Trial Application requirements

A Clinical Trial Application for conducting clinical trials in Rwanda including bioavailability studies should be made to the Authority prior to the initiation. The content and format of clinical trial application is composed of three modules:

a) **Module I**: Administrative and protocol related information about the trial;
b) **Module II**: Information related to the Quality (Chemistry, Manufacturing and Control) summaries about the investigational products to be used in the proposed trial;
c) **Module III**: Other Supporting Information

The contents of each module of clinical trial application dossier are summarized in the table provided below:

Module I	**Administrative Information and Protocol Related Information**
1.1	**Administrative Information**
1.1.1	Signed and dated Clinical Trial Application Cover letter
1.1.2	Signed and dated clinical trial application form-**ANNEX-I**
1.1.3	Valid Ethical Clearance Certificate from Rwanda National Ethics Committee
1.1.4	Curriculum vitae (CVs) of Principal investigator(s) and Co-investigator(s)
1.1.5	Copy of Valid GCP Certificates for both Principal Investigator(s) and co-Principal investigator (s)
1.1.6	Signed and dated Joint declaration between Sponsor & Principal Investigator for sufficient funds in the prescribed format (**ANNEX-III**)
1.1.7	Signed and dated declarations by the Principal investigator and/or Co-investigators (**ANNEX-IV**)

1.1.8	Valid Local Insurance Policy Covering trial participants
1.1.9	Signed and dated Sponsor/ Principal investigator contractual Agreement
1.1.10	Letters of Access authorizing Authority to access related files (Drug Master Files, Site Reference Files) must be submitted
1.1.11	Clinical Trial Site Agreement/contract
1.1.12	Collaborative note from Rwanda Biomedical Center for clinical trial on products used under public health programs(HIV,TB,Malaria,etc),if applicable
1.1.13	Minutes of the discussions and conclusions of the pre-submission meeting or other relevant correspondence with the Authority, if applicable
1.1.14	List of Competent Authorities to which the same application has been submitted and details of decisions, if available
1.1.15	Proof of registration of the trial with a WHO recognized Clinical Trial Registry. Preferably, trials may be registered with the Pan African Clinical Trials Registry (PACTR)
1.1. 1 6	Evidence of payment of prescribed fees
1.2	**Clinical Trial Protocol-related Information**
1.2.1	A copy of the final proposed protocol(s), including the version number. The trial protocol must be signed by the sponsor and the investigator prior to the start of the clinical trial (ICH E6 8.2.2)
1.2.2	A copy of the Informed Consent Forms (ICFs) in English, French and Kinyarwanda signed and stamped by the Rwanda National Ethics Committee that includes a statement regarding the risks and anticipated benefits to the clinical trial participants as a result of their participation in the clinical trial
1.2.3	Copy of Participant Information Leaflet (PIL)
1.2.4	Copy of Case Report Forms (CRFs) to be used for data collection
1.2.5	Capacity building plan including training and updating of staff involved in the trial
1.2.6	Good Clinical Laboratory Practice (GCLP) accreditation certificate
1.2.7	Signed Charter of DSMB and CVs of Members if applicable
1.2.8	Signed and dated Materials Transfer Agreement (MTA) if applicable
Module II	**Information related to the Quality of Investigational Product** (Chemistry, Manufacturing, and Control Summaries)
2.1	Investigational Product (IP) Dossier containing the Quality Overall Summary and showing the chemistry, manufacture, and control (CMC) as per Common technical document (CTD) format in ANNEX-V, non-clinical data, and Data from previous clinical use (if applicable). Non-clinical data reports should be included in the dossier as per the requirements in the latest version of ICH M3.
2.2	A copy of the current Investigator's Brochure (IB), supplemented as appropriate with up-to-date safety, non-clinical, and available clinical data

2.3	Copy of valid Good Manufacturing Practice (GMP) Certificate or Confirmation document of the authority that the manufacturer complies with PIC/S or GMP inspection report or ISO Certificate for medical device/IVD
2.4	A copy of the identification labels for both primary and secondary packaging (outer and inner packaging) of Investigational product labels
2.5	Investigational product package Insert/s for mark if applicable
2.6	Mock-up labels for the Investigational Product(s)
2.7	Copy of the summary of product characteristics (SmPC) or a copy of the certificate of pharmaceutical product (COPP) of the investigational products if applicable
2.8	Copy of Certificate of analysis for the batches of the investigational products to be used in a clinical trial if applicable
2.9	Composition of the placebo (placebo-controlled trials**,** information on the placebo is also required including a description of the manufacturing process, a qualitative and quantitative list of ingredients, specifications, batches, stability and facility information) or diluent if applicable
2.10	Copy of the import authorization in case the investigational product is not imported directly to the trial site
Module III	**Other Supporting Information**
3.1	Additional supporting quality information such as publications
3.2	Literature References

Note: Non-compliance and non-conformity to the regulatory requirements prescribed in these guidelines shall lead to the clinical trial application rejection. The Clinical Trial Application shall be accepted for review if more than 70% of the applicable required documents are provided. This shall include but not be limited to the signed, dated application letter and forms, duly signed protocol, updated IB, proof of payment of applicable fees, declarations, and agreement between the sponsor and principal investigator. Therefore, sponsors, investigators and Clinical Research Organizations (CROs) are encouraged to submit a completed clinical trial application dossier to avoid rejection and delays in the review process.

Application for compassionate use of unauthorized investigational products shall follow requirements set out in the latest version of AVAREF Guidance and Considerations on Compassionate Use Access Application for compassionate use of unauthorized investigational products shall follow requirements set out in the latest version of AVAREF Guidance and Considerations on Compassionate Use Access.

Additional requirements for medical devices clinical trials

In addition, the following documentation will be required for clinical trials of medical devices:

1) Device description, intended use, design and User manual of the device

2) Marketing authorization from other countries if applicable
3) Risk assessment and standard list
4) Sterilization validation certificate if applicable
5) Electrical safety certificate if applicable
6) Software as medical device classification if applicable.

7.1 Conduct of clinical trials involving medical devices and diagnostics

The design, conduct, recording and reporting of clinical investigations carried out in human subjects to assess the safety or performance of medical devices should be as prescribed in the ISO 14155-2011 (en) Clinical investigation of medical devices for human subjects – Good Clinical Practice and ISO14971: 2007 Medical devices – application of risk management to medical devices guidelines

2.2.1 Submission of clinical trial application dossier

The clinical trial application dossier to the following address:

Director General
Rwanda Food and Drugs Authority
Email: info@rwandafda.gov.rw
P.O. Box 1948 Kigali, Rwanda.

2.2.2 Clinical Trial Application Fees

An application shall be accompanied by a non-refundable application fee as prescribed in the Regulations No CBD/TRG/004 related to regulatory service tariff/fees and fines. The application fees should be paid on the Rwanda FDA accounts:

a) National Bank of Rwanda (BNR): 1000047658 entitled ‘’ Rwanda FDA’’ in Frw
b) National Bank of Rwanda (BNR): 1000047666 entitled ‘’ Rwanda FDA’’ in USD
   Swift code is: BNRRWRWRW
c) Bank of Kigali (BK): 100025143684entitled "Rwanda FDA" in Frw
d) Bank of Kigali (BK): 100025143765 entitled "Rwanda FDA" in USD
   Swift code is: BKIGRWRW

Note: The authority is not reliable for transfer charges.

2.2.3 Clinical Trial Protocol

The content and format of the clinical trial protocol and its amendments should comply with the requirements set out in the latest version of the ICH GCP guidelines. Site specific information may be provided on separate protocol page(s), or addressed in a separate agreement for multicentre clinical trials. The protocol and its amendment should be those reviewed by the Rwanda National Ethics Committee and signed by the both sponsor and principle investigator. The clinical trial protocol template (ANNEX-II) is provided as a guide capturing key section of ICH GCP guidelines.

2.2.4 Investigator's Brochure

The Investigator's Brochure (IB) is a compilation of the clinical and nonclinical data on the investigational product(s) that are relevant to the trial of the product(s) in human participants. The content and format of the Investigator's Brochure (IB) and its updates should comply with the requirements set out in the latest version of the ICH GCP guidelines. The approved summary of product characteristics (SmPC) may be used in place of the Investigational Brochure (IB) if the investigational product is marketed and is used according to the terms of the marketing authorization. If the conditions of use in the clinical trial differ from those authorized, the SmPC should be supplemented with a summary of relevant non-clinical and clinical data that support the use of the IP in the clinical trial.

2.2.5 Informed Consent and Assent

The informed consent informed consent should comply with regulatory requirements and abide with ICH GCP guidelines and the ethical principles that have their origin in the Declaration of Helsinki. Note that, the language used in the ICF shall be in English, French and Kinyarwanda and approved by Rwanda National Ethics Committee.

2.2.6 Ethical Clearance

A valid Ethical Clearance certificate issued by RNEC is required for all phases of clinical trials. The Authority shall give its position after the applicant has submitted ethical clearance. The Authority shall allow parallel submission of clinical trial applications to facilitate the sponsor and principal investigators. In this case, the evidence of submission to RNEC shall be required and any change made to the protocol by RNEC will be submitted to the Authority.

2.2.7 Insurance cover of trial participants.

All trial participants must be satisfactorily insured against possible injuries that must arise during the conduct of clinical trial. The valid evidence insurance policy issued by the local insurance company for participants shall be submitted to Authority prior to the study initiation.

The insurance certificate shall contain at least the following elements:

a) policy number,
b) starting date and expiry Date,
c) insured (Policy Holder/Sponsor),
d) title of insured protocol or protocol number,
e) number of trial participants and
f) List all events that are covered by the insurance policy e.g. deaths, permanent and temporary impairment of health conditions, etc.

2.2.8 Data and Safety Monitoring Board/Committee (DSMB/C)

An Independent Data Monitoring committee may be 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. The Sponsor shall include charter of work, membership and curriculum vitae of all the DSMB members when applicable. DSMB shall sign the charter and copy of updated CVs shall be submitted. It is recommended that at least one member of the DSMB is Rwandese.

2.2.9 Materials Transfer Agreement (MTA)

Where applicable, an appropriate MTA which defines the rights, obligations and restrictions for the provider (PI) and recipient(s) (External Laboratory) with respect to the materials and any derivatives to be Transferred, as well as any confidential information exchanged with the material shall be provided. The MTA shall specify:

a) The type of materials to be transferred
b) The local laboratory or institution from which the samples shall be transferred
c) The destination of the samples (intermediary and final destination)
d) The type of analyses to be carried out by the recipient(s)
e) Competence of the recipient(s) of the materials for the listed analyses to be carried out

The MTA shall be duly signed and dated by the Sponsor, PI and the recipient(s) of the materials at external laboratory.

2.2.10 Investigational Product (IP) Dossier

The investigational product dossier (IPD) gives information related to the quality of any IP (i.e. including reference product and placebo), manufacture and control of the IP, and data from non-clinical studies and from its clinical use shall be provided according to the ICH CTD format. The applicant shall fill in the summary of the quality of the Investigational product in the Quality Overall Summary template as per **ANNEX-V** as well as additional Quality information as outlined in the template, should be completed as stipulated in the guidelines.

Any additional information that can support the chemistry, manufacturing and control (CMC) of the Investigational Product including but not limited to non-clinical studies, clinical studies and the relevant batch analysis results should be provided as attachments.

Non-clinical data shall be required together with the application package according to the latest version ICH M3 Non-clinical safety studies for the conduct of human clinical trials. Generally, in many cases where the IP has a marketing authorization, the investigational product dossier is not required and summary of product characteristics shall be sufficient. However, for placebo-controlled studies, a qualitative list of the ingredients in the placebo shall be submitted.

2.2.11 Evidence of Good Manufacturing Practices (GMP) compliance

To support the quality of the investigational product (s), the Authority shall rely and accept a valid GMP certificate or confirmation of GMP compliance or GMP inspection report issued by but not limited to:

a) Stringent Regulatory Authorities/WHO listed authorities;
b) Competent Authority of countries that are standing PIC/s members;
c) World Health Organization (WHO) prequalification program;
d) Authorities operating at least at maturity level 3(ML3)
e) Competent Authority that has a recognition agreement with the Authority;
f) EAC Joint GMP inspection procedure.

In case the investigational product is manufactured in a country whose GMP control system is not recognized by the Authority, but the clinical trial has been authorized by one of the above-stated bodies a, b, c, d, e, and f, the decision from that body may be considered.

3.0. Requirements for amendment of approved clinical Trial

3.1 Substantial amendments

The substantial amendment are major changes to the terms of the protocol or any other trial-supporting documentation that is likely to have significant impact and affect the safety and integrity of trial participants, the scientific value of the clinical trial, the conduct or management of the clinical trial, and the quality or safety of any investigational product. All substantial amendment require approval by the Authority.

Sponsors and investigators are required to file Clinical Trial Application Amendment (CTAA) for changes to the protocol and investigational product made after the original CTA that will impact on the safety of the trial participants or will affect the analysis and the interpretation of the safety and efficacy of the drug(s) under investigation. CTAA must be filed and approved by the Authority before such amendments are implemented when the proposed amendments to the protocol or investigational product (s):

a) Affect the selection, assessment, or dismissal of a clinical trial participants;
b) Affect the evaluation of the clinical efficacy of the investigational products;
c) Alter the risk to the health of a clinical trial participants;
d) Affect the safety evaluation of the investigational products or
e) Extend the duration of the treatment.

If such amendments are necessary to protect the life of participants, an urgent amendment may be implemented but the investigator shall inform the ethics committee and the Authority of such amendments with immediate communication (e-mail) within 48 hours. An application for approval of the amendment, which clearly identifies the change and the rationale for immediate implementation of the change, shall be submitted within 15 days after the date of implementation of the amendment.

The substantial amendments submitted when the CTA is under review will not be accepted. He /she sponsor should withdraw the active CTA and submit the amendment as a new CTA. However, non-substantial amendments shall be notified and shall be handled as additional information to the application.

3.1.1 Non-substantial amendments

The non-substantial amendments shall not require the approval of the Authority, but, shall be submitted as notification including the rationale of the change and supporting document must be submitted within 15 days of the implementation of the change. A line list of all notifications must be submitted along with the annual progress report.
The changes may be implemented and notify to the Authority. The recorded changes shall be availed to the Authority upon request during GCP inspection at the trial site. The examples of non-substantial amendment that require notification are provided as **ANNEX VII**

3.2 Filing a Clinical Trial Application Amendment

The CTAA shall be submitted to the Authority in the same way as a new CTA. The regulatory requirements shall differ depending on the type of amendment.
The sponsor or principal investigator shall submit the following documents:

a) Signed and dated cover letter of Clinical Trial Application for amendment
b) Copy of the Clinical Trial Approval Certificate
c) Signed and dated clinical trial application form for an amendment
d) Valid Ethical Clearance Certificate from Rwanda National Ethics Committee
e) Copy of the most recently authorized protocol, including version number.
f) Updated protocol highlighting the proposed amendments if applicable
g) Copy of ICF with changes clearly highlighted if the amendment affects the ICF
h) Addendum to the IB describing any new Quality information, if applicable
i) Supporting data as required depending the amendment of quality of the investigational products (revised CMC information with track changes that have been submitted in the initial clinical trial application, and summary of changes on the CMC information) as applicable.
j) Evidence of payment of prescribed fees.

The authority reserves the rights to request any other documents deemed necessary to support the safety of the trial participants.

Note: Each amendment related to an IP and that leads to a new potential risk for the trial participants must be considered as a substantial amendment.

3.3 Requirements for Renewal of Clinical Trial Authorization

In case the implementation period of the trial is more than one (1) year, the sponsor or principal investigator apply for renewal of Clinical Trial Authorization to continue the implementation of the trial one (1) month before the expiration of the certificate previously issued. The application shall consist of the following documents:

a) Signed and dated Clinical Trial Application letter for renewal;

b) Copy of the Clinical Trial Approval Certificate to be renewed;
c) Valid Ethical Clearance Certificate from Rwanda National Ethics Committee;
d) Valid Local Insurance Policy Covering trial participants;
e) Copy of protocol and its amendments (if applicable) that is being implemented;
f) Updated investigational brochure if applicable;
g) Updated progress report of the implementation of the trial according to the format provided in the guidelines on GCP in Rwanda.

In case of the extension of the trial implementation period, the applicant shall provide justification, all above-mentioned documents, and any other documentation deemed necessary by the Authority.

3.4 Application for import of Investigational Products

The sponsor or principal investigator shall be required to obtain an import permit for importation of Investigational products after authorization of the trial. A copy of the import authorization is required if the investigational product is not directly imported from the manufacturing country to the trial site.

The full requirements for importation and exportation of IP are detailed in guidelines for importation and exportation of Pharmaceutical products. In case of exportation of leftover for the Investigational Products after the completion of the trial, the sponsor or principal investigator shall obtain export permit or destruction certificate from the Authority.

3.5 Requirements for labelling and blinding of Investigational Products

The following information shall be labelled on the carton, inner label and the blisters or strips of the investigational drug product for a clinical trial:

Parameters	**Unit carton or subject kit**	**Inner Labels**	**Blister/Strips/ Vials**
Clinical Trial Protocol Number	√	√ *	√
No, of Subjects or Initial of subject	√**	√**	√**
Investigational Drug Product name or code	√	√	√
Dosage form	√	√*	√**
Name of Active substance	√	√	√
List of excipients	√	√*	√*
Strength	√	√	√
Instructions for use	√**	√ **	√**
Lot number	√**	√	√
Batch number	√	√**	√**
Manufacturing date	√	√**	√
Expiry date	√	√	√

For clinical Trial use only/Cautionary statement	√	√*	√
Name and address of Manufacturer	√***	√***	√***
Route of administration	√	√	√
Storage condition	√	√	√
Pack size (Unit/Vol)	√	√	√

NA Not Applicable

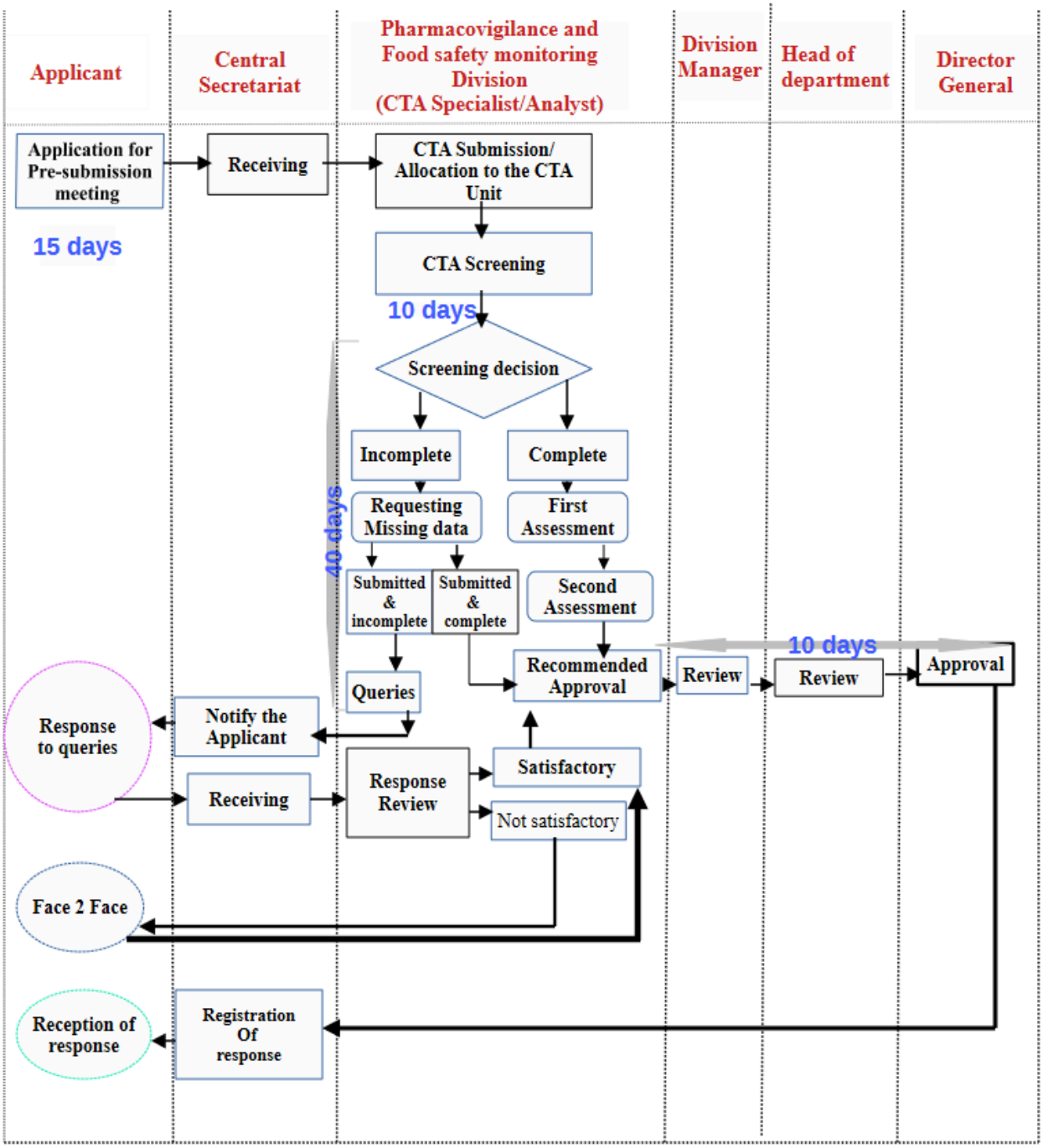
* Exempted for small label such as ampoule and vial.

** Where applicable

*** With letter of authorization where it applies

If the product is supplied without an outer carton, the information that is required on the outer carton should be stated on the inner carton. In blinded trials, the coding system for the investigational product(s) should include a mechanism that permits rapid identification of the product(s) in case of a medical emergency, but does not permit undetectable breaks of the blinding.

APPENDIX I: Clinical Trial Application Process Flow chart



APPENDIX II: Phases of Clinical Trials

Phase I

These are the first trials of a new active ingredient or new formulations in man, often carried out in healthy volunteers. 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. These trials are tested in a small group of people between 20 to 100 health volunteers.

Phase II

These trials are performed in a limited number of subjects and are often, at a later stage, of a comparative (e.g. placebo-controlled) design. Their purpose is to demonstrate therapeutic activity and to assess short-term safety of the active ingredient 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. These trials are tested in a larger group of people generally 100–300 participants with a specific disease.

Phase III

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 generally in 300 to 3,000 volunteers who have the disease or condition.

Phase IV

Studies performed after marketing of the pharmaceutical 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 pharmaceutical products.

APPENDIX III: List of possible amendments to an approved trial

CHANGES RELATED TO CLINICAL PROTOCOL		
#	**Example of changes include but are not limited to the following:**	**Type**
1	Criteria, tests or procedures required to select or dismiss a clinical trial participant. These include changes to eligibility criteria, tests or procedures for selecting the study population, as well as tests, procedures, or criteria for dismissing clinical trial participants prematurely or at the end of the trial;	Amendment
2	Criteria, tests or procedures required for the ongoing assessment of clinical trial participants, including assessment of safety, or evaluation of safety and efficacy. This includes protocol changes as a result of serious unexpected ADRs;	Amendment
3	Study design, study population, duration of use, objectives, or hypotheses, including adding or discontinuing a study arm that was not included as a provision in the original CTA protocol;	Amendment
4	Changes in the primary efficacy endpoint(s), important secondary efficacy endpoints (e.g., those that could be used in support of a marketing application), safety endpoints, sample size estimation, or addition of interim analyses that will affect the analysis and interpretation of the study results;	Amendment
5	Dose level, dosage schedule, or treatment duration;	Amendment
6	Changes to the post-treatment follow-up period that may affect the safety evaluation of the drug.	Amendment
7	Adding or removing a concomitant medication, which may impact on the analysis of efficacy or increase the risk to clinical trial participants;	Amendment
8	Criteria for expedited reporting of serious, unexpected adverse drug reactions;	Amendment
9	Increases in blood volume, changes in procedures, enrolling additional subjects in PK studies or confirmatory testing in PK studies that were not specified in the original CTA protocol; and/or	Amendment
10	Aspects of the conduct of the study that may increase the risk to the health of clinical trial participants.	Amendment
11	Increasing the screening period or other administrative changes to accommodate logistical constraints in study conduct that do not affect the safety of the trial participants	Notification
12	Minor changes to the inclusion and exclusion criteria, such as laboratory chemistry cut-off values that reflect clinical practice and improve the safety of clinical trial subjects;	Notification
13	Changes to administrative information such as new contact names and numbers and ages of individuals, organizations, or other entities, involved in the conduct of the trial;	Notification
14	Updating the ICF with new safety information that does not require a protocol amendment;	Notification
15	Annual Investigator Brochure updates	Notification
16	Changes to the quality information that does not affect the quality or safety of the investigational product	Notification
CHANGES RELATED TO QUALITY (CMC) OF INVESTIGATIONAL PRODUCT		

	DRUG SUBSTANCE (Biologics and Radiopharmaceuticals)	
#	**Example of changes include but are not limited to the following:**	
1	Replacement or addition of a manufacturing site involving:	
	a. production of the starting material, intermediate, or drug substance	Amendment
	b. testing (e.g., release, stability)	Notification
2	Change in the manufacturing process for the drug substance intermediate, involving:	
	a. the fermentation process [for example (e.g.), scale-up, new bioreactor technology, use of new raw materials of biological origin]; or change in the route of synthesis of the radiopharmaceutical drug substance or critical component*	Amendment
	b. the purification process (e.g., addition/removal/replacement of a purification step)	Amendment
3	Change in the specifications for the drug substance involving:	
	a. deletion or replacement of a test, relaxation of an acceptance criterion or addition of a test for a new impurity	Amendment
	b. addition of a test (other than a test for new impurity) or tightening of an acceptance criterion	Notification
4	Change in the primary container closure system(s) for the storage and shipment of the drug substance provided the proposed container closure system is at least equivalent to the approved container closure system with respect to its relevant properties, and the change does not concern a sterile drug substance	Notification
5	Change in the shelf life for the drug substance, involving:	
	a) Extension i) if the approved shelf life is less than or equal to 18 months	Amendment
	ii) if the approved shelf life is more than 18 months	Notification
	b) Reduction (due to stability concerns)	Amendment
	DRUG PRODUCT (Biologics and Radiopharmaceuticals)	
#	**Type of Change**	**Type**
1	Replacement or addition of a drug product manufacturing site involving:	
	a. production of a drug product (including primary packaging)	
	b. secondary packaging	
	c. testing [for example (e.g.), release, stability]	
2	Change in the drug product manufacturing process (e.g., scale-up, changes to the formulation process); change from manual synthesis of positron-emitting radiopharmaceutical to use of automatic synthesis unit or change in type.	Amendment
3	Deletion of a drug product manufacturer / manufacturing site, primary or secondary packaging site or testing site	Notification
4	Change in the specifications for the drug product, involving:	
	a) deletion or replacement of a test, relaxation of an acceptance criterion or addition of a test for a new impurity	Amendment
	b) addition of a test (other than a test for new impurity) or tightening of an acceptance criterion	Notification
5	Change in the shelf life for the drug product, involving:	

	a. Extension i) if the approved shelf life is less than or equal to 18 months	Amendment
	ii) if the approved shelf life is more than 18 months	Notification
	b. Reduction (due to stability concerns)	Amendment
6	Change in the storage conditions for the drug product	Amendment
7	Changes in final product dosage form (e.g., liquid to lyophilized formulation)	Amendment
8	Changes in final product strength	Amendment
9	Change in diluent, involving replacement or addition of a diluent for a lyophilized powder or concentrated solution by a diluent, which is commercially available in Canada, is water for injection (WFI) or a salt solution, and after reconstitution, there is no change in the drug product specifications outside of the approved ranges.	Notification
10.	Change in radiolytic protective agent or antioxidant	Amendment
DRUG SUBSTANCE (Pharmaceuticals)		
#	**Type of Change:**	**Type**
1	Replacement or addition of a manufacturing site involving:	
	a. production of drug substance	Amendment
	b. testing (e.g., release, stability)	Notification
2	Change in the manufacturing process for the drug substance intermediate or starting material (e.g., reaction conditions, solvents, catalysts, synthetic routes, reagents, etc.)	Amendment
3	Change in the batch size for the drug substance (no impact on quality)	Notification
4	**Change in the specification for the drug substance involving test and acceptance criteria:**	
	a. Deletion or replacement of a test, relaxation of an acceptance criterion, or addition of a test for a new impurity	Amendment
	b. addition of a test (other than a test for a new impurity) or tightening of an acceptance criterion	Notification
5	Change in the re-test period (or shelf life) for the drug substance, involving:	
	a. Extension	Notification
	b. Reduction (due to stability concerns)	Amendment
DRUG PRODUCT (Pharmaceuticals)		
1	Addition of a dosage form or strength	Amendment
2	Change in the composition of a dosage form	Amendment
3	Qualitative or quantitative addition, deletion or replacement of a colour or flavour with no negative impact on stability	Notification
4	Change in diluent, involving replacement or addition of a diluent for a lyophilized powder or concentrated solution	Amendment
5	Replacement or addition of a drug product manufacturer / manufacturing site involving:	

	a. Production of an immediate release drug product (tablet, capsule, liquids, semi-solids) within the same Manufacturer	Notification
	b. Production of an immediate release drug product (tablet, capsule, liquids, semi-solids) to a new Manufacturer	Amendment
	c. Production of a modified release product	Amendment
	d. Production of a sterile drug product	Amendment
	e. Primary packaging (non-sterile products)	Notification
	f. Testing (e.g., release, stability)	Notification
6	Change in the drug product manufacturing process	Amendment
7	Change in the specification for the drug product tests and acceptance criteria, involving:	
	a. Deletion or replacement of a test, relaxation of an acceptance criterion, or addition of a test for a new impurity	Amendment
	b. addition of a test (other than a test for a new impurity) or tightening of an acceptance criterion	Notification
8	Change in the shelf life for the drug product, involving:	
	a. Extension	Notification
	b. Reduction (due to stability concerns)	Amendment
9	Change in the storage conditions for the drug product	Amendment

ENDORSEMENT OF THE GUIDELINES

	Author	**Authorized by**	**Checked by**	**Approved by**
Title	Division Manager of Pharmacovigilance & Food Safety Monitoring	Head of Food & Drugs Inspections & Safety Monitoring Department	Quality Assurance Analyst	Director General
Names	**NTIRENGANYA Lazare**	**Dr. Eric NYIRIMIGABO**	**NDAYAMBAJE Théogène**	**Dr Emile BIENVENU**
Signature				 Digitally signed by Rwanda FDA (Director General) Date: 2023.04.06 10:34:17 +02'00'
Date	04/04/2023	04/04/2023	05/04/2023	06 / 04 / 2023

ANNEX-I: Clinical Trial Application Form (CTA)

Format: QMS/FMT/002 Revision No: 1 Effective Date: 20 June 2022		Department/Division /Office/Unit	FDISM/PVSM/CT
Document Type: **Form**			Doc. No : FDISM/PVSM/FOM/xxx
RWANDA FDA Rwanda Food and Drugs Authority	Title: **Clinical Trial Application**		Revision Number : 01 Revision Date: : 28/02/2023 Effective Date : 28/02/2023 Review Due Date : 28/02/2023 Ref Doc. : FDISM/PVSM/GDL/005

Clinical Trial Application Form (CTA)		☐ **Routine CTA** ☐ **Non-Routine CTA**
1.	Title of the Study:	
2.	Protocol Number :	
3.	Protocol version number	
4.	Protocol date:	
5.	Clinical trial Phase	
6.	Trial objectives	
7.	Trial Design:	
8.	Investigational product's name, number or identifying mark	
9.	Indications	
10.	Comparator product (if applicable	
11.	Concomitant medications (if applicable	
12.	Number of Participants	
13.	Trial Site (s)	
14.	Duration of the trial	
15.	Amount paid for this application	
16.	Sponsor's names	Names: Institution: E-mail address: Phone number (with country code):
17.	Principal Investigator's names	Names: Institution E-mail address: Phone number (with country code):
18.	Contact Person names and Full address	Names: Institution E-mail address:

		Phone number (with country code):	
DECLARATION BY THE APPLICANT			
19.	I, (*Insert the names of Sponsor or PI*) the undersigned, hereby declare that I have submitted all required documentations, and have disclosed all information which may influence the approval of this application I, hereby declare that all information contained or referenced in this application is complete, accurate and is not false or misleading. I, agree and ensure that once the above said clinical trial is approved, will be conducted according to the submitted protocol, legal, ethical and regulatory requirements of Rwanda FDA		
20.	**Names of applicant**	**Signature**	**Date**

ANNEX- II: Clinical Trial Protocol Format

Format: QMS/FMT/002 Revision No: 1 Effective Date: 20 June 2022		Department/Division /Office/Unit	FDISM/PVSM/CT
Document Type: **Form**			Doc. No : FDISM/PVSM/FOM/xxx
RWANDA FDA Rwanda Food and Drugs Authority	Title: **Clinical Trial Protocol Format**		Revision Number : 01 Revision Date: : 28/02/2023 Effective Date : 28/02/2023 Review Due Date : 28/02/2023 Ref Doc. :FDISM/PVSM/GDL/xxx

This template should be filled in and submitted in **Microsoft word format** with times new roman style font size 12 black ink)	
GENERAL INFORMATION	
Title of Study	
Protocol Identification Number/code	
Protocol Version Number (where applicable)	
Date of Protocol	
Rwanda FDA Application Number	
Ethical Clearance Number/ Date of Approval	
Name of Investigational Product or Intervention	
Therapeutic Classification	
Dosage Form(s) and Strength(s)	
Route(s) of Administration	
Name of Comparator Product (where applicable)	
Name and address(es) of the Applicant	
Name and address(es) of the Sponsor	
Name and address(es) of the Principal Investigator (PI)	
Name and address(es) of the Study Monitor	
Name and address(es) of Study Site(s)	
Name and address of the manufacturer of investigational product	

Name and address of the manufacturer of comparator product (if applicable)		
Phase of Trial		
Duration of study		

1. BACKGROUND AND RATIONALE

(Insert a brief, concise introduction into the clinical problem and previous treatments and developments, i.e., pertinent data from previous preclinical/clinical pharmacology studies and therapeutic exploratory studies taking into account relevant scientific literature (citations by consecutive numbering, with list at end of this section; important or not readily available references may be included with the paper submission, if appropriate). This section should also contain information on the new drug). Provide rationale for conducting the study in Rwanda

2. OBJECTIVE OF THE TRIAL

(Insert the objectives that are the same as the objectives contained in the protocol. Include the primary objective and secondary objectives)

Primary Objective(s):

Secondary Objective(s):

3. STUDY ENDPOINTS

(Insert the endpoints that are the same as the endpoints contained in the body of the protocol. Include the primary endpoint and important secondary endpoints)

Primary Endpoint(s):

Secondary Endpoint(s):

4. STUDY DESIGN

4.1 *Insert summary description of the type/design of trial to be conducted (e.g. double-blind, placebo-controlled, parallel design). Provide a simple summarized snapshot of your study design not to exceed a single page. This section should include a diagram that provides a quick to 1 page. Please present an overview of your study design in a schematic diagram and tables. The data presentation can be adapted depending on the nature of your study and can be customized according to your protocol. Example: complete the tables with study-specific information and adapt the table(s) to illustrate your study design.*

Arm 1	*Sample size*	*Intervention A*

Arm 2	*Sample size*	*Intervention B*

Include instructions for progressing to next phase (if applicable):

Include a schematic diagram to show the design, procedures and stages including study arms, visits, time-points, interventions etc.

4.2 *Summary of the randomization method and procedures to allocate participants to treatment groups;*

4.3 *Blinding (methods of blinding (masking) and other bias reducing techniques to be used);*

4.4 *Summary description of the trial treatment(s) and the dosage and dosage regimen of the investigational product(s), including packaging, and labeling of the investigational product(s);*

4.5 *Maintenance of trial treatment randomization codes and procedures for breaking codes;*

4.6 *Total study duration (anticipated starting/ finishing dates);*

4.7 *Expected duration for each subject including post treatment period etc;*

5. STUDY PARTICIPANTS

5.1 Participants' characteristics, Age ranges of participants, Gender, use of vulnerable participants, and justification

5.2 *Provide a brief description of specific characteristics of the trial participants (e.g. disease/ stage/ indication/ conditions/ treatment etc.) as applicable and of diagnostic criteria and assessment*

5.3 *State the Inclusion criteria:*

5.4 *State the Exclusion criteria*

6. PREMATURE WITHDRAWAL / DISCONTINUATION CRITERIA

6.1 ***Withdrawal criteria:***

6.1.1 *Enumeration of all conditions / criteria and management for drug/ patient's withdrawal or (premature) discontinuation, including voluntary withdrawal by subject without prejudice to future treatment by the physician. The type and timing of the data to be collected for withdrawn participants.*

6.1.2 *State whether and how participants are to be replaced.*

6.1.3 *The follow-up for participants withdrawn from investigational product treatment/trial*

6.1.4 *Treatment*

6.2 *State the stopping rules" or "discontinuation criteria" for individual participants, parts of trial and entire trial;*

7. INVESTIGATIONAL DRUG FORMULATION

7.1 *(Brief description of the study drug(s) and formulation to be used in the clinical trial. The relationship to the formulations used in the preclinical and/or other clinical trials should be delineated, as applicable. This may also include disclosure of the formulation intended to be marketed and/or any bridging studies which may be necessary, planned, initiated and/or already performed if different formulations have been used during clinical development.)*

7.2 *Instructions for safe handling;*

7.3 *State the accountability procedures for the investigational product(s), placebos and comparator(s) and disposal;*

8. DOSAGE REGIMEN

8.1 *Rationale for dose selection*

8.2 *Provide the following regarding the treatment(s) to be administered:*

8.2.1 *The name(s) of all the product(s):*

8.2.2 *Dose(s):*

8.2.3 *The dosing schedule(s):*

8.2.4 *The route/mode(s) of administration:*

8.2.5 *The treatment period(s):*

8.2.6 *Follow-up period(s) for participants for each investigational product treatment/trial treatment group/arm of the trial:*

8.2.7 *Concomitant Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial:*

8.2.8 *Procedures for monitoring participant's compliance:*

8.2.9 *Wash-out period (Description for pre-, during- and post-trial, as applicable)*

9. PRE-STUDY SCREENING AND BASELINE EVALUATION

(Describe in summary the process of clinical validation for participation in the clinical trial, including methodology / schedule of events.)

10. TREATMENT / ASSESSMENT VISITS

(Insert the schedule of all events / visits / procedures during the clinical trial)

11. EFFICACY VARIABLES AND ANALYSIS

11.1 *Description and validation of primary endpoint(s), i.e. responses/changes from baseline over time in relation to clinical trial events. Description and validation of related secondary changes (secondary endpoints) following from clinical trial events.*

11.2 *Provide specification of the efficacy parameters.*

11.3 *Describe the methods and timing for assessing, recording, and analyzing efficacy parameters*

12. ASSESSMENT OF SAFETY

12.1 *Specification of safety parameters:*

12.2 *The methods and timing for assessing, recording, and analyzing safety parameters:*

12.3 *Procedures for eliciting reports of and for recording and reporting adverse events and intercurrent illnesses.*

12.4 *The type and duration of the follow-up of subjects after adverse events*
12.5 *RISKS: (Identify potential risks and mitigation strategies (e.g. need for and risks associated with long term immunosuppression)*
12.6 *DATA and SAFETY MONITORING PLAN (DSMP):* *(Summarize the Data and Safety Monitoring Plan. Describe measures that will be implemented to minimize risk to study subjects e.g. specific inclusions/exclusions; plans to ensure medical intervention in the case of an adverse event for subjects; plans for surveillance, detection and management of specific adverse events that might or could occur; potential use of an Independent Safety Monitor or Data Safety Monitoring Board (DSMB)* 12.7 *Immune Monitoring and immunosuppression: (Describe and justify the plan for immunosuppression and immune monitoring (if applicable)*
13. ASSAYS/METHODOLOGIES
13.1 *Briefly describe any specialized assays or methodologies that will be used in this clinical study or supporting study/studies (Provide a more detailed summary of assay methods and summarize assay qualification/validation. Indicate where specialized testing will be conducted)* 13.2 *The names and contact addresses of the laboratories to be used for the study;* 13.3 *State the location of the attached draft Material Transfer Agreements (MTAs) in the submission;* 13.4 *State the duration for long term storage of samples and the area to be stored*
14. STATISTICAL ANALYSIS PLAN
14.1 *Specify the planned sample size to be used in the study and its justification*
14.2 *Summary of description of the statistical methodologies to be used to evaluate the effectiveness of the investigational product, including the hypotheses to be tested, the parameters to be estimated, the assumptions to be made and the level of significance and the statistical model to be used.* 14.3 *Analysis of trial parameters (primary/ secondary endpoints), population, demographics, as applicable.* 14.4 *Efficacy analysis methods and results of efficacy end-point analysis.* 14.5 *Safety analysis methods and results of safety end-point analysis.* 14.6 *Exploratory end-point analysis: evaluation effect(s) (or lack of effects) of relevant biochemical/ pharmacological etc parameters, as applicable.*

14.7 *Pharmacokinetic endpoint analysis, as applicable.*

14.8 *Interim analysis and role of Data Safety Monitoring Board, as applicable*

15. OUTCOME CRITERIA

(Describe criteria that would define whether you would or would not move forward with the subsequent development plan, based upon primary and designated secondary objectives)

16. DATA MANAGEMENT

(Describe procedures for recording, processing, handling, and retaining raw data and other study documentation)

17. MONITORING PLAN

(Summary of the monitoring plan)

State the location of the detailed monitoring plan in the submission

18. ETHICAL CONSIDERATIONS

18.1 *State the ethical clearance reference number and institutions that have approved the trial*

Institution review Board ethical clearance: Number and date

RNEC ethical clearance number and Date:

18.2 ***Insurance Details:***

18.2.1*Insert local Insurance Company name and address:*

18.2.2*policy cover number:*

18.2.3*Validity:*

18.2.4*Expiry Date:*

18.2.5 *State the location of the Insurance cover in the submission:*

18.2.6 *Number of insured participants*

18.3 ***Participant Information sheets and Informed Consent forms:***

(The contents should be as per ICH guidelines, these guidelines and declaration of Helsinki)

18.3.1*State the version number and dates for both English and Kinyarwanda*

18.3.2*State the location of the Participant Information sheets and Informed Consent forms in the submission*

18.4 *State the amount to be reimbursed to the participants*

18.5 *Treatment and/or management of participants and their disease condition(s) after completion of trial*

18.6 *Follow-up of trial study participants after the conclusion of the trial*

18.7 *In case of transfer of materials, provide Material Transfer Agreement (MTA) highlighting among other things, the following:*

18.8 *Identification of the provider and recipient*
18.9 *Identification of the material and the volume of material*
18.10 *Definition of the trial and how the material will and will not be used.*
18.11 *Maintenance of confidentiality of background or supporting data or information, if any*
18.12 *Indemnification and warranties (where applicable)*
18.13 *Details on post-trial access to the products*
19. BENEFIT/RISK ASSESSMENT
Evaluation of the anticipated benefits and risks of participating in the trial and proposed measures to address the known and potential risks of participating in the trial and to protect participants

ANNEX-III: Joint Declaration for Sufficient Funds

Format: QMS/FMT/002 Revision No: 1 Effective Date: 20 June 2022	Department/Division/Office/Unit	Pharmacovigilance and Food Safety Monitoring Division
Document Type: **Form**		Doc. No : FDISM/PVSM/FOM/xxx
RWANDA FDA Rwanda Food and Drugs Authority	Title: **Joint Declaration for Sufficient Funds**	Revision Number : 01 Revision Date: : 28/02/2023 Effective Date : 28/02/2023 Review Due Date : 28/02/2023 Ref Doc. : FDISM/PVSM/GDL/005

The Joint Declaration for Sufficient Funds should be completed and signed by Sponsor and National Principal Investigator concerning to Complete Study)

Title of the study:	
Protocol:	
Investigational Product(s):	

I, <*insert full name*>, Sponsor /representing the sponsor (*delete whichever is not applicable*) and
I, <full name>, Principal Investigator/National Principal Investigator

hereby declare that sufficient funds have been made available to complete the above-mentioned study according to legal, ethical, and regulatory requirements currently enforced in Rwanda.

Done at ……

SPONSOR	**National /Principal Investigator**:
Name: Address: E-mail address: Phone number: Signed:	Name: Address: E-mail address: Phone number: Signed:

ANNEX-IV: Declaration by principal investigator or co-investigator

Format: QMS/FMT/002 Revision No: 1 Effective Date: 20 June 2022	Department/Division/Office/Unit	Pharmacovigilance and Food Safety Monitoring Division
Document Type: **Form**		Doc. No : FDISM/PVSM/FOM/xxx
RWANDA FDA Rwanda Food and Drugs Authority	Title: **Declaration by principal investigator or co-investigator**	Revision Number : 01 Revision Date: : 28/02/2023 Effective Date : 28/02/2023 Review Due Date : 28/02/2023 Ref Doc. : FDISM/PVSM/GDL/005

Note that all investigators should fill and sign this form	
Title of clinical trial:	
Role in clinical trial:	
Title of clinical trial:	
Clinical trial protocol number:	
Investigational Product:	
Clinical trial site:	
DECLARATION	

I, *(Insert Full names*), the **principal investigator or co-investigator *(****delete as applicable****)*** in above mentioned study, hereby DECLARE that:

1. I am familiar with the International Conference on Harmonization-Good Clinical Practice (ICH-GCP) and understand the responsibilities and obligations of the Principle Investigator (PI) within the context of this study.

2. I have notified the Rwanda FDA of any aspects of the study with which I do not/am unable to, comply. (If applicable, this may be attached to this declaration.)

3. I 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).

4. I will conduct the trial as specified in the protocol and in accordance with Rwanda FDA requirements and ICH – GCP principles.

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

6. I will not commence the trial before written authorization from the National Ethics Committee and Rwanda FDA has been obtained.

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

representatives.

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

9. 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*].

10. I have*/have not (delete as applicable) previously been the principal investigator at a site which has been closed due to failure to comply with ICH-GCP (*Attach details).

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

Principal Investigator:	**Date**	**Signature**

ANNEX-V: Investigational Product Quality Overall Summary Template

Format: QMS/FMT/002 Revision No: 1 Effective Date: 20 June 2022		Department/Division/Office/Unit	Pharmacovigilance and Food Safety Monitoring Division
Document Type: **Form**			Doc. No : FDISM/PVSM/FOM/xxx
RWANDA FDA Rwanda Food and Drugs Authority	**Investigational Product Quality Overall Summary Template**		Revision Number : 01
			Revision Date: : 28/02/2023
			Effective Date : 28/02/2023
			Review Due Date : 28/02/2023
			Ref Doc. : FDISM/PVSM/GDL/005

*This template should be filled in and submitted in **Microsoft word format** with New times roman style font size 12 black ink). Details on this summary should as inserted as prescribed in the CTD module 3.)*	
Title of Study	
Protocol Identification Number/code	
Protocol Version Number (where applicable)	
Date of Protocol	
Rwanda FDA Application Number	
Name of Investigational Product or Intervention	
Therapeutic Classification	
Dosage Form(s) and Strength(s)	
Route(s) of Administration	
Clinical trial Design *(extract from the protocol)*	
Name of Comparator Product (where applicable)	
Name and address(es) of the Applicant	
Name and address(es) of the Sponsor	
Name and address(es) of the Principal Investigator (PI)	
Name and address(es) of the Study Monitor	
Name and address(es) of Study Site(s)	
Name and address of the manufacturer of investigational product	
Name and address of the manufacturer of comparator product (if applicable)	
Phase of Trial	
Proprietary (Brand) Name of FPP	
Non-proprietary or Common Name of Drug Substance (Medicinal Ingredient)	

Company Name	
Dosage Form(s)	
Strength(s)	
Country from which the Clinical Supplies were Obtained for the Lot to be Used in this Clinical Trial (as well as the market status in that country)	

2.3. S ACTIVE PHARMACEUTICAL INGREDIENT (NAME, MANUFACTURER)

2.3. S.1 General Information (name, manufacturer)

2.3. S.1.1 Nomenclature (name, manufacturer)

(a) Recommended International Non-proprietary name (INN):

(b) Compendial name, if relevant:

(c) Chemical name(s):

(d) Company or laboratory code:

(e) Other non-proprietary name(s) (e.g., national name, USAN, BAN):

(f) Chemical Abstracts Service (CAS) registry number:

Note: For Phase I Trials only (a) and (b) is required

2.3. S.1.2 Structure (name, manufacturer)

(a) Structural formula, including relative and absolute stereochemistry:

(b) Molecular formula:

(c) Molecular mass:

2.3. S.1.3 General Properties (name, manufacturer)

(a) Physical description (e.g., appearance, colour, physical state):

(b) Physical form (e.g., preferred polymorphic form, solvate, hydrate):

(c) Solubilities (e.g., aqueous/non-aqueous solubility profile, tabular format, reporting in mg/mL):

(d) pH and pKa values:

(e) Other relevant information:

2.3. S.2 Manufacture (name, manufacturer)

2.3. S.2.1 Manufacturer(s) (name, manufacturer)

(a) Name, address, and responsibility of each manufacturer, including Contractors, and each proposed production site or facility involved in the manufacturing of the batches to be used in this clinical trial:

(b) List of referenced Drug Master Files (DMFs) and DMF Numbers (copies of

DMF letters of access should be located in Module 1):

2.3. S.2.2 Description of Manufacturing Process and Process Controls (name, Manufacturer)

(a) Flow diagram of the synthetic process(es):

Note: For Phase II & III include also the following should be submitted: -

(b) Detailed narrative description of the manufacturing process(es):

2.3.S.2.3 Control of Materials (name, manufacturer)

(a) For Active Pharmaceutical Ingredient manufactured with reagents obtained from sources that are at risk of transmitting Bovine Spongiform Encephalopathy (BSE)/Transmissible Spongiform Encephalopathy (TSE) agents (e.g., ruminant origin), provide an attestation (with supporting documentation, if applicable) confirming that the material is free of BSE/TSE agents:

Note: For Phase II & III include also the following should be submitted:

(b) Information on starting materials

2.3. S.2.4 Controls of Critical Steps and Intermediates (name, manufacturer)

(a) Summary of the controls performed at critical steps of the manufacturing

(b) Process and on intermediates:

2.3. S.3 Characterization (name, manufacturer)

2.3. S.3.1 Elucidation of Structure and other Characteristics (name, manufacturer)

(a) List of studies performed (e.g., IR, UV, NMR, MS, elemental analysis) and Summary of the interpretation of evidence of structure:

(b) Discussion on the potential for isomerism and identification of Stereochemistry (e.g., geometric isomerism, number of chiral centres and configurations):

(c) Summary of studies performed to identify potential polymorphic forms (including solvates):

(d) Summary of studies performed to identify the particle size distribution of the Active Pharmaceutical Ingredient:

(e) Other characteristics:

2.3. S.3.2 Impurities (name, manufacturer)

a. Identification of potential and actual impurities arising from the synthesis, manufacture and/or degradation:

b. List of drug-related impurities (e.g., starting materials, by-products, intermediates, chiral impurities, degradation products, metabolites), including chemical name, structure and origin:

Drug-related Impurity	Structure	Origin

(chemical name or descriptor)		

(c) List of process-related impurities (e.g., residual solvents, reagents, catalysts), including compound name and step used in synthesis:

(d) Actual levels of impurities (e.g., drug-related and process-related) found in Batches used in nonclinical and clinical studies:

Impurity (drug-related and process-related)	Acceptance Criteria	Results (include batch number and use) (e.g., clinical)		

2.3. S.4 Control of the Active Pharmaceutical Ingredient (name, manufacturer)

2.3. S.4.1 Specification (name, manufacturer)

(a) Specification for the Active Pharmaceutical Ingredient:

Test	Acceptance Criteria	Analytical Procedure (Type and Source)

2.3. S.4.2 Analytical Procedures (name, manufacturer)

(a) Summary of the analytical procedures (e.g., suitability, key method parameters, conditions):

2.3. S.4.3 Validation of Analytical Procedures (name, manufacturer)

(a) Tabulated summary of the validation information (e.g., system suitability testing, validation parameters and results):

2.3. S.4.4 Batch Analyses (name, manufacturer)

(a) Description of the batches to be used in this clinical trial (or representative batches):

Batch Number	Batch Size	Date of Manufacture and Site of Production	Use (e.g., clinical)

(b) Summary of results for the batches to be used in this clinical trial or Representative batches (should include tests, types of analytical procedures (type and source), and actual results):

2.3. S.4.5 Justification of Specification (name, manufacturer)

(a) Justification of the Active Pharmaceutical Ingredient specification (e.g., manufacturing experience, stability, historical batch analysis results, safety considerations):
For Phase one trial only Batch analysis report is required.

2.3. S.6 Container Closure System (name, manufacturer)

(a) Description of the container closure system(s) for the storage and shipment of the Active Pharmaceutical Ingredient:

2.3. S.7 Stability (name, manufacturer)

2.3. S.7.1 Stability Summary and Conclusions (name, manufacturer)
(a) Summary of stability studies to support this clinical trial (e.g., studies conducted, protocols used, results obtained):

(b) Proposed storage conditions and re-test period (or shelf life, as appropriate):

2.3. S.7.2 Stability Protocol and Stability Commitment (name, manufacturer)

(a) If full long term stability data is not available at the time of filing, provide a summary of the stability protocol and a commitment for the continued monitoring of the Active Pharmaceutical Ingredient stability according to the protocol:

2.3. S.7.3 Stability Data (name, manufacturer)

(a) The actual stability results (i.e., raw data) may be found in:

(b) Summary of analytical procedures and validation information for those
Procedures not previously summarized in 2.3.S.4 (e.g., analytical procedures used only for stability studies):

2.3. P FINISHED PHARMACEUTICAL PRODUCT (NAME, DOSAGE FORM)

2.3.P.1 Description and Composition of the FPP (name, dosage form)

(a) Description of the dosage form:
(b) Composition of the dosage form:

(i) Composition, i.e., list of all components of the dosage form, and their amounts on a per unit basis (including overages, if any):

Component and Quality Standard (and Grade, if applicable)	Function	Strength (label claim)			
		Quantity per unit	%	Quantity per unit	%

(i) Composition of all *components that are mixtures* (e.g., colorants,
coatings, capsule shells, imprinting inks):-
a) Description of reconstitution diluent(s), if applicable:
b) Type of container closure system used for accompanying reconstitution diluent, if applicable:
c) Qualitative list of the components of the placebo samples to be used in this
Clinical trial, if different from the components listed in 2.3. P.1(b):

2.3. P.2 Pharmaceutical Development (name, dosage form)

(a) Discussion on the development of the dosage form, the formulation,
Manufacturing process, etc.:
(b) For sterile, reconstituted products, summary of compatibility studies with Diluents/containers:

2.3. P.3 Manufacture (name, dosage form)

2.3. P.3.1 Manufacturer(s) (name, dosage form)

(a) Name, address, and responsibility of each manufacturer, including contractors, and each proposed production site or facility involved in the manufacturing of the batches to be used in this clinical trial:

(b) List of referenced Drug Master Files (DMFs) and DMF Numbers (copies of DMF letters of access should be located in Module 1):

(c) Attestation that the dosage form was manufactured under Good Manufacturing Practices (GMP) conditions:

2.3. P.3.2 Batch Formula (name, dosage form)

(a) List of all components of the dosage form to be used in the manufacturing process, and their amounts on a per batch basis (including overages, if any):

Strength (label claim)	
Batch Size(s) (number of dosage units)	
Component and Quality Standard (and Grade, if applicable)	Quantity per batch
Total	

2.3. P.3.3 Description of Manufacturing Process and Process Controls (name, dosage form)

(a) Flow diagram of the manufacturing process:

(b) Detailed narrative description of the manufacturing process, including Equipment type and working capacity, process parameters ***(for Phase II & III trials***)

(b) For sterile products, details and conditions of sterilization and lyophilization:

2.3. P.3.4 Controls of Critical Steps and Intermediates (name, dosage form)

(a) Summary of controls performed at the critical steps of the manufacturing Process and on isolated intermediates (***for Phase II & III trials***)

2.3. P.4 Control of Excipients (name, dosage form)

2.3. P.4.1 Specifications (name, dosage form)

Specifications for non-compendial excipients and for compendial excipients Which include supplementary tests not listed in the monograph(s) may be found in:

(a) List of referenced Drug Master Files (DMFs) and DMF Numbers (copies of DMF letters of access should be located in Module 1):

2.3. P.4.5 Excipients of Human or Animal Origin (name, dosage form)

(a) List of excipients that are of human or animal origin (including country of origin):

(b) Summary of the information (e.g., sources, specifications, description of the
Testing performed, viral safety data) regarding adventitious agents for excipients of human or animal origin:
For excipients obtained from sources that are at risk of transmitting Bovine
Spongiform Encephalopathy (BSE)/Transmissible Spongiform Encephalopathy (TSE) agents (e.g., ruminant origin), provide an attestation (with supporting documentation, if applicable) confirming that the material is free of BSE/TSE agents:

2.3. P.4.6 Novel Excipients (name, dosage form)

(a) Summary of the details on the manufacture, characterization, and controls,
With cross references to supporting safety data (nonclinical and/or clinical) on novel excipients (i.e., those used for the first time in a FPP or by a new route of administration):

2.3. P.5 Control of FPP (name, dosage form)

2.3. P.5.1 Specification(s) (name, dosage form)

(a) Specification(s) for the FPP:

Test	Acceptance Criteria	Analytical Procedure (Type and Source)

2.3. P.5.2 Analytical Procedures (name, dosage form)

(a) Summary of the analytical procedures (e.g., key method parameters, conditions, suitability):

2.3. P.5.3 Validation of Analytical Procedures (name, dosage form)

(a) Tabulated summary of the validation information (e.g., system suitability testing, validation parameters and results):

2.3. P.5.4 Batch Analyses (name, dosage form)

(a) Description of the batches to be used in this clinical trial (or representative batches):

Strength and Batch Number	Batch Size	Date of Manufacture and Site of Production	Input Drug Substance Batch	Use (e.g., clinical)

`

(b) Summary of results for the batches to be used in this clinical trial or

Representative batches (should include tests, types of analytical procedures (type and source), and actual results):

Note: For Phase one trial only Batch analysis report is required.

2.3. P.5.5 Characterization of Impurities (name, dosage form)

(a) Information on the characterization of impurities, not previously provided in 2.3. S.3.2 (e.g., summary of actual and potential degradation products):

2.3. P.5.6 Justification of Specification(s) (name, dosage form)

(a) Justification of the Active Pharmaceutical Ingredient specification (e.g., manufacturing experience, stability, historical batch analysis results, safety considerations):

2.3.P.7 Container Closure System (name, dosage form)

(a) Description of the container closure systems, including unit count or fill size, container size or volume:

(b) Materials of construction of each primary packaging component:

(c) For sterile products, details of washing, sterilization and depyrogenation

d) Procedures for container closures:

2.3. P.8 Stability (name, dosage form)

2.3. P.8.1 Stability Summary and Conclusions (name, dosage form)

(a) Summary of stability studies to support this clinical trial (e.g., studies conducted, protocols used, results obtained):

(i) Description of stability study details:

Storage Conditions (oC, % RH, light)	Strength and Batch Number	Batch Size and Date of Manufacture	Container Closure System	Completed (and Proposed) Test Intervals

(ii) Summary and discussion of stability study results:

(b) Proposed storage conditions and shelf life (and in-use storage conditions and in-use period, if applicable):

2.3. P.8.2 Post-approval Stability Protocol and Stability Commitment (name, dosage form)

(a) If full long term stability data is not available at the time of filing, provide a summary of the stability protocol and a commitment that the stability of the clinical trial samples or representative batches will be monitored throughout the duration of the clinical trial or proposed shelf life:

2.3. P.8.3 Stability Data (name, dosage form)

(a) The actual stability results (i.e., raw data) may be found in:

(b) Summary of analytical procedures and validation information for those Procedures not previously summarized in 2.3.P.5 (e.g., analytical procedures used only for stability studies):

5. Additional Requirements for Clinical trials for medical devices

An application to authorize a clinical trial involving a medical devices or diagnostics shall be made in accordance with provisions provided in section 2 of these guidelines. In addition, the following documentation will be required;

a) Device Description, design and materials including User manual, catalogue of IFU of the device.
b) Marketing history
c) Risk assessment and standard list
d) Toxicology and biological safety
e) Sterilization validation
f) Electrical safety
g) Safety and usefulness of medicinal substance
h) Safety and appropriateness of use of tissues of animal origin
i) Signed and approved protocol with data compiled as prescribed in ANNEX-II and current ISO standards.
j) Certificate of ISO/ Quality audit (ISO 13485) for manufacturer of the device if applicable.

ANNEX-VI : Protocol Pre-Submission Synopsis

Format: QMS/FMT/002 Revision No: 1 Effective Date: 20 June 2022		Department/Division/Office/Unit	Pharmacovigilance and Food Safety Monitoring Division
Document Type: **Form**			Doc. No : FDISM/PVSM/FOM/xxx
RWANDA FDA Rwanda Food and Drugs Authority	Title: **Protocol Pre-Submission Synopsis Template**		Revision Number : 01 Revision Date: : 28/02/2023 Effective Date : 28/02/2023 Review Due Date : 28/02/2023 Ref Doc. : FDISM/PVSM/GDL/005

Protocol Pre-Submission Synopsis Template			
1.	Title of the Study:		
2.	Sponsor name:		
3.	Investigational Product (s)		
4.	Background and Rationale (Brief)		
5.	Indication (s)		
6.	Clinical trial Phase		
7.	Trial objectives	Primary objectives: Secondary Objectives):	
8.	Trial Design		
9.	Trial End points	Primary endpoints: Secondary endpoints:	
10.	Number of Participants		
11.	Eligibility criteria	Inclusion criteria: Exclusion criteria:	
12.	Trial Site (s)		
13.	Duration of the trial		
	Date	**Names**	**Signature**

ANNEX-VII: Clinical Trial Amendment Application Form (CTA-A)

Format: QMS/FMT/002 Revision No: 1 Effective Date: 20 June 2022		Department/Division/Office/Unit	Pharmacovigilance and Food Safety Monitoring Division
Document Type: **Form**			Doc. No : FDISM/PVSM/FOM/xxx
RWANDA FDA Rwanda Food and Drugs Authority	**Clinical Trial Amendment Application Form (CTA-A)**		Revision Number : 01 Revision Date: : 28/02/2023 Effective Date : 28/02/2023 Review Due Date : 28/02/2023 Ref Doc. : FDISM/PVSM/GDL/005

This form should be filled and signed by applicant for substantial amendment for an already approved clinical trial

A. DETAILS OF THE APPROVED ORIGINAL PROTOCOL

Reference Number of the approved Clinical Trial	
Date of approval of original protocol (dd/mm/yyyy)	
Clinical Trial Title	
Principal Investigator approved for the clinical trial	
Number of sites approved for the clinical trial	
Number of subjects approved for the clinical trial	
Applicant of the current amendment (Sponsor or principal investigator)	
Contact person responsible for this application	First name: Surname name: E-mail: Tel:

B. SUMMARY OF PROPOSED CHANGES

Amendment title, number and natures supporting documentation: *List of all types of supporting documents that you will submit*

Summary of current	**Proposed change details:**
Reason/rationale for change(s): *Please provide the rationale for each change if more than one*.	
Multi-centre trials: *Will this amendment apply to all approved site(s)?*	☐ **YES** ☐ **NO**
If No: Specify the sites for which the amendment will apply	

C. DOCUMENTATION CHECKLIST	
Valid ethical approval of the proposed change(s)	☐ **YES** ☐ **NO**
Proof of payment of amendment fees as per Rwanda FDA regulations	☐ **YES** ☐ **NO**
Revised Protocol with version number (if applicable)	☐ **YES** ☐ **NO**
Other relevant supporting documentation in line with the amendment	☐ **YES** ☐ **NO**
Valid ethical approval of the proposed change(s)	☐ **YES** ☐ **NO**

D. DECLARATION (by applicant)

I, (*Insert the Sponsor or PI*) the undersigned, hereby declare that I have submitted all required documentations, and have disclosed all information which may influence the approval of this application

☐ There are no changes being made other than those applied for in this submission, except for possible editorial changes. Any other changes will be applied for separately.

☐ The information submitted is true and correct.

Names:	**Signature:**	**Date:**