RWANDA FDA
Rwanda Food and Drugs Authority

QMS No.: DIS/CRC/007/RwandaFDA/2020

CLINICAL TRIAL DOCUMENTATION REQUIREMENTS

INTRODUCTION

The Rwanda Food and Drugs Authority (Rwanda FDA) is the regulatory authority in Rwanda mandated among other regulatory functions to regulate, approve and inspect the conduct of clinical trials. This Document highlights detailed requirements that need to be followed by Investigators and Sponsors when submitting their applications for approval to conduct 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 trials. The following documentation are elaborated for the general public and in particular companies and individuals intending to conduct clinical trials in Rwanda.

However, new application to conduct a clinical trial 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:
    a) The introduction of a completely new concept of device into clinical practice where components features and/or methods of action, are previously unknown;
    b) 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;
    c) Where a device, either CE-marked or non-CE-marked, is proposed for a new purpose or function;
    d) Where in vitro and/or animal testing of the device cannot mimic the clinical situation
3. 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
4. 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.

    It is necessary to emphasize that no company/person shall import, procure or manufacture a drug product, cosmetic or medical device for the purpose of a clinical Trial in Rwanda unless she/he is a holder of a valid clinical trial approval. The conduct of all clinical trial must be in accordance with the terms of the approval and the provisions of Good Clinical Practice Regulations. (Refer to https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf)

A. CLINIAL TRIAL APPLICATION REQUIREMENTS:

1. PRE-CLINICAL TRIAL APPLICATION (CTA) MEETING

a) An application for a pre-CTA consultation meeting should be made by the sponsor and submitted to the Director General of Rwanda FDA
b) The pre-meeting creates an opportunity for the Sponsor and the Regulator to deliberate on the potential study plan, address areas of conflict if any, prior to submission of the clinical trial application.
c) The application should include proposed date and time for the meeting and a brief synopsis (hard and electronic copies) of the proposed study listing questions (if any) to be addressed by Rwanda FDA, during the meeting.
d) A confirmation of the date and time of meeting shall be duly conveyed to the Sponsor within 30 calendar days after the receipt of meeting request

2. CLINICAL TRIAL APPLICATION (CTA)

The application may be delivered physically or by courier to Rwanda FDA. An application to conduct a clinical trial shall be addressed to the Director General of Rwanda FDA with the following supporting documents:

a) Cover letter addressed to Director General of Rwanda FDA
b) A duly filled and signed clinical trial application form obtained from Rwanda FDA **(Annex 1)**
c) General investigational plan
d) Clinical trial Protocol (detailed content **Annex 2)**
e) Investigators' brochures
f) Capacity building plans including training and updating of staff involved in the trial.
g) Clinical study reports (accomplished Clinical trial phases)
h) National Ethics Committee Clearance

i) Participant Information Leaflet (PIL).
j) Informed Consent Forms (English, French and Kinyarwanda)
k) Curriculum vitae (CVs) of Principal investigator and Co- investigators
l) Joint declaration by Sponsor (or representative) and National Principal Investigator in prescribed format **(Annex 3)**
m) Evidence of accreditation of the designated Laboratories or other evidence of Good Laboratory Practice (GLP) and assay validation.
n) Letters of Access (if applicable) authorizing Rwanda FDA to access related files (Drug master Files, Site Reference Files) must be submitted.
o) Filled in Quality Overall Summary – Chemical Entities Template. **(Annex 4)**
p) Declarations by Principal investigator and Co- investigators **(Annex 5)**
q) Evidence of agreement between the Sponsor and the Investigator.
r) Case Report Forms (CRFs)
s) Serious Adverse Events reporting form **(Annex 6)**
t) Certified copy of insurance policy cover of study participants
u) Certificate of Good Manufacturing Practice (GMP) for manufacture of the trial product and/or placebo
v) Trial product labels and package Insert/s for other trial medicines.
w) Mock up labels for the Investigational products.
x) List and Charter of the Data Safety Monitoring Board/Committee (DSMB).
y) Declaration of Conflict of Interest, Financial Disclosure by the investigator.
z) Evidence of payment of prescribed fees

3. ADDITIONAL REQUIREMENTS FOR CLINICAL TRIALS IN 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
k) Certificate of ISO/ Quality audit (ISO 13485) for manufacturer of the medical device

4. CLINICAL TRIAL AUTHORISATION TIMELINES

The approval and Authorization to conduct the clinical trial in Rwanda shall be issued upon satisfactory review of the submitted application package within 60 working days.

5. TARIFFS

All applicable fees for clinical trials shall be paid according to the regulation N° CBD/TRG/004 related to Regulatory service tariff/fees and charges currently enforced accessible on Rwanda FDA website on the following link: http://www.rwandafda.gov.rw/web/fileadmin/Regulation_governing_service_fees_Tariff_and_Fines_Version2_Final.pdf

The application fees should be paid on one of the following Rwanda FDA bank accounts:

- BNR: 1000047658 Entitled '' RWANDA FDA'' in FRW
- BNR: 1000047666 entitled '' RWANDA FDA'' in USD
- BK:00040 06972093 63 entitled "RWANDA FOOD AND DRUGS AUTHORITY" in FRW
- BK:00040 06972094 64 entitled "RWANDA FOOD AND DRUGS AUTHORITY" in USD

6. OBLIGATION TO CONDUCT CLINICAL TRIAL IN RWANDA

1. The study is to be conducted strictly in accordance with the approved protocol and Rwanda FDA regulatory requirements.
2. Any amendment to the protocol shall be subject to the approval of the Rwanda FDA in line with the regulatory requirements.

3. Rwanda FDA shall carry out inspections at the approved trial site(s).
4. Fatal or life threatening SUSARs should be submitted not later than 7 calendar days after the sponsor has information that the case reported fulfils the criteria for a fatal or life-threatening SUSAR, with any follow up information to be reported within a further 8 calendar days.
5. All other SUSARs and SAE should be submitted not later than 15 calendar days after the sponsor has information that the case fulfilled the criteria for a SUSAR
6. A progress report shall be submitted to Rwanda FDA during the conduct of the Clinical trial **on monthly basis** for study not exceeding 6 months, **on quarterly basis** for studies from seven months to eleven months and on **a six months basis** for one year study and above.
7. Final Report of the Clinical Trial shall be submitted to Rwanda FDA at the end of the study.
8. All correspondences should be addressed to the Director General of Rwanda FDA

7. TERMINATION OF CLINICAL TRIAL

a. **Premature termination**

If a clinical trial is terminated by the principal investigator or sponsor in its entirety, the principal investigator or sponsor must inform Rwanda FDA not later than 15 days after the date of the termination; and must:

a) Provide Rwanda FDA with the reason(s) for the termination and its impact on the proposed or ongoing clinical trials in respect of the investigational medicinal product including issues related to accountability and disposal of investigational products as well as maintenance of records.

b) As soon as possible, inform all co-investigators of the termination and of the reasons for the termination and advise them in writing of potential risks to the health of clinical study participants or other persons including ensuring that patients continue to receive medical care.

c) Submit confirmation that the dispensing or importation of the drug to the discontinued sites has been stopped.

d) Submit Confirmation that reasonable measures to ensure the return of all unused quantities of the drug will be taken.

b. **Suspension, termination or withdrawal of a clinical trial by Rwanda FDA**

Rwanda FDA may suspend, terminate or withdraw authorization of a clinical trial if the conditions of authorization of a trial have been violated or if there is an information raising doubts about the safety or scientific validity of the trial, or the conduct of the trial at a particular trial site

Done at Kigali, on 9th April, 2020

Dr. Charles KARANGWA
Ag. Director General

Annex 1: CLINICAL TRIAL APPLICATION FORM (CTA)

To be completed by Applicants for all Clinical Trials

Study Title:

Protocol No:

Version No: **Date of protocol:**

Investigational product's name, number or identifying mark:

Comparator product (if applicable):

Concomitant medications (if applicable):

Date(s) of Rwanda FDA approval of previous protocol(s):

Sponsor:

Applicant:

Contact Person:
Address:
Telephone Number: **Fax Number:**
Cell phone Number:
E-mail address:

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Date original application received: **Proposed Clinical Trial Committee meeting date:**

Application/Reference No.:
Application Fee paid:

Signature: **Date:**

(All future communications to Rwanda FDA regarding the application should quote the above

ANNEX 2: OVERALL SUMMARY/SYNOPSIS – CLINICAL TRIAL PROTOCOL TEMPLATE

1. 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	

(Instructions; Please insert the protocol summary in respective sections below the subtitles and delete the guidance notes in blue.)

2.	**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
	Assessor's comments:
3.	**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):**
	Assessor's comments:
4.	**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):**
	Assessor's comments:
5.	**Design**
5.1	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.

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

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

5.4 Summary description of the trial treatment(s) and the dosage and dosage regimen of the investigational product(s), including packaging, and labelling of the investigational product(s);

5.5 Maintenance of trial treatment randomization codes and procedures for breaking codes;

5.6 Total study duration (anticipated starting/ finishing dates);

5.7 Expected duration for each subject including post treatment period etc;

Assessor's comments:

6. Study participants

6.1 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

6.2 State the Inclusion criteria:

6.3 State the Exclusion criteria

Assessor's comments:

7. Premature Withdrawal / Discontinuation Criteria

7.1 **Withdrawal criteria:**

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.

.2 State whether and how participants are to be replaced.

.3 The follow-up for participants withdrawn from investigational product treatment/trial Treatment

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

8. Drug Formulation

8.1 (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.)

8.2 Instructions for safe handling;

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

Assessor's comments:

9. Dosage Regimen

9.1 Rationale for dose selection

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

9.2.1 The name(s) of all the product(s):

9.2.2 Dose(s):

9.2.3 The dosing schedule(s):

9.2.4 The route/mode(s) of administration:

9.2.5 The treatment period(s):

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

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

9.2.8 Procedures for monitoring participant's compliance:
9.2.9 Wash-out period
(Description for pre-, during- and post-trial, as applicable)

Assessor's comments:

10. 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.)

11. Treatment / Assessment Visits

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

Assessor's comments:

12. Efficacy Variables and Analysis

12.1 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.

12.2 Provide specification of the efficacy parameters.

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

Assessor's comments:

13. Assessment of Safety

13.1 Specification of safety parameters:

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

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

13.4 The type and duration of the follow-up of subjects after adverse events

13.5 RISKS: (Identify potential risks and mitigation strategies (e.g. need for and risks associated with long)
13.6 term immunosuppression)

13.7 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)

13.8 Immune Monitoring and immunosuppression: (Describe and justify the plan for immunosuppression and immune monitoring (if applicable)

Assessor's comments:

14. Assays/methodologies

14.1 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)

14.2 The names and contact addresses of the laboratories to be used for the study;

14.3 State the location of the attached draft Material Transfer Agreements (MTAs) in the submission;

14.4 State the duration for long term storage of samples and the area to be stored

Assessor's comments:

15. Statistical analysis plan

15.1 Specify the planned sample size to be used in the study and its justification

15.2 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.

15.3 Analysis of trial parameters (primary/ secondary endpoints), population, demographics, as applicable.

15.4 Efficacy analysis methods and results of efficacy end-point analysis.

15.5 Safety analysis methods and results of safety end-point analysis.

15.6 Exploratory end-point analysis: evaluation effect(s) (or lack of effects) of relevant biochemical/ pharmacological etc parameters, as applicable.

15.7 Pharmacokinetic endpoint analysis, as applicable.

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

Assessor's comments:

16. 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)

17. Data management
(Describe procedures for recording, processing, handling, and retaining raw data and other study documentation)
18. Monitoring plan
(Summary of the monitoring plan) State the location of the detailed monitoring plan in the submission
Assessor's comments:
19. Ethical considerations
19.1 State the ethical clearance reference number and institutions that have approved the trial Institution review Board ethical clearance: Number and date NIMR ethical clearance number and Date:
19.2 **Insurance Details:** 19.2.1 Insert local Insurance Company name and address: 19.2.2 policy cover number: 19.2.3 Validity: 19.2.4 Expiry Date: 19.2.5 State the location of the Insurance cover in the submission:
19.3 **Participant Information sheets and Informed Consent forms:** (The contents should be as per ICH guidelines, these guidelines and declaration of Helsinki) 19.3.1 . State the version number and dates for both English and Swahili versions 19.3.2 State the location of the Participant Information sheets and Informed Consent forms in the submission
19.4 State the amount to be reimbursed to the participants
19.5 Treatment and/or management of participants and their disease condition(s) after completion of trial
19.6 Follow-up of trial study participants after the conclusion of the trial
19.7 In case of transfer of materials, provide Material Transfer Agreement (MTA) highlighting among other things, the following:
19.8 Identification of the provider and recipient
19.9 Identification of the material and the volume of material
19.10 Definition of the trial and how the material will and will not be used.
19.11 Maintenance of confidentiality of background or supporting data or information, if any
19.12 Indemnification and warranties (where applicable)
19.13 Details on post-trial access to the products
Assessor's comments:

ANNEX 3: JOINT DECLARATION BY SPONSOR (OR REPRESENTATIVE) AND NATIONAL PRINCIPAL INVESTIGATOR CONCERNING SUFFICIENT FUNDS TO COMPLETE STUDY

Title of the study:

Protocol:

I, <full name>, representing <sponsor or representative)

and

I, <full name>, Principal Investigator/National Principal Investigator

hereby declare that sufficient funds have been made available to complete the above-mentioned study.

Signed **Date**

SPONSOR (or representative)
Name
Address
Contact details

Signed **Date**

PRINCIPAL INVESTIGATOR (or National PI)
Name
Address
Contact details

ANNEX 4: QUALITY OVERALL SUMMARY – CHEMICAL ENTITIES CLINICAL TRIAL APPLICATION

(This template should be filled in and submitted in **Microsoft word format** with bookman old style font size 11 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	

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Assessors Recommendation: ☐ **Recommended** (no outstanding issues) ☐ **Query raised** ☐ **Rejected**	**Comments (if any)**	
Name of 1st Assessor		
Signature of 1st Assessor		**Date assessment**
Name of 2nd Assessor		

Signature of 2nd Assessor		**Date of assessment**

ASSESSOR'S INTRODUCTION / DISCUSSION:

PROPOSED COMMENTS/QUERIES TO BE FORWARDED TO THE APPLICANT:

INTRODUCTION

(a) Information on the comparator product:

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)	

(b) If the information in any section (or subsection) has previously been submitted (in its entirety, without changes), and approved by Rwanda FDA, do not resubmit that section. Provide the following information on the cross-referenced submission(s):

Section(and subsections)	Cross-Referenced Submission Name	Rwanda FDA approval certificate number	Date Approved

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/nonaqueous 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 Process and on intermediates:

2.3. S.3 Characterisation (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:

(i) 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 (chemical name or descriptor)	Structure	Origin

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

(c) 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 FPP (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	%

(ii) Composition of all components that are mixtures (e.g., colourants, coatings, capsule shells, imprinting inks): -

(c) Description of reconstitution diluent(s), if applicable:
(d) Type of container closure system used for accompanying reconstitution diluent, if applicable:

(f) 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)

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

c) 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 Characterisation 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 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:

StorageConditios (^{o}C, % 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):

ATTACHMENTS

Attachment Number	Subject

ANNEX 5: DECLARATION BY PRINCIPAL INVESTIGATOR and CO-INVESTIGATOR

Name:
Title of the study:
Protocol and site:

I, the undersigned, 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 analysed 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).

Annex 6: SAE REPORTING FORM

CIOMS FORM

SUSPECT ADVERSE REACTION REPORT	

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE Years	3. SEX	4-6 REACTION ONSET Day	Month	Year	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)										☐ PATIENT DIED ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION ☐ INVOLVED PERSISTENCE OR SIGNIFICANT DISABILITY OR INCAPACITY ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)		20 DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA
15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION	21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA
17. INDICATION(S) FOR USE		
18. THERAPY DATES (from/to)	19. THERAPY DURATION	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER		
	24b. MFR CONTROL NO.	
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE ☐ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL	
DATE OF THIS REPORT	25a. REPORT TYPE ☐ INITIAL ☐ FOLLOWUP	

ANNEX 7: ADR/AEIFI REPORTING FORM

RWANDA FDA
P O. Box 84 Kigali
info@rwandafda.gov.rw
www.rwandafda.gov.rw

ADVERSE DRUG REACTION/ADVERSE EVENT FOLLOWING IMMUNIZATION REPORTING FORM

Type of Report	**Seriousness of ADR/AEFI**	**Category of Suspected Product**
Initial☐ Follow up☐	Serious☐Not Serious☐	Medical product☐ Vaccine☐

I.PATIENT INFORMATION

Patient ID/initials: _____**Gender**: Male ☐Female

☐**Weight**(kg)_____ **Height** (m): _____Pregnancy Status: **YES** ☐ **NO**

☐**Date of birth***:* _____/____/_____

Patient Address: Village _____Cell: _____

Sector: _____District: _____ Phone Nº _____

Patient's Medical History (Provide any relevant medical history and laboratory results including dates (if done):
……
……
……
……
……
……
……
……
……

II. INFORMATION ON ADVERSE EVENT(S)

Brief description of the ADR/AEFI:

(a) Information on Onset:
Date of ADR/AEFI onset: ____ /_____/_____(dd/mm/yyyy)
Time of onset: _____/___ _/_____ (hours, Min, Sec)
Date ADR/AEFI stopped: _____ / ____/_____(dd/mm/yyyy)

(d) Adverse Event Evolution/ Outcome:
Recovered ☐ Recovering ☐ Recovered with sequelae ☐
Not recovered ☐ Congenital abnormality ☐ Death ☐ Unknown ☐

(b)Severity of the ADR/AEFI: Mild ☐ Moderate ☐ Severe ☐ Unknown ☐

Reason for seriousness: Prolonged hospitalization☐Disability ☐Congenital abnormality☐Death☐Life threatening☐

(e)Causality of the ADR/AEFI (If performed):

Certain☐Probable/Likely ☐Possible ☐Unlikely ☐Unclassifiable ☐

(c) Action Taken:

Drug withdrawn ☐ Dose increased ☐ Dose reduced ☐Dose not changed ☐Substituted ☐Antidote ☐**Other☐*(Specify):***
……
……
……
……
……

(f) Optional information:

☐Therapeutic Failure *(Provide information on medicine (s) or vaccine (s) that showed lack of efficacy*…….
☐Medication errors *(Provide details of medication errors)*
……
….

III. INFORMATION ON SUSPECTED PRODUCT

A. Details of suspected medicinal product Source/Supplier:……

Product brand name&manufacturer	**Generic name/ /Strength/ Dosage form**	**Route of Administration**	**Dose and frequency**	**Starting Date and Time**	**Stopping Date and Time**	**Batch Nº. & Expiry date**	**Indications (Reason for use)**

Other medicines used at the same time and/ or in the last one month (including herbal medicines)							

B. Details of Suspected Vaccine					Diluent (if applicable)		
Name of vaccine	**Date of vaccination**	**Time of vaccination**	**Dose (1st, 2nd, 3rd etc.)**	**Batch/Lot N°&Expiry date**	**Name of diluent**	**Batch/Lot N°& Expiry date**	**Date & time of re-constitution**

IV. REPORTER INFORMATION					
Name of reporter:		Qualification:		Phone number	
Health Facility Name:		District:		Report Reference N°	
E mail Address of Reporter:		Contact/Tel N°:		Date of report:	
Note: Reporters and patients' identity are held in strict confidentiality by Rwanda FDA and protected to the fullest extent of the Law					