RWANDA FDA
Rwanda Food and Drugs Authority

GUIDELINES ON GCP INSPECTION OF CLINICAL TRIALS IN RWANDA

APRIL, 2023

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FOREWORD

Rwanda Food and Drugs Authority (Rwanda FDA) was established by the Law N° 003/2018 of 09/02/2018. Rwanda FDA is a regulatory authority that has the mandate of regulating and inspecting clinical trials, among others, as stipulated for in article 8, paragraph 7 and 12 of the said Law.

Furthermore, the provisions of the technical regulations N° FDISM/PVSM/TRG/001 governing the conduct and inspection of clinical trials especially in its article 34 and 38, Rwanda FDA issued Guidelines N° FDISM/PVSM/GDL/009 on Good Clinical Practices (GCP) Inspection of Clinical Trials in Rwanda.

The purpose of inspecting clinical trials is to ensure that the trials are conducted in accordance with the standards of Good Clinical Practices (GCP). GCP is an international ethical and scientific quality standard for designing, conducting, performing, monitoring, auditing, recording and reporting clinical trials that involve the participation of human subjects.

Compliance with this standard provides public assurance that the rights, safety, and well-being of trial participants are protected; consistent with the principles that have their origin in the Declaration of Helsinki, and that the quality, reliability, and integrity of data collected are credible.

These Guidelines detail the steps and processes required during the GCP inspection of clinical trial conduct to ensure the effective protection of trial participants and compliance with requirements as well as the clinical trial protocol.

Strict adherence to these guidelines will facilitate the acceptance of clinical data by international regulatory authorities, especially since these guidelines adopt the basic principles outlined by the International Committee on Harmonization of Good Clinical Practice (ICH-GCP) with some customization to fit the local requirements.

I am confident that the publication of these Guidelines will mark another milestone in our efforts to strengthen clinical research in Rwanda. The Authority acknowledges all the efforts of key stakeholders who participated in the development and validation of these guidelines.

Dr. Emile BIENVENU
Director General

Digitally signed by
Rwanda FDA
(Director General)
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GUIDELINES DEVELOPMENT HISTORY

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23/07/2021	0	First issue
31/03/2023	1	1. The reference number was changed from DIS/GDL/043 to No FDISM/PVSM/GDL/009_1 as per the current SOP on document control. 2. Criteria for designing, conducting, recording, and reporting clinical trials were included in line with the latest version of ICH GCP and AVAREF guidelines; 3. Frequency of trial monitoring based on risk included; 4. Considerations for inspection of multicentre trials were included; 5. Section related to remote GCP inspections was included; 6. Formats and forms were updated to include a section related to the trial administrative formation 7. Necessary editorial changes in line with SOP on document control were included.

TABLE OF CONTENTS

ACCRONYMS AND ABBREVIATIONS

ALCOA **:** Attributable, Legible, Contemporaneous, Original and Accurate

AVAREF : African Vaccine Regulatory Forum

CAPA : Corrective Action and Preventive Action

CRF : Case Report Form

CRO : Contract Research Organization

DSMB : Data and Safety Monitoring Board

GCP : Good Clinical Practice

IB : Investigator's Brochure

ICH **:** International Conference on Harmonization of Technical

IP : Investigational Product

IRB **:** Institutional Review Board

RNEC **:** Rwanda National Ethics Committee

SAE **:** Serious Adverse Event

SOPs **:** Standard Operating Procedures

SUSAR : Suspected Unexpected Serious Adverse Reaction

TMF : Trial Master File

GLOSSARY

In these Guidelines, unless the context otherwise states:

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

"Authority" Means Rwanda Food and Drugs Authority or its acronym "Rwanda FDA", established under the article 2 of the Law N° 003/2018 of 09/02/2018.

"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).

"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 to, written, electronic, magnetic, and optical records, and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken.

"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.

"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 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.

"Investigator" An individual who conducts a clinical investigation.

"Sub-investigator" Any member of a clinical trial team, supervised by the investigator at a trial site and allowed to perform critical trial-related procedures

"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.

"Monitor" The person responsible for ensuring that the study is performed at the agreed progression and that it is conducted, recorded and reported in accordance with the protocol, SOPs, GCP, GLP and the Authority requirement(s).

"Phase I trials" These are 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.

"Phase II trials" These trials are performed in 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 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 of medicinal 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, among others. are normally considered as trials for new pharmaceutical products.

"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 principal 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.

"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.

"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

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, performing, monitoring, auditing, recording and reporting clinical trials that involve the participation of human subjects.

These guidelines provide a set of harmonized procedures to conduct GCP inspection of clinical trials in all phases including bioequivalence studies. Further objectives include ensuring that there is a basis to assure ethical, scientific and data integrity of clinical trials. It may be used by inspectors from the Authority or in joint GCP inspections with RNEC according to the Joint Institutional Collaboration Framework (MoU) between Rwanda FDA and RNEC. It can support recognition of GCP inspection findings and regulations actions for clinical trials between countries that apply the same standards and procedures of GCP inspection.

The areas for the GCP inspection of clinical trial conducted in Rwanda include but not limited to the clinical site organisation, administrative aspects, protocol compliance, informed consent, safety reporting, Source of data verification (SDV), IP management, Clinical sample management, Trial Master File, Trial Management & Monitoring of related clinical trial data.

These guidelines will help the Authority to establish a conducive environment for clinical trial conduct and oversight to ensure sustainable quality, scientifically sound clinical trials conducted in an acceptable and ethical way. Therefore, inspectors and inspected team are urged to adhere to the provisions of these guidelines while planning, preparing, conducting, and reporting clinical trial inspections.

1.1 Scope

These Guidelines apply to the GCP inspection of all clinical trials approved by the Authority and conducted at investigator site (s), sponsor facility (ies), CROs, and other establishments involved in clinical trials deemed necessary.

The areas of the inspection include but are not limited to data and information relating to regulatory approvals, ethics review committee approval, protocols, consent forms, case report forms, IP management, safety reports (SAEs and SUSARs), clinical trial reports (progress and final reports), participant and participant data, sponsors, investigators and personnel involved in the trial, and laboratory data.

1.2 Objectives of GCP Inspections

The objectives to conduct clinical trials inspections are:

a. To safeguard the rights, safety and well-being of trial participants;

b. To verify the quality and integrity of the clinical trial data submitted to the Authority;
c. To assess the compliance with the protocol and applicable regulations, guidelines and standard operating procedures;
d. To assess whether a clinical trial system is suitably designed, controlled, maintained and documented to fulfil the objectives for which it has been set up;
e. To identify areas for quality improvement;
f. To investigate a complaint about the conduct of the study at a particular site;
g. To verify the implementation of corrective actions and preventive actions.

1.3 GCP Inspection Criteria

Rwanda FDA ensures that the rights, safety and well-being of trial participants are protected, and that the results of the clinical trials are accurate and credible. During GCP inspection, Rwanda FDA shall therefore ensure compliance with criteria for designing, conducting, recording, and reporting clinical trials as per the latest version of the ICH GCP Guidelines and Rwanda FDA regulatory requirements:

a) **Clinical trial regulatory requirements:** All clinical trials should have obtained Clinical trial Authorization to conduct the trial and being conducted in compliance with the latest version of ICH GCP guidelines;
b) **Approved Protocol and its supplementary documents**: The Authority shall verify that the approved protocol is being followed at the trial sites to meet the trial objectives;
c) **Ethical considerations:** Rwanda FDA shall verify that the trial is conducted in accordance with ethical principles, including obtaining informed consent from participants, ensuring their privacy and confidentiality, and protecting vulnerable populations;
d) **Investigator qualifications**: Rwanda FDA shall verify at the site's investigators have the appropriate qualifications, training, and experience to conduct the trial
e) **Trial site organization**: Rwanda FDA shall verify at the site has adequate settings including working space, consultation area, laboratories, pharmacy, and equipment to ensure safe, consistent, and proper conduct of the trial;
f) Management of investigational product(s): Rwanda FDA shall verify at the site that the conditions for investigational products are acceptable and that the investigational product(s) is supplied only to the eligible trial participants as per specified dose(s) in the approved protocol. The inspectors shall verify and ensure that the receipt, use, return, and disposal of the investigational product(s) at the trial sites are controlled and documented adequately in line with Rwanda FDA regulatory requirement(s);
g) **Trial Monitoring**: Rwanda FDA shall verify that the trial is monitored to ensure that it is being conducted in compliance with the protocol and that the safety and well-being of participants are being protected;
h) **Documentation and record keeping**: Rwanda FDA shall verify that the trial-related data and documentation to ensure that they are accurately recorded and properly stored to ensure data integrity;
i) **Safety reporting:** Any adverse events that occur during the trial should be reported to Rwanda FDA and Rwanda National Research Ethics Committee;

j) **Data analysis**: Rwanda FDA shall verify that the trial data are analysed using appropriate statistical methods;
k) **Reporting in clinical trials:** Rwanda FDA shall verify that the results of the trial are reported in a clear and concise manner, and in accordance with Rwanda FDA regulatory requirements;
l) **Quality assurance and quality control systems:** Rwanda FDA shall ensure that written SOPs to ensure that trials are conducted and data are generated, documented (recorded), and reported in compliance with the approved protocol, GCP guidelines, and Rwanda FDA regulatory requirement(s).

2. TYPES OF GCP INSPECTIONS

Rwanda FDA conduct the following three main types of inspection for Clinical trial in Rwanda:

a. Routine GCP inspection;
b. Triggered GCP inspections;
c. Follow-up GCP inspection.

The clinical trial sites may be inspected before granting the regulatory approval, while the trial is on-going, when trial participants are being enrolled in a trial or completed on a routine basis or sometimes when triggers by a complaint or there is a suspicion of serious non-compliance integrity issues and/or scientific/ethical misconduct. Generally, GCP inspections are announced. However, unannounced inspections may be possible.

2.1 Routine GCP Inspections

Routine inspections are inspections performed on a regular basis to monitor GCP compliance in the absence of specific trigger elements. These inspections are announced in advance and apply to ongoing clinical trials. The duration of the inspection and the number of inspectors will vary depending on the complexity of the clinical trial and the activities taking place at the site. They are typically scheduled for 3-5 days per site.

2.2 Triggered GCP Inspections

Triggered GCP inspections are conducted when there is a suspected concern due to either the actual issues observed or the potential impact of deviations from GCP on the conduct of the study as a whole or at a particular site or when a serious breach of GCP occurred. In addition, products with a major impact factor could be considered to require special attention. This type of inspection may be done announced or unannounced and apply to ongoing or completed clinical trials.

2.3 Follow up GCP inspections

A follow up is also referred to as re-inspection or re-assessment of the site. It is performed specifically to monitor the result of corrective and preventive actions of the site following previous inspection(s). Depending on the nature of the observation(s), and the work required the follow up inspection could be carried out within the agreed timelines after the previous inspection. The follow up inspection is limited to specified clinical trial non-compliances that have been observed.

3. INSPECTION PROCESS

3.1 GCP Inspection Prioritization

The Authority shall use a risk-based approach to select sites for GCP inspections. The Authorized trials with higher risk are more likely to be inspected. The majority of GCP inspections shall be routine inspections of clinical trials that are ongoing or completed. However, other types of inspections including triggered inspections may also occur. The duration of the GCP inspection shall vary depending on the complexity of the clinical trial, risk involved and activities conducted at the site and shall be scheduled for 3-5 days per site.

The selection of trial sites for the GCP inspection includes, but is not limited to the following criteria:

a. Nature of intervention or investigation product;
b. Clinical trial phase;
c. Inclusion of vulnerable populations in the trial;
d. Size of the trial (number of trial participants and sites).
e. Route of administration of the investigational product;
f. Significant or frequent reports of serious adverse events;
g. Complaint on the conduct of the trial reported to the Authority.

3.2 Inspection Team

The GCP inspections of a clinical trial site must be performed by GCP inspectors appointed by the Authority according to the procedures in place. However, the Authority may involve experts in the GCP inspection of the clinical trial whose qualifications and experience correspond to the proposed clinical trial. In addition, the Authority may conduct joint inspections at the clinical trial site to ensure the safety and protection of participants in clinical trials and the integrity of collected data.

The inspection team will be constituted considering the phase or type of trial, the investigational product, and other variables considered relevant on a case-by-case basis. The inspectors should be well qualified and have valid GCP certification obtained within three (3) years as per ICH-GCP guidelines. The team will have a lead GCP inspector responsible for coordinating the inspection, collating the information from team members, and finalizing the inspection report.

3.3 GCP Inspection of Multicentre trials

Multicentre trials are usually conducted simultaneously by several investigators at different sites implementing the same protocol and its supplementary documents. The trial sites with more participants or frequent serious adverse event reports will be prioritized. However, the non-compliance of the GCP inspection from one clinical trial site can trigger further GCP inspections at other site (s) that were not planned for inspection.

In case of multi-centre clinical trials carried out in more than one country including Rwanda, the non-compliance of the GCP inspection performed by other regulatory authorities will trigger further inspection of the trial site (s) in Rwanda in order to ensure the protection and well-being of the trial participants in Rwanda.

3.4 Notification of GCP inspection

The Authority shall contact the inspectee notifying the date(s) of inspection one (1) months prior to the proposed announced inspection dates and ask to confirm the proposed dates. A subsequent reminder by the Authority may be sent within fourteen (14) days in case the inspectee fails to confirm the availability. If the inspectee fails to confirm the proposed inspection date, the Authority shall conduct the triggered GCP inspection.

The notification will identify the trial to be inspected and proposed sites. In relation to triggered or follow up inspections, the Authority may provide a shorter notice period. The following information shall be requested by the Authority:

a. Participant status per trial site (number of randomized, dropout rate, number of SAEs reported per site, among others.) at trial initiation or during the trial;
b. Copies of Standards Operating Procedures (SOPs) along with amendments (e.g., monitoring procedures, informed consent procedures, SAEs reporting Procedures, Pharmacy Management Procedures, among others);
c. Trial-specific document such as Trial Master File (TMF) or Investigator Site File (ISF), a copy of the current protocol and protocol amendment and informed consent form, source data verification guidelines, investigational product management and accountability, product handling instructions, laboratory manual, randomisation code, breaking procedure, monitoring plans and reports;
d. Updated CV of principal investigator or co-investigators, and members of the DSMB if applicable;
e. In case of computerized system, the PI or sponsor may provide access to the system
f. Any other document deemed necessary by the Authority.

In case the GCP inspection dates are confirmed by both parties, the PI or sponsor shall submit the signed cover letter and aforementioned data to the Authority electronically or hard copy within fourteen (14) days of the receipt of the notice of GCP inspection to the following address:

The Director General
Rwanda Food and Drugs Authority
P.O. Box 1948 Kigali, Rwanda.
E-mail: ***info@rwandafda.gov.rw***.

3.5 Preparation for GCP inspection

The GCP inspection schedule and Clinical Trial GCP Inspection Checklist will be shared to the principal investigator within five (5) working days in order to prepare for the upcoming inspection. Each member of the inspection team should become familiar with all the relevant documents, including the study protocol(s), clinical trial report(s), case report forms, adverse event reports, trial site information, and other related documentation. The inspectee should ensure that access is provided to all trial records, including trial participant medical records, Investigator Site File, Trial Master File, Case Report Forms and applicable standard operating procedures, where applicable.

4. CONDUCT OF GCP INSPECTIONS

4.1 Opening meeting

The opening meeting between the inspector(s) and the inspectee(s) will:

a. Introduce the inspector(s) to the inspectee(s) and identify their roles and responsibilities
b. Confirm the GCP inspection schedule;
c. explain the scope of inspection and GCP Inspection regulatory framework;
d. give a brief overview of the trial site;
e. provide a short summary of the methods and procedures to be used for the conduct of the inspection;
f. confirm the availability of resources, access to records and facilities required for the GCP Inspection, and clarify matters relating to confidentiality;

4.2 Verification and collection of information during GCP inspection

After the opening meeting, the inspection begins. The inspectors assess the site compliance with both regulatory requirements and GCP standards. The essential documents to be reviewed during GCP inspection will depend on the stage of the trial as per regulatory requirements and provisions of the latest version of AVAREF and ICH GCP guidelines.

The GCP inspection checklist (**ANNEX-I**) shall be used to record observations or comments, non-compliance and recommendation for improvement. The scope and activities examined during the inspections undertaken by the Authority may include different aspects.

4.2.1 Legal and administrative aspects

During the inspection, the inspection team shall verify whether the site is ready to conduct clinical trials. This includes verification of the authenticity and validity of the documents issued by the Authority and other relevant bodies.

a. Ethical Clearance

During the Inspection, the inspection team shall verify relevant records relating to ethics to ensure the protection of the rights and welfare of participants in clinical trials. This verification shall include but not limited to:

i. Validity and authenticity of RNEC ethical clearance and consent forms (reference number, dates, signatures, and stamp, among others);
ii. Reports submitted to the RNEC related to the serious adverse events occurring during the trial implementation and follow up as well as other relevant communications with RNEC if any;
iii. Approval given for any advertisement, recruitment, screening, compensation and payments of trial participants.

b. Regulatory Authority approval

The inspection team shall ensure that:

i. Clinical Trial Approval Certificate was granted to conduct the trial prior to its initiation;
ii. Revisions and changes/amendments to the protocol and related documents were granted approval prior to implementation.
iii. Serious adverse events (SAEs) and other reports were submitted to the authority according to the timelines of relevant regulations and guidelines.

4.2.2 Organisational aspects

The inspection team will verify the compliance of the procedures and practices carried out by the investigator with those set out in the protocol and reports submitted to the Authority.

a. Implementation of the trial at the site

The site has to be ready to conduct clinical trials. Depending on the activities undertaken by the site, areas such as a clinic, pharmacy and laboratories should have enough space with appropriate

infrastructure and equipment. The access to the storage of investigational products (IPs) and other services should be controlled as appropriate.

b. Organisation and personnel

The investigator is responsible for ensuring that an investigation is conducted according to the approved protocol, the investigational plan, and applicable regulations and guidelines. The contract between the sponsor and the investigator has to clearly define the responsibilities of each party. The inspectors shall verify if:

i. The clinical trial agreement (contract, Memorandum of Understanding) is still valid, i.e., dated, period covering the trial, signatures by all parties;
ii. The academic qualification and work experience as stated in the curriculum vitae and training records;
iii. The research team complies with the multidisciplinary aspect as per trial requirements;
iv. Training records are available and updated by checking certificates of training and training log or reports;
v. The training subjects were relevant to the trial objectives being implemented at the trial site.

c. Facilities and equipment

Each site should be equipped with adequate, calibrated and maintained equipment depending on the type of clinical trial to be conducted.

d. Implementation of the protocol

The Clinical trial should be conducted in accordance with the provisions of the approved study protocol and/or amendments. During the inspection, inspectors shall verify if:

i. The approved protocol is being implemented;
ii. all trial participants enrolled met the inclusion and exclusion criteria;
iii. dosing, meals (fed and fasting), sample collection were done as stipulated in protocol;
iv. randomization, product information, reporting of serious adverse events, and preparation of reports are compliant with the requirements;
v. there are no deviations from the approved protocol;
vi. violations to the protocol were reported;
vii. Reporting of results was/being done as required.

e. Management of biological samples

The aim of checking the management of biological samples is to examine conditions, and documentation regarding collection, analysing, storage and shipping conditions (if applicable) for proper management of biological samples. Laboratory of a Clinical research site should be able to analyse samples as specified in the protocol. In case the testing is outsourced, the contracts should define the responsibilities and scope of each party including sample transport, storage, preparation and methods used as well as reporting of results. The inspectors shall review the contracts and appropriate SOP for sample handling at the time of inspection.

f. Organisation of the documentation

The site needs to have archiving facilities with sufficient space to ensure the protection of records from damage, i.e. fire, water, humidity, and deterioration. The site has to have procedures and records to place and retrieve documents and trial data. During the inspection, SOPs and records to archive electronic data and electronic records shall be verified.

g. Monitoring and auditing

The Sponsors generally perform site monitoring of a clinical trial to assure high quality trial conduct. The sponsor may perform such monitoring directly, or may utilize the services of an outside individual or organization (e.g., contract research organization). The "on site" monitors review individual case histories in order to verify adherence to the protocol, ensure the ongoing implementation of appropriate data entry and quality control procedures, and verify adherence to GCP principles.

h. Use of computerised systems

The use of validated computerized systems to generate data should be encouraged. Computer hardware, software, and associated documents (e.g., user manual) that create, modify, maintain, archive, retrieve, or transmit in digital form information related to the conduct of a clinical trial should be validated. During the course of inspection, it will be necessary to ascertain their validation status. Computer system features, security, maintenance and controls, back up and data recovery should be inspected to ensure data integrity. The inspection team will ensure the availability of a central computerized system that is protected to ensure the backup or data recovery of clinical trials.

4.2.3 Informed consent of trial participants

The aim is to determine whether informed consent was obtained in accordance with ICH GCP principles. The trial participants have to be informed of the advantages and disadvantages of participating in a trial. This includes information on the IP, possible adverse events, insurance, and other issues. The inspection team will verify and confirm that:

a. The required information was presented to the participant, verbally and in writing;
b. If each participant signed the ICF prior to participating in the trial;
c. The contact details of the investigator or secretariat were given to trial participant(s).

4.2.4 Review of the trial participant data

The aim of trial subject data review is to check whether the investigator team conducted the clinical trial according to the approved protocol and its amendments by source data verification. In the source data verification, it will be necessary to evaluate the source records taking into account their organisation, completeness and legibility. The description of the source data inspected should be reported by the

inspector. It will be necessary to evaluate whether corrections to the data recorded in the CRF were done according to the latest version of the ICH Good Clinical Practice (signed and dated by the authorised person who did it and providing justification, if necessary). For a number of participants that will be determined within the inspection plan, (the sample might include the first and last patient enrolled among others) the following should be checked:

a. Characteristics of the participant the clinical trial;
b. Participant' visits calendar;
c. Efficacy and safety assessment data;
d. Concomitant therapy and intercurrent illness;
e. Safety management and reporting.

4.2.5 Data integrity in clinical trial

During the course of inspections, the authority shall verify the integrity of data generated in clinical trial and to assure the protection of trial participants, in addition to ensuring that clinical trial is conducted according to the applicable regulations and guidelines.

An open reporting culture in research sites should be encouraged as fundamental to data integrity promotion throughout the data lifecycle, including processes from generation or recording of data to destruction, if needed, and the intervening processes.

Decisions made, based on the outcome of clinical trials, rely on the integrity of the results and data obtained during the study. The data should be complete, attributable, legible, contemporaneous, original and accurate, commonly referred to as "ALCOA+". This applies to all data and information as reflected in manual records and electronic data from computerized systems.

4.2.6 Management of the investigational product(s)

The aim is to verify whether all the activities related to the management of Investigational Product(s) has been done according to the protocol and appropriate SOPs at trial site. Clinical research sites usually have a pharmacy where IPs are stored and dispensed under appropriate conditions. The inspection team during the inspection shall very and confirm that:

a. access is controlled and that access records reflect entry and exit against the clinical trial activities such as dates for receiving and storage of IPs, dispensing, issuing, returns, and disposal;
b. SOP content for the various activities including receiving, checking, storage, dispensing, labelling, and reconciliation of IPs. Verify the related records to ensure compliance with the protocol and SOPs;
c. SOP and records to monitor the conditions under which the IPs are stored. Verify the labelling requirements against the room storage conditions such as temperature and relative humidity

observed from the calibrated devices. If there values outside the specifications, verify if they were investigated and if any prospective impact on the IPs was assessed;

d. Records relating to the IP, such as import license, proof of purchase, shipping letter, storage conditions during transport, certificate of analysis, stock card, and dispensing record including dates, quantity and signatures;
e. Check the suitability of storage conditions and their records (fridge, freezer and controlled substances, among others);
f. Cross check the records such as label sheets, randomization, CRFs, and reconciliation record for the IPs;
g. Whether IP labels contain the correct information such as the study number, "for clinical trial use only", participant number, period, randomization, dosage form, and route of administration, as appropriate;
h. SOP for safe disposal of damaged or expired IPs.

The inspectors should check where required that these documents have been signed and dated by the responsible persons according to the site SOP and/or applicable requirements related to the management of Investigational Products. If access to any record or copying is denied, or there is any withholding of documents or denial of access to areas to which the inspector has legal access, the refusals should be documented and included in the inspection observations or report.

4.3 Interview with Research Team Members

During the Inspection, the team of inspectors will interview the research team member to determine how the clinical trial is or being conducted. The interview responses may trigger the deep review of essential documents pertaining to the clinical trial being inspected.

4.4 Inspection of trial site facilities, equipment and system

The team of Inspectors shall inspect facilities equipment and system used to conduct the clinical trial being inspected and take appropriate documented evidence to support the inspection report where necessary. The inspection team shall inspect the following units: consultation room, laboratory, pharmacy, data management room, trial equipment and instrument, clinical trial documentation, and other applicable infrastructure covering the trial operations.

4.5 Generating GCP inspection findings

The GCP inspection evidences should be evaluated against the inspection criteria in order to determine inspection findings. These findings can indicate compliance or non-compliance with inspection criteria. The inspection findings should include compliance and good practices along with their supporting evidence, opportunities for improvement, and any recommendations to the inspectee. The findings should be well documented in a clear, concise manner using the inspection checklist (**ANNEX -I**) adopted from AVAREF and supported by objective evidence.

4.6 Clinical Trial Inspection Closing Meeting

At the end of the inspection, a closing meeting with the purpose of presenting inspection findings to the inspectee(s) will be held at the clinical trial site. During the closing meeting, on the last day of inspection, the preliminary findings noted during inspection will be highlighted. This meeting will help to ensure that the results of the inspection are clearly understood and that there is no misunderstanding by both parties. This is also an opportunity to discuss the findings, request/provide clarifications and supporting documentation, as needed, and also ask questions.

The inspector(s) or the inspectee(s) will also sign the Memorandum Form of GCP findings (**ANNEX-II**) listing all the non-compliant findings noted during the clinical trial inspection of which a copy will be left at the investigator's site.

4.7 Remote GCP inspections

During public health emergencies, the Authority may remotely perform GCP inspections where access to the clinical sites is difficult. If a remote inspection reveals issues that require on-site inspection, or the inspection objectives could not be met remotely, the site shall be physically inspected.

4.8 Grading of clinical trial inspection findings

The grading of findings from GCP inspections of Clinical Trial sites are classified into three risk categories: critical (Risk-1), Major (risk-2), Minor (risk 3) and other findings.

4.8.1 Critical findings

Critical findings are conditions, practices or processes that adversely affect the rights, safety or well-being of the participants and/or the quality and integrity of data or that represent a serious violation of regulations and guidelines. They present the situation that result in fatal, life-threatening or unsafe conditions for study participants. The critical findings may include fraud, adulteration, misrepresentation, falsification of records, absence of source documents and falsified data are classified as critical findings.

4.8.2 Major findings

The major findings are conditions, practices or processes that describes a situation where a marked finding, other than a critical one, may result in undue health risks for the clinical trial participants or in other persons and/or could invalidate the data.

4.8.3 Minor findings:

Minor findings are conditions, practices or processes that would not be expected to adversely affect the rights, safety or well-being of the participants and/or the quality and integrity of data. The minor findings imply the necessitate actions for improvement of conditions, practices and processes.

4.8.4 Other findings:

Other findings are conditions, practices or processes that inspection team may highlight in the report on how to improve quality or reduce the potential for a deviation to occur in the future.

4.8.5 Considerations for grading of GCP inspection findings

The GCP inspection findings classification may vary depending on circumstance, severity of the findings, corrective actions and preventive actions that may be taken and nature of the investigational product. In some circumstances an otherwise major findings may be categorised as critical. However, a finding reported after a previous inspection and not corrected may be given higher classification.

4.9 Outcome of GCP inspections

The results of a GCP inspection is inspection report and a close out letter describing the outcome with the applicable regulations and guideline(s) issued by the Authority. The overall inspection report concludes that the clinical trial site is:

a. **Compliant**- only minor and major observations were reported;
b. **Non-Compliant**-one or many critical observations; or a repetition of major observations reported during a previous inspection and may result in suspension or termination of the trial.

4.9.1 Clinical trial Inspection Report

Once the inspection has been completed, an inspection report will be written in the format shown in the **ANNEX-IV** and is issued to the sponsor/investigator within twenty (20) working days from the last day of inspection. The inspectee is required to acknowledge the receipt of GCP report and propose corrective and preventive actions (CAPAs) to all highlighted findings within fifteen (15) working days.

In case CAPAs are satisfactory, the Authority will issue the Inspection closing letter. However, if CAPAs are not satisfactory, additional actions will be requested by the Authority and when necessary, a follow up inspection may be conducted for verification. Once the CAPA is deemed acceptable, the Authority will send a GCP inspection close out letter.

4.9.2 Transparency & Confidentiality during GCP Inspections

The Authority will conduct GCP inspections of authorized clinical trials in a transparent manner from preparation, planning and conduct of inspections in accordance with provisions of regulations, guidelines

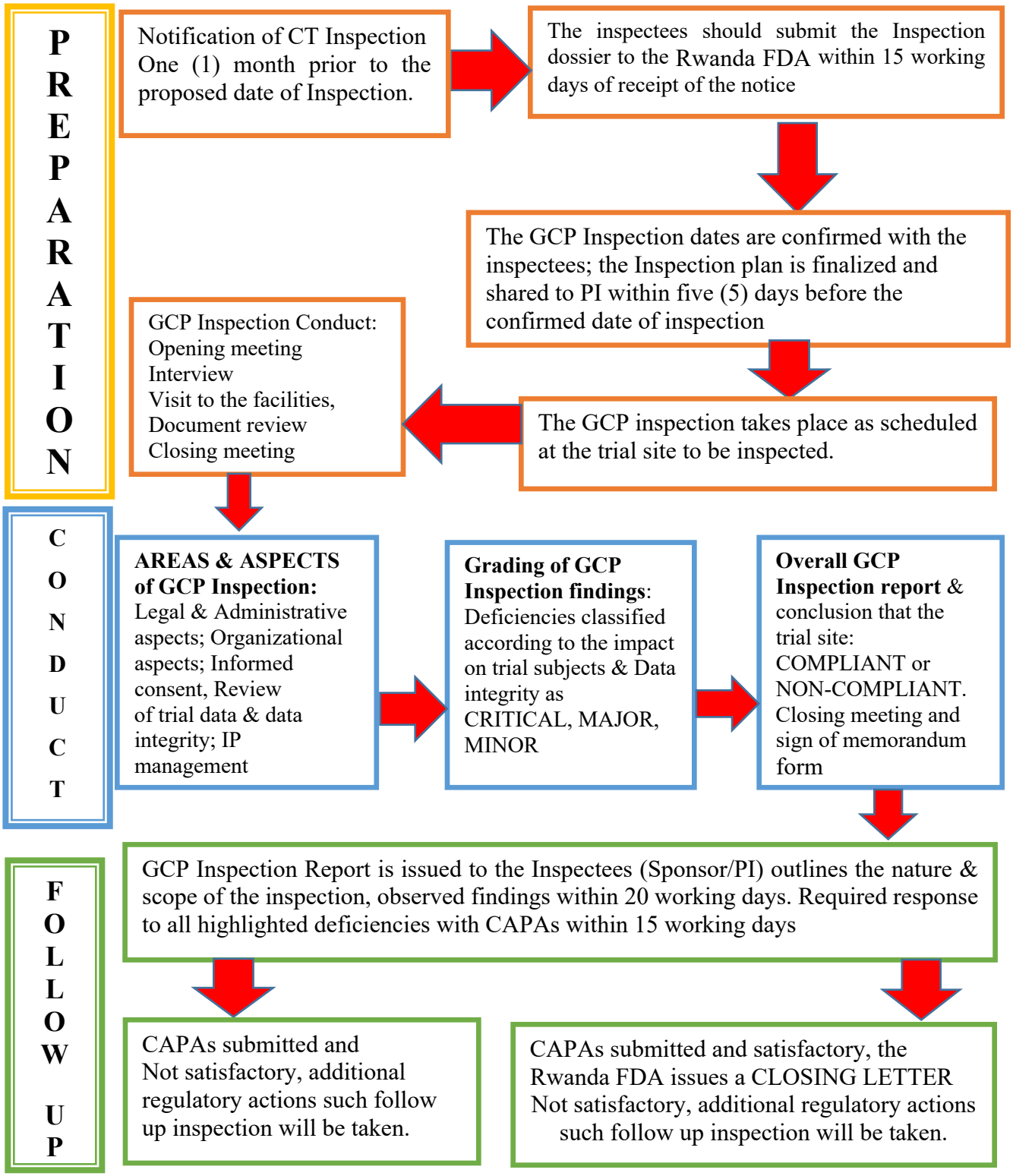
and standards operations procedures in place. All trial site will be inspected using the same inspection standards and tools. The rights of trial participants in terms of privacy and confidentiality must be protected and maintained.

5. REGULATORY ACTIONS DURING GCP INSPECTIONS

Based on the findings of the GCP inspection, the Authority may proceed with administrative regulatory actions if the inspectee fails to address critical and major findings according to the provisions of regulations and laws enforced in Rwanda. However, the Authority may not wait for CAPA to administrative regulatory actions in cases of deliberated misconduct such as fraudulent documentation or continuation of the clinical trial can have an adverse effect on trial participants. The following regulatory actions depending on the GCP inspection findings may be taken:

a. Issuance of a warning letter;
b. Temporary suspend of the trial;
c. Permanently terminate the trial and revocation of clinical trial Approval certificate
d. Blacklist the principal investigator or sponsor;
e. File case for court proceedings.

APPENDIX: GCP INSPECTION PROCESS FLOW CHART



ENDORSEMENT OF THE GUIDELINES

	Author	Authorized by		Approved by
Title	**DM/Pharmacovigilance & Food Safety Monitoring**	**HoD/ Food & Drugs Inspections & Safety Monitoring**	**Quality Assurance Analyst**	**Director General**
Names	**NTIRENGANY A Lazare**	**Dr. Eric NYIRIMIGABO**	**NDAYAMBAJE Théogène**	**Dr Emile BIENVENU**
Signature				 Digitally signed by Rwanda FDA (Director General) Date: 2023.04.06 21:54:13 +02'00'
Date	01/04/2023	01/04/2023	06/04/2023	06 / 04 / 2023

ANNEX -I: CLINICAL TRIAL GCP INSPECTION CHECKLIST

Format: QMS/FMT/002 Revision No: 1 Effective Date: 20 June 2022	Department/Division/Office/Unit	Pharmacovigilance and Food Safety Monitoring Division
Document Type: **Checklist**		Doc. No : FDISM/PVSM/CKL/001
RWANDA FDA Rwanda Food and Drugs Authority	Title: **Clinical Trial GCP Inspection**	Revision Number : 01 Revision Date: : 30/03/2023 Effective Date : 07/04/2023 Review Due Date : 06/04/2026 Ref Doc. :FDISM/PVSM/GDL009

ADMINISTRATIVE INFORMATION OF THE TRIAL	
Date of Inspection	DD/MM/YYYY
Clinical trial(s) names	
Rwanda FDA CTAC number	
Trial protocol title	
Trial site address	
Total number of sites	
Investigational product(s)	
Names and contact of Principal Investigator	
Name of the site	
Physical Address of the site	
Protocol Number	
Stage of the trial *[Tick as appropriate]:*	☐ Before commencement ☐ Ongoing ☐ Completed
Principal Investigator	
Sub/Co-Investigator	1…… 2…… 3…… 4……
Regulatory Authority approval date Version &Date	…….. …… …… ……
Ethical Approval date for informed consent form	1)…… 2)……
Names of Inspectors	1……

	2…… 3…… 4……
Screening date 1st Participant	
How many Participants enrolled	
Randomization date of 1st Participant	
How Many participants withdrew from the study?	
How many participants completed the study	
How many SAEs were reported	

DATA INTEGIRITY	**YES**	**NO**	**NA**
There is a written data integrity policy			
There is an SOP describing principles of data integrity ensuring ALCOA+			
Data and results were reviewed and considered complying to data integrity requirements. (If "no", complete comments section below)			
Comments:			

FACILITY INSPECTION			
CONSULTING AREA	**YES**	**NO**	**NA**
1. Is the consulting area where the Clinical trial team evaluates the participants during visits adequate in size?			
2. Are there lock-up cupboards for confidential documents?			
3. Is the trial specific equipment available in the consulting room?			
4. If not, is the area where procedures are performed adequate and easily accessible?			
COMPLIANCE TO THE TRIAL PROTOCOL			
1. Is the trial being carried out in accordance with the trial protocol provisions?			
2.Are the SOP mentioned in the protocol being implemented? *(Note: You can provide a detail of SOP mentioned*) 1. …… 2……. 3…….			
3. Was the dose in the protocol the same as the dose dispensed?			
PROCEDURE ROOM			
1. Are all protocol specified equipment calibrated and validated?			
2. Are SOPs on how to use equipment available?			
3. Is the blood sampling area kept according to infection control procedures?			
4. Is an SOP on handling of biological waste available?			
5. Is an emergency trolley available in the procedure area?			
5.1 Is the trolley locked and are keys available and controlled?			

5.2 Is the emergency trolley frequently checked?			
5.3 Are medicines stored within their expiry dates?			
5.4 Are oxygen and accessories available checked and signed?			
5.5 Are investigators ALS trained?			
Comments:			

PHARMACY MANAGEMENT (INVESTIGATIONAL PRODUCTS STORAGE AREA)			
	YES	**NO**	**NA**
1. Are the Pharmacy access controlled, temperature and humidity?			
2. Are Investigational products stored as per temperature or humidity?			
3. In case of vaccines are a spillage SOP available and the study team trained to handle such an incidence?			
4. Are electronic or hand-written logs available?			
5. Is an SOP on how to handle electricity or temperature failure in the pharmacy available?			
6. Are the investigational products for different studies clearly identified and stored in separate lock-up cupboards?			
Comments:			

ARCHIVE	**YES**	**NO**	**NA**
1.Is there an agreement between the Sponsor and the Clinical trial site/CRO on archiving of documentation			
2. Was access to the archive facility restricted?			
3. Are records of retrieval of documents from the archive available?			
4. Was the archive storage area fireproof and pest controlled			
Comments:			

CLINICAL LABORATORY	**YES**	**NO**	**NA**
1. Is the clinical laboratory at the same site?			
2. If not, are procedures in handling biological samples clearly documented?			
3. Is the laboratory accredited for the tests to be performed?			
4. Are all testing procedures used in the laboratory validated?			
5. Are all instruments adequate?			
6. Are all instruments and equipment calibrated and maintained/			
7. Are updated signed CVs of analysts available?			
8. Are the frequencies of QC checks for each instrument before analysis documented?			
9. Are there SOPs for receipt, storage of chemicals and preparation of solution available?			

10. Is an SOP for waste disposal (e.g.: organic and biological waste) available?			
11. Are normal values ranges for medical/laboratory/technical procedures and/or tests and wherever applicable their updates during the trail available?			
Comments:			
STUDY SPECIFIC INSPECTION			
CONTRACT AND AGREEMENTS	**YES**	**NO**	**NA**
1. Did the contract or the protocol describe any transfer of responsibility between the sponsor and the investigator?			
2. Was a confidentiality agreement signed between the sponsor and the investigator(s)?			
3. Was there a signed and dated financial agreement between the sponsor and the investigator available?			
4. Was an insurance certificate that covers the duration of the study available?			
5. Was there a signed conflict of interest declaration?			
6. Has the final version of the protocol been signed by all appropriate persons?			
Comments:			
REGULATORY APPROVALS	**YES**	**NO**	**NA**
1. Was regulatory approval for the protocol obtained before the start of the study?			
2. Was the version number of protocols used in the study versus the version number of the approved protocol identified?			
3. Was regulatory approvals of any new investigators obtained?			
INVESTIGATOR BROCHURE	**YES**	**NO**	**NA**
1. Was an investigator brochure and updates available on file with the date and version corresponding to that submitted Rwanda FDA			
2. Was an investigator brochure and updates available on file with the date and version corresponding to that submitted Rwanda FDA			
INFORMED CONSENT	**YES**	**NO**	**NA**
1. Was the informed consent form version that was used approved by RNEC?			
2. Was a written SOP used to solicit informed consent?			
3. Did all the subjects sign the consent form before any study related procedure?			
4. Did all the subjects receive a copy of the signed informed consent form?			
5. Did participants receive information regarding insurance?			
6. Was an assessment of understanding of the contents of the informed consent done?			
7. Did the principal investigator or person designed by the principal			

investigator conduct the informed consent appropriately			
8. Were the participants given sufficient time to decide whether or not to participate in the study?			
Comments:			
RESPONSIBILITIES OF THE INVESTIGATOR	**YES**	**NO**	**NA**
1. Were updated CV and adequate training certificate available? (check for GCP training)			
2. Did the investigator have sufficient personnel for the conduct of the study?			
3. Was a record of the pre-trial training for all staff available?			
4.Were the signatures of the staff involved in the study recorded?			
5. Was a participant identification log available?			
6. Was a participant enrolment log available?			
7. Were the facilities at the site adequate for safe and proper conduct of the trial?			
8. Did the investigator have a contingency plan for medical care in case of emergency?			
9. Were significant trial related duties and functions delegated to qualified persons documented?			
10. Were all the inclusion criteria and none of the exclusion criteria met by participants?			
11. Was the sixth monthly progress report sent to the RNEC?			
12. Was the sixth monthly progress report sent to the regulatory Authority?			
13. Were treatment compliance documented for all participants?			
14. Were all SAEs/AEs reported within the specified timelines to Rwanda FDA			
15. Were all SAEs/AEs reported within the specified timelines to the Sponsor?			
Comments:			
INVESTIGATIONAL PRODUCT	**YES**	**NO**	**NA**
1. Were the records of shipping letters of the investigational product(s) (e.g.: dates, batch numbers, quantities, letters) from the Sponsor to the investigator available?			
2. Were all study medications kept in a securely locked, temperature-controlled area accessible only to authorized persons?			
3. Were the records of storage conditions e.g.: temperature control log available?			
3. Were records of the products used available as dosage form. Strength, batch number, expiry date, certificate of Analysis, other coding that identifies the specific characteristic of the product tested?			
4. Were Valid certificates of analyses (CoA) for the study products available? (Check stability, expiry dates)			
5. Were instructions for handling investigational product and trial related			

materials available?			
6. Was the dispensing of the investigational product done according to the protocol/SOPs?			
7. Was dispensing done by a registered Pharmacist or b y a person with a dispensing license?			
8. Did the labelling of the investigational products reflect clinical research purposes only?			
9. was there a record of reconciliation at the end of the dispensing?			
10. Were retention samples available?			
11. Were there proof that conditions as stated in the protocol have been maintained during shipment and storage of products?			
12. Was drug accountability done?			
13. Were decoding procedures (for blinded trials) available?			
14. Was documentation on disposal of investigational products available?			
Comments:			

RECORD KEEPING AND DATA HANDLING	**YES**	**NO**	**NA**
1. Were records of key trial related procedures e.g.: CRF, source documents			
2. Was a signature sheet reflecting signatures and initials of all persons We're authorized to make entries and or corrections on CRFs available?			
3. Were corrections to the CRF/eCRF verified during the inspection done in such a way that it leaves an audit trial?			
4. Were the CRFs verified during the inspection signed, initiated and dated by the investigator?			
5. Did each page of the case report form identify the participant and the study?			
6. Was there an SOP for data entry/corrections in the CRF?			
7. Was the security of data protected in the eCRF?			
8. Were there any discrepancies between Adverse Events recorded in the source documents and those reported in the CRF?			
9. Was follow up to all the adverse events reported satisfactory?			
10. Were concomitant therapies included in the CRF verified during the inspection?			
Comments:			

QUALITY ASSURANCE	**YES**	**NO**	**NA**
1. Did a quality system exist to ensure compliance with GCP/GLP training?			
2. Was records available for training of staff, including proof of GCP training?			
3. Was there a procedure available for internal monitoring of the quality system?			
4. Was an audit certificate available?			

5. Was there documentation on SOP training?			

General Comments:

#	Print name	Functions	Signature

ANNEX-II: FORM OF MEMORANDUM OF GCP INSPECTION FINDINGS

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/008
RWANDA FDA Rwanda Food and Drugs Authority	Title: **Memorandum of GCP Inspection Findings**	Revision Number : 01 Revision Date: : 30/03/2023 Effective Date : 07/04/2023 Review Due Date : 06/04/2026 Ref Doc. :FDISM/PVSM/GDL/009

#	ADMINISTRATIVE INFORMATION	
	Clinical trial(s) names	
	Rwanda FDA CTAC number	
	Trial protocol title	
	Trial site address	
	Total number of sites	
	Investigational product(s)	
	Names and contact of Principal Investigator	
	Date of inspection	
	Number of Findings	

#	GCP Findings details	Comments

#	GCP Findings details	Comments

#	Inspectee' names	Functions	Signature

#	Inspectors' names	Functions	Signature

ANNEX-III: FORM FOR GRADING OF CLINICAL TRIAL INSPECTION FINDINGS

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/020
RWANDA FDA Rwanda Food and Drugs Authority	Title: **Grading of Clinical Trial GCP Inspection Findings**	Revision Number : 00 Revision Date: : 30/03/2023 Effective Date : 07/04/2023 Review Due Date : 06/04/2023 Ref Doc. :FDISM/PVSM/GDL/009

#	**ADMINISTRATIVE INFORMATION**		
	Clinical trial(s) names		
	Rwanda FDA CTAC number		
	Trial protocol title		
	Trial site address		
	Total number of sites		
	Investigational product(s)		
	Names and contact of the Principal Investigator		
	Clinical Site (s) inspected		
	CRITICAL FINDINGS [*Tick as appropriate*]	**YES**	**NO**
1.	Conduct of clinical trial that is not authorized by the Rwanda FDA		
2.	Sponsor imported Investigational product (IP) without import license from Rwanda FDA		
3.	Use of prohibited substance(s) without having received prior authorization from the Authority		
4.	Misrepresentation or falsification of information of data submitted to obtain authorization to conduct clinical trials		
5.	Clinical trial on-going after the authorization has suspended or cancelled		
6.	The application for an amendment that contains falsified, misleading or deceptive information		
7.	Failure to notify the Authority after amendments were implemented in cases where the clinical trial endangered the health of trial participants or other persons		
8.	Evidence of fraud such as "fabricating" trial participants, falsification of study data		
9.	Lack of records of SAEs which occurred from trials inside and/or outside Rwanda		
10.	Lack of records in respect of use of investigational product in a clinical trial.		
11.	Lack of records with respect to the enrolment of clinical trial participants		
12.	Lack of records of qualifications of the PI to conduct the clinical trial		
13.	Failure to report serious and unexpected adverse drug reactions to the Authority		
14.	Change of IP in Clinical trial without Authorization from the Authority		

15.	The sponsor failed to ensure sufficient and robust monitoring of the trials, leading to data integrity issues		
16.	The investigator lost control of data between database lock and pdfs being sent to the site		
17.	Updated documents containing new expected adverse reactions that had not previously been approved as substantial amendments were used for expectedness assessments.		
18.	Other findings not listed (add rows)		
	MAJOR FINDINGS [*Tick as appropriate***]**		
1.	Information contained in the trial application was incomplete or incorrect.		
2.	Failure to disclose all clinical trial sites to the Authority.		
3.	Failure to provide all necessary information, not previously provided in the application, prior to the sale or importation of a drug at a clinical trial site.		
4.	Failure to notify the Authority when changes made to the chemistry and manufacturing information or to the approved protocol.		
5.	Failure to implement an amendment at a clinical trial site.		
6.	Failure to provide to the Authority with information regarding an immediate amendment to the protocol		
7.	Clinical trial was not conducted in accordance with the protocol		
8.	Protocols not amended, informed consents not amended, and/or subjects not advised/re-consented when information becomes available regarding health and safety concerns, or use of the clinical trial drug which endanger the health of the clinical trial subject or other person.		
9.	Failure to obtain RNEC approval prior to implementation of amendments to protocol or informed consents forms		
10.	Informed consents not administered properly or not signed and dated		
11.	Informed consent not obtained from trial participants before enrollment in the trial or after major amendments to the informed consent form		
12.	No source data to substantiate clinical trial results		
13.	Sponsor did not notify the Principal Investigator of serious unexpected adverse drug reactions that occurred at other sites		
14.	No procedures in place for reporting new safety information to the Principal Investigator		
15.	Significant clinical endpoint data not collected on time, not correctly recorded, or not accurately transcribed/transferred to case report forms.		
16.	No systems in place for drug accountability		
17.	Source data was not verified for quality, completeness and integrity		
18.	Systems and procedures that assure the quality of every aspect of the clinical trial were not implemented		
19.	The informed consent did not contain all of the required information		
20.	Individuals involved in the conduct of the clinical trial are not qualified by education, training or experience to perform their respective tasks		
21.	Incomplete documentation of protocol deviation		

22.	Lack of documentation that Sponsor was informed of protocol deviations		
23.	No security procedures in place for electronic records or electronic signatures		
24.	The electronic data system was not validated		
25.	Sponsor has no or incomplete records of all adverse events which occurred inside or outside Rwanda		
26.	Incomplete records respecting the enrolment of clinical trial participants		
27.	No records concerning shipment, receipt, use, disposition, return or destruction of the investigational products		
28.	Quantities of drug not accounted for through the various stages of shipment, receipt, disposition, return or destruction of the lot of the investigation		
29.	Copies of the protocol/amendments and informed consents approved by the EC not retained for each clinical trial site		
30.	Absence of RNEC attestation for each clinical trial site stating that it has reviewed and approved the protocol, the informed consent and that it functions in compliance with GCP		
31.	Incomplete records in respect of the use of a drug in a clinical trial		
32.	Sponsor did not comply with the prescribed timeline for reports of fatal or life-threatening adverse drug reactions		
33.	Sponsor did not inform the Rwanda FDA that the clinical trial was discontinued in its entirety or at a clinical trial site within 15 days after the date of the discontinuance		
34.	Sponsor did not provide to the Rwanda FDA with the reasons for the discontinuance and its impact on the proposed or on-going clinical trials		
35.	Sponsor did not inform all Investigators of the discontinuance of a trial, the reason for the discontinuation or did not advise them in writing		
36.	Sponsor, after having discontinued a clinical trial, resumed selling or importing the drug without having submitted the required information to the Rwanda FDA.		
37.	Clinical trial ongoing at one or more sites after Sponsor stated that the trial was discontinued at those sites		
38.	Other findings not listed (add rows)		
	MINOR FINDINGS [*Tick as appropriate*]		
1.	Sponsor did not maintain copies of previous investigator's brochures pertaining to the clinical trial drug.		
2.	Date for the commencement of a clinical trial at one or more trial sites was earlier than that stated in the application.		
3.	Sponsor did not notify Rwanda FDA in writing within 15 days after the date of the change that requires notification.		
4.	Delegation of tasks incomplete, signature log incomplete.		
5.	Correction of data not initiated and/or dated.		
6.	Minor errors in transcribing data from source documents to case report forms.		
7.	Source data stored in unsecured location.		
8.	Labelling of the products not complying with requirements.		

	Other findings not listed (add rows)		
	SUMMARY OF EVENTS [*Tick as appropriate***]**		
1.	Rwanda FDA approval for Protocol and amendments		
2.	Ethics approval for Protocol and amendments		
3.	Ethics approval for Informed consent form		
4.	Annual ethics approval Renewal		
5.	General screening Trial specific screening		
6.	Randomization		
7.	Dosing/administration after approvals		
8.	Number of subjects enrolled		
9.	Number of subject withdrawals		
10.	Number of subjects lost to follow up		
11.	Number of subjects who completed the study		
12.	Number of SAEs reported		
13.	Number of protocol deviations and violations		
14.	Was CAPA taken?		
15.	Is there a Risk Management Plan and it is being adhered to?		

#	**Inspectee' name**	**Functions**	**Signature**

Comments from Internal Clinical Trial Technical Committee

Names of Chair of ICTTC	**Date**	**Signature**

ANNEX-IV: TEMPLATE FOR CLINICAL TRIAL SITE GCP INSPECTION REPORT

Rwanda Food and Drugs Authority
Nyarutarama Plaza, KG 9 Avenue
P.O. Box: 1948 Kigali - Rwanda
Email: info@rwandafda.gov.rw
website: www.rwandafda.gov.rw

QMS N°: FDISM/PVSM/FMT/013
Revision No: 0
Effective Date: 07/04/2023

CLINICAL TRIAL SITE GCP INSPECTION REPORT

GCP INSPECTION Report N°	
Trial Protocol title:	
Inspected Sites and address	
Type of inspection :	☐ Routine ☐ Triggered ☐ Follow-up *[Tick as appropriate]*
Status of Trial implementation	☐ Before commencement ☐ Ongoing ☐ Completed trial *[Tick as appropriate]*
Principal Investigator and site address	
CTAC reference number	
Names of lead Inspector(s):	
Names of Inspector(s):	
Other Clinical trial Sites not inspected:	
Inspection dates:	From: DD-MM-YYYY to DD-MM-YYYY
Inspection Report date:	DD-MM-YYYY
Due date for reply from Inspectee:	DD-MM-YYYY
BACKGROUND OF TRIAL	
Brief description of the Trial <*Insert comments as appropriate*> Reason and scope of the inspection 2.1.1. Opening meeting <*Insert comments as appropriate*> 2.1.2 Closing Meeting <*Insert comments as appropriate*>	

DOCUMENTS REVIEWED

Study specific documents reviewed in preparation for the GCP inspection:
List the documents, version number and date, amending as applicable, for example:

- Protocol and amendments version xxx
- Investigator Brochure version xxx

Rwanda National Ethics Committee (RNEC)/ Rwanda FDA
Site initiation report version xxx
safety reports/SUSARs
Monitoring Plan version xxx
Site personnel interviewed:

ORGANIZATION AND MANAGEMENT

< Insert summary comments as appropriate>
Facility and Equipment
< Insert summary comments as appropriate>
Management of Investigational Product (s)
< Insert comments as appropriate>
Documentation and Trial Master File
< Insert comments as appropriate>
(Contract and agreements, regulatory approvals, compliance to the trial protocol, investigator brochure, informed consent, ethical clearance, Patient information leaflet, safety reporting forms, progress and close out reports among others.)
Record Keeping and data Handling
< Insert comments as appropriate>
(Use of computerized systems, Data integrity in clinical trial, Efficacy and safety assessment data Safety management and reporting
Monitoring and Auditing
< Insert comments as appropriate>
Clinical Laboratory (Management of biological samples, among others)
< Insert comments as appropriate>
Quality assurance
< Insert comments as appropriate>

GCP Inspection Report Summary

The summary should be stand-alone i.e. the reader should be able to understand it without needing to refer to the main body of the report. There should be nothing in the summary that is not in the main body of the report.

This was a < insert type of GCP inspection to match the GCP inspection plan, for e.g. Routine, internal/contracted Investigator Site GCP inspection > conducted on the < insert as applicable, for e.g. Protocol number and name>study by the QA department or Contract inspector on behalf of the QA department. The inspection was conducted at <insert title, name and designation of inspectee and address where inspection was conducted, e.g. Dr/Prof Name & Surname, Principal Investigator (PI) at Name of Site in Location, Suburb, City, Country>.

The inspection was conducted per the inspection plan dated DD-MM-YYYY

The purpose of the inspection was to confirm<amend as applicable for e.g. whether the safety and rights of the research participants were protected, and the study was conducted per the approved protocol, all applicable Good Clinical Practices (GCPs), national and international regulatory requirements and the Declaration of Helsinki>.

The focus of the inspection was on <insert as applicable, matching to inspection plan e.g. participant data and site procedures>.

Name & Surname, joined the site in Month and Year. Comment on the PI's oversight and evidence of involvement in the trial.

Critical observations: number

Major observations: number

Minor observations: number

Critical observations were noted relating to elaborate on the critical observations observed.

Major observations were noted relating to elaborate on the major observations observed.

The inspector/s concluded that <provide a summary of the adequacy of the site, PI oversight, quality of the data, among others.>.

Details of the observations made during the inspection are documented in the section "inspection observations and action plan" of this report. An appropriate Corrective and Preventive Action (CAPA) (as applicable) for each observation documented must be provided by the inspectee (s), together with the name of the person responsible to implement the CAPA and the planned date for completion (or date completed).

Grading of GCP Inspection findings

The inspection finding are graded per the criteria as detailed below. Several minor (or major) observations may collectively be considered as equal to a major (or critical) observation.

Critical findings:

A finding with a significant risk of or having a major impact on participant safety, data integrity or study outcome, and / or seriously affects regulatory compliance or could lead to regulatory action.

Major findings:

A finding that is a significant deviation from GCP / regulatory requirements, procedural documents, or regulatory / industry expectations, with actual or potential effect on participant safety, data integrity or study outcome.

Minor findings:

A finding which does not affect the safety of participants or significantly affect the integrity of study results or study outcome, but is not compliant with GCP / regulatory requirements, or regulatory / industry expectations.

Other findings:

A suggestion for improvement to quality, safety or efficiency.

Quality of the data, ethical conduct and GCP compliance

<Insert comment as appropriate>

Recommendations for the acceptability of the clinical trial data

<Insert comment as appropriate and rows as appropriate>

This inspection *report is not intended to be an all-inclusive list of deficiencies and represents only those detected*

during the inspection. Corrective and/or preventive actions should be implemented across participants, or sites as applicable.

REPORT APPROVALS				
	Names	**Position**	**Date**	**Signature**

ANNEX - V: FORM FOR GCP INSPECTION FINDINGS AND CAPA

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/032
RWANDA FDA Rwanda Food and Drugs Authority	Title: **GCP Inspection Findings and CAPA**	Revision Number : 00 Revision Date: : 30/03/2023 Effective Date : 07/04/2023 Review Due Date : 06/04/2023 Ref Doc. :FDISM/PVSM/GDL/009

#	ADMINISTRATIVE INFORMATION	
	Clinical trial(s) names	
	Rwanda FDA CTAC number	
	Trial protocol title	
	Trial site address	
	Total number of sites	
	Investigational product(s)	
	Names and contact of Principal Investigator	
	Date of inspection	
	Number of Findings	

#	Grading	Reference	Findings details	Proposed CAPA and Timelines
	Critical,	ICH GCP E6 (R2), *Regulations*	*Document the first sentence as a brief summary of the observation. Add details as necessary.* *E.g.: Management of IP at the site was inadequate.*	*Add more lines as appropriates*
	Critical	ICH GCP E6 (R2) *Regulations*	*Add an example to substantiate the observation e.g. The pharmacist did not complete the IP inventory log every day*	*Add more lines as appropriates*
	Major,	ICH GCP E6 (R2) section 4.6 *Regulations*	*Add an example to substantiate the observation e.g. The pharmacist did not complete the IP inventory log every day*	*Add more lines as appropriates*

#	Grading	Reference	Findings details	Proposed CAPA and Timelines
	Major,	ICH GCP E6 (R2) *Regulations*	*Add an example to substantiate the observation e.g. The pharmacist did not complete the IP inventory log every day*	*Add more lines as appropriates*
	Minor	ICH GCP E6 (R2) *Regulations*	*Add an example to substantiate the observation. You may add more rows if applicable, by clicking outside the end of this row on the right.*	*Add more lines as appropriates*
	Minor	ICH GCP E6 (R2) section 4.6 *Regulations*	*Add an example to substantiate the observation. You may add more rows if applicable, by clicking outside the end of this row on the right.*	*Add more lines as appropriates*

#	Inspectee' name	Functions	Signature