RWANDA FDA
Rwanda Food and Drugs Authority

REGULATIONS GOVERNING THE CONDUCT AND INSPECTION OF CLINICAL TRIALS IN RWANDA

(Rwanda FDA Law Nº 003/2018 of 09/02/2018, Article 9)

REGULATION DEVELOPMENT HISTORY

First issue date	31/12/2020
Effective date of this revision	Refer to the approval date

Document revision history

Date of revision	**Version number**	**Changes made and/or reasons for revision**
31/12/2020	0	First issue
18/06/2021	1	1. Provisions that require prior authorization from the Authority to conduct of clinical trials in Rwanda included; 2. Provisions that all clinical trials shall be reviewed using the same requirements for all applicants; 3. Provisions that approved, rejected, and summary of evaluation reports of clinical trial applications, suspended and/or terminated clinical trials shall be publicly available, and register should be updated on regular basis; 4. Article 16 on Disclosure of Conflicts of Interests in the Conduct of Clinical Trial included for more transparency; 5. Article 39 on Authorization of clinical trial conduct during public health emergencies was updated to include the circumstances under which the Authorization may be granted; 6. Provisions on reliance in clinical trials were included; 7. Article 27 was updated to include timelines for non-routine applications and an internal tracking system; 8. Article 31 was updated to include Safety Monitoring and Reporting of SAEs and SUSARs; 9. Typos in the previous version were removed and necessary editorial changes were made; 10. Subject replaced by trial participant; 11. The table revision history was included;

31/03/2023	2	1. The Title was updated to include Inspection to reflect the adopted name of the regulations in the initial versions 2. The reference number was changed from CBD/TRG/015 Rev_1 to No FDISM/PVSM/TRG/001 Rev_2 as per current document control SOP. 3. Article 5 was updated to include provisions on the use of experts in clinical trial monitoring; 4. Article 15 for renewal of Clinical Trial Approval Certificate was updated to include provisions on requirements for renewal or reinstatement of clinical trial approval; 5. Article 17 was updated to include provisions for registering clinical trials in public registries accepted by WHO guidelines; 6. Article 27 was updated to include AVAREF timelines in case of emergencies; 7. Article 30 was updated to include reasons for the suspension or termination of a clinical trial; 8. Article 32 related to the manufacture of investigational products and the criteria for accepting GMP certificates for imported IMPs was revised; 9. Article 39 was updated to include the provisions on quick access to compassionate use products; 10. Article 41 was updated to include language English, French, and Kinyarwanda. 11. Article 43 updated administrative sanctions under Annex-A; 12. Article 44 on repealing was included; 13. Necessary editorial changes were included in line with the current SOP on document control.

	3	1. The Title was updated to include clinical to reflect the scope of the regulations in line with the current regulatory ecosystem; 2. The reference number was changed from No FDISM/PVSM/TRG/001_Rev_2 to No.: DD/PVCT/TRG/001_ Rev 3 as per current document control SOP; 3. Article 4 was updated to include New terminology "Non-clinical vs pre-clinical" in line with the updated version of Glossary of Rwanda FDA Terms and Definitions 4. Article 14 was updated to include the provisions on approval of preclinical /clinical studies; 5. Article 17 was updated to include the provisions on publication of summarized evaluation reports; 6. Article 35 was inserted with provisions for qualification of GCP Inspectors; 7. Article 42 was inserted with provisions for performance monitoring in clinical trials oversight; 8. Article 40 was updated to include provisions for rolling reviews of clinical trials during public health emergencies or unmet medical needs 9. Necessary editorial changes for clarity were included in line with the current SOP on document control: Article 18, Article 6, Article 40, and Article 14.

ADOPTION AND APPROVAL OF THE REGULATIONS

In exercise of the powers conferred upon Rwanda Food and Drugs Authority by Article N° 9 of the Law N° 003/2018 of 09/02/2018 establishing Rwanda FDA and determining its mission, organization and functioning, hereby adopts these regulations No.:DD/PVCT/TRG/001 version 3 Governing the Conduct and Inspection of Clinical Trials in Rwanda.

Prof. Emile BIENVENU
Director General

ARRANGEMENT OF THE REGULATIONS

CHAPTER ONE: GENERAL PROVISIONS

Article One: Purpose of these Regulations

The purpose of these regulations is to create favourable conditions for conducting clinical trials with the highest standards of safety for participants and increased transparency of trial information.

These regulations enforce the legal framework for application, assessment, approval, rejection and inspection of clinical trials, bioequivalence and/or bioavailability studies for human participants.

Article 2: Citation

These regulations are cited as "*Regulations Governing the Conduct and inspection of Clinical Trials in Rwanda*."

Article 3: Scope

These regulations apply to all clinical trials including Bioavailability and Bioequivalence studies as provided in the Law establishing the Authority.

Article 4: Definitions

In these regulations, unless the context otherwise requires:

1. **"Adverse drug reactions"** means all noxious and unintended responses to an investigational medicinal product related to any dose or all unintended noxious responses to a registered medicinal product that occurs at doses normally used in humans for prophylaxis, diagnosis, or therapy of diseases or modification of physiological function;
2. **"Adverse event"** means any untoward medical occurrence in a patient or study participant administered a pharmaceutical product and which does not necessarily have a causal relationship with the treatment;
3. **"Applicant**" means a person and including a Sponsor, Contract Research Organization or in the case of investigator-initiated academic research studies, research institution or principal investigator, applying for a permit to conduct a clinical trial;
4. **"Assemble"** in relation to investigational medicinal product means and include- (a) enclosing the product, with or without other medicinal products of the same description, in a container that is labelled before the product is used or supplied; or (b) where the product, with or without other medicinal products of the same description, is already enclosed in the container in which it is to be used or supplied and is labelled before the product is used or supplied;
5. **"Authority"** means the Rwanda Food and Drugs Authority or its acronym "Rwanda FDA."
6. **"Blinding or masking"** means a procedure in which one or more parties to a clinical trial are kept unaware of the treatment assignment;
7. **"Case report form"** means a document that is used to record data on each study participant during the course of the trial, as defined by the protocol;

8. **"Clinical trial or study"** means an investigation or series of investigations consisting of a particular description by, or under the direction of a medical practitioner, dentist or veterinary surgeon to the patient or animal where there is evidence that drugs, medical devices or herbal drugs of that description have effects which may be beneficial to and safe to the patient and animal in question and the administration of the drugs, medical devices or herbal drugs is to ascertain beneficial and harmful effects;
9. **"Clinical trial or study report"** means a written description of a clinical trial or study of any therapeutic or prophylactic agent conducted in human study participants in which the clinical and statistical description, presentations and analyses are fully integrated into a single report;
10. **"Clinical trial site"** means an investigator site, Sponsor's office, contract research organization, data management Centre or any other establishment involved in a clinical trial;
11. **"Code"** means the identification code assigned by the investigator to each clinical trial study participant to protect the study participant's identity and used instead of the study participant's name when the investigator reports adverse events or other trial-related data;
12. **"Compliance''** (concerning trials) means adherence to all the trial-related requirements, Good Clinical Practice (GCP) requirements, and the applicable regulatory requirements.
13. **"Confidentiality"** means maintenance of the privacy of trial participants including their personal identity and all personal medical information;
14. **"Coordinating investigator"** means an investigator assigned the responsibility for the coordination of investigators at different center participating in a multicenter trial;
15. **"Contract research organization"** means a person or an organization contracted by the Sponsor to perform one or more of a Sponsor trial-related duties and functions;
16. **"Data and safety monitoring board"** means 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;
17. **"Direct access"** means permission to examine, analyze, verify and reproduce any records and reports that are important to the evaluation of a clinical trial;
18. **"Essential documents"** means documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced;
19. "Ethical clearance" means an authorization to conduct a clinical trial issued by an approved institute for medical research;
20. **"Fee"** means the fee prescribed in regulation No CBD/TRG/004 related to regulatory Services tariff /fees and fines;
21. **"Good clinical practice"** means a standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials that assure that the data and reported results are credible and accurate and that the rights, integrity, and confidentiality of study participants are protected;
22. **"Good manufacturing practice"** means that part of quality assurance which ensures that investigational medicinal products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization;
23. **"Herbal medicine"** means any labeled preparation in pharmaceutical dosage form that contains one or more substances of natural origin as active ingredients that are derived from plants;
24. **"Informed consent"** means participant voluntary confirmation of willingness to participate in a particular trial, and the documentation thereof;

25. **"Inspection"** means 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 clinical trial site;
26. **"Investigational product"** in relation to a drug, medical device and herbal drug means a pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use;
27. **"Investigator"** means a qualified person (physician, dentist, Pharmacist, Anaesthetist, Veterinary doctor and any other qualified persons) who conducts a clinical trial at a trial site;
28. **"Investigator brochure"** means a compilation of the clinical and non-clinical data on the **investigational** product which is relevant to the study of the investigational product in human study participants;
29. **"Monitor"** means a person appointed by, and responsible to, the Sponsor or Contract Research Organization for the monitoring and reporting of progress of the trial and for verification of data;
30. **"Multi-centre clinical trial"** means a clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator;
31. **"National Ethics Committee"** means an independent body in Rwanda constituted of **medical** professionals and non-medical members, whose responsibility is to verify that the safety, integrity and human rights of participants in a particular trial are protected and to consider the general ethics of the trial, thereby providing public reassurance. National Ethics Committee shall be constituted and operated so that its tasks can be executed free from bias and from any influence of those who are conducting the trial;
32. **"National registry"** means a database created by the Authority that houses and manages information about a clinical trial submitted by an applicant;
33. **"Pharmacovigilance"** means the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem;
34. **"Pre-clinical/Non-clinical studies "** means biomedical studies not performed on human study participants;
35. **"Principal investigator"** means a pharmacist, physician, dentist, veterinarian or other qualified person, resident in Rwanda and member of good standing of a professional body, responsible for the conduct of clinical trial at a clinical trial site;
36. **"Pharmaceutical Product"** means any substance capable of preventing, treating human or animal diseases and any other substance intended for administration to a human being or an animal in order to diagnose diseases, restore, correct or carry out modification of organic or mental functions in clinical trials;
37. **"Protocol"** means a document which states the background, rationale and objectives of a clinical trial and describes its design, methodology and organization, including statistical considerations, and the conditions under which it is to be performed and managed;
38. **"Protocol amendment"** means a written description of changes to or formal clarification of a protocol;
39. **"Quality assurance"** means all those planned and systematic actions that are established to ensure that a trial is performed and data are generated, documented, recorded, and reported in compliance with good clinical practices;

40. **"Quality control"** means the operational techniques and activities undertaken within a quality assurance system to verify that the requirements for quality of the clinical trial-related activities have been fulfilled;
41. **"Randomization"** means the process of assigning study participants to treatment or control groups using an element of chance to determine the assignments in order to reduce bias;
42. **"Serious adverse event or serious adverse drug reactions"** means any untoward medical occurrence that at any dose may cause death, life threatening, hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity; or congenital anomaly or birth defect.
43. **"Sponsor"** means an individual, company, institution or organization who takes responsibility for the initiation, management and, or financing of a clinical trial;
44. **"Substantial amendment"** means change to the terms of the protocol or any other trial supporting documentation that is likely to have significant impact and affect the safety and integrity of trial participants, the scientific value of the research, the conduct or management of the research, and the quality or safety of any investigational medicinal product used in research
45. **"Non-substantial amendment"** means changes to the details of a trial study which have no significant implications for the study participants, conduct, management and scientific value of the research
46. **"Trial or study participant"** means an individual who participates in a clinical trial either as a **recipient** of the investigational medicinal product or as a control;
47. **"Trial or study site"** means the location(s) where clinical trial-related activities are conducted;
48. **"Unexpected adverse drug reaction"** means an adverse reaction with the nature or severity not consistent with the applicable product information.

CHAPTER II: APPLICATION, REVIEW, INSPECTION, AND REPORTING PROCESS

Article 5: General Principles

The Authority ensures that a dedicated entity for clinical trial oversight activities is established within its organizational structure. The entity shall oversee all daily activities related to the conduct and inspection of clinical trials and advise the Authority accordingly.

In order to ensure that clinical trials respect the rights, safety, dignity and well-being of participants are protected and the data generated are reliable and robust, the Authority shall have competent staff to perform clinical trial oversight activities. When deemed necessary, the Authority may involve external experts in clinical trial whose qualification and experience correspond to the specific needs in the clinical trial regulations.

Every person involved in the conduct and inspection of a clinical trial shall provide complete and accurate information attesting to the absence of conflicting interests in the trial.

The sponsor or the investigator shall submit clinical trial reports as prescribed by the Authority in relevant guidelines.

All sponsors, researchers, research centres, Contract Research Organizations (CROs), and all relevant stakeholders involved in the clinical Trial shall comply with latest version of ICH GCP guidelines.

The Authority shall carry out inspection at the trial sites and all other facilities used or being used for the purpose of the clinical trial to ensure compliance with ICH GCP guidelines and provisions of these Regulations.

Amendments relating to the conduct, design, methodology, investigational product, or the investigator or site(s) of the clinical trial and which may have substantial impact on the safety or rights of the participant or on the reliability and robustness of the data generated in the clinical trial, shall be subject to approval by the Authority.

Article 6: ICH-GCP Principles

All clinical trials, including Bioavailability and Bioequivalence studies, shall be designed, conducted, recorded, monitored and reported in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the latest version of ICH GCP guidelines and the provisions of these regulations.

Before a trial is initiated, foreseeable risks and inconveniences shall be weighed against the anticipated benefit for the individual trial subject and society. A trial shall be initiated and continued only if the anticipated benefits overweigh the risks.

The rights, safety, and well-being of the trial participants are the most important considerations and shall prevail over the interests of science and society.

The available non-clinical and clinical information on an investigational product shall be adequate to support the proposed clinical trial.

Clinical trials shall be scientifically sound and described in a clear and detailed protocol.

A trial shall be conducted in compliance with the protocol that has received prior ethical clearance from the National Ethics Committee in accordance to the relevant law governing research on human beings and the Approval from Authority.

The medical care given to, and medical decisions made on behalf of the trial participants shall always be the responsibility of a qualified physician, dentist or pharmacist when appropriate.

Each individual involved in conducting a trial shall be qualified by education, training, and experience to perform his or her respective task(s).

Freely given informed consent or assent shall be obtained from every trial participant prior to clinical trial participation.

All clinical trial information shall be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification. This principle applies to all records irrespective of the type of media used.

The confidentiality of records that could identify trial participant shall be protected, respecting the privacy and confidentiality rules in accordance with the applicable laws.

Investigational products shall be manufactured, handled, and stored in accordance with applicable Good Manufacturing Practices (GMP). They shall be used in accordance with the approved protocol.

Systems with procedures that assure the quality of every aspect of the trial shall be implemented. Those systems shall focus on the aspects that are essential to ensure trial participant protection and reliability of trial results.

Article 7: Requirements for a clinical trial pre-submission meeting

An application for the clinical trial pre-submission meeting can be made by the sponsor or Principal Investigator and submitted to the Authority.

The pre-submission meeting shall include the proposed date and time and a brief synopsis (electronic copies) of the proposed study listing questions, if any, to be addressed by Authority. A confirmation of the date and time of the meeting shall be duly conveyed to the Sponsor or principal investigator according the timelines set out in the clinical trial application guidelines.

Article 8: Clinical trial application

A person who desires to conduct a clinical trial shall submit an application dossier according to the regulatory requirements described in the clinical trial application guidelines issued by the Authority.

All clinical trial applications shall comply with the requirements as determined by the Authority in the guidelines on clinical trial application and shall be accompanied by data establishing the evidence that the product/intervention has a potential clinical benefit such as but not limited to efficacy, performance, quality and safety;

An application for a clinical trial shall be made by a Sponsor or Investigator who shall submit a power of attorney attesting that she/he is a duly appointed agent;

The clinical trial application and its amendment shall be accompanied by proof of payment of non-refundable applicable fees.

Article 9: Review process of clinical trial applications

All clinical trial applications shall be reviewed based on the same requirements as described in the guidelines for clinical trial applications irrespective of the applicant. The Authority shall, upon being satisfied by the application, conduct a review of the protocol and other essential documents to verify compliance with quality, safety, and efficacy requirements pertaining to the investigational product (s).

The Authority shall issue guidelines, Standard Operating Procedures (SOPs), forms, and tools for review procedures. The Authority may, during the review of the clinical trial, require the applicant to submit additional information, data, or clarification to support the clinical trial application within thirty (30) working days. Where the Authority requires additional information, data or clarification pursuant to the second paragraph of this Article, the processing of the application shall not proceed until when the applicant makes a submission.

Pursuant to the requirements of the second paragraph of this Article, the applicant may, by giving reasons in writing, request for an extension of time for the submission of additional information, data or clarification requested by the Authority.

In case the applicant fails to submit the required information without a formal request for extension according to provisions of the second paragraph of this Article, the application shall be considered withdrawn.

If the applicant fails to provide satisfactory responses three consecutive (3) times for the same requested information according to the second paragraph of this Article, the application shall be rejected.

Article 10: Authorization to conduct clinical trials in Rwanda

The conduct of a clinical trial in Rwanda requires prior authorization from the Authority. Authorization for conducting clinical trial shall be granted to all categories of products and circumstances described in the clinical trial application guidelines.

Article 11: Reasons for rejection of clinical trial application

The Authority shall reject clinical trial applications where it is satisfied that:

a) The information and regulatory documents as set out in the clinical trial application guidelines have not been provided.
b) The application contains false or misleading information;
c) The information provided is insufficient to enable the Authority to assess the safety and risks of the investigational product or clinical trial;
d) Queries raised by the Authority in relation to the application were not adequately addressed;
e) The applicant failed to obtain ethical clearance from Rwanda National Ethics Committee.
f) The use of the investigational product (s) for the purposes of the clinical trial endangers the health of a clinical trial participant or any other person;
g) The objectives of the clinical trial will not be achieved;
h) Any other scientific grounds as may be determined by the Authority.

Article 12: Amendment to clinical trial application

After the authorization of the clinical trial, the sponsor may make amendments to the protocol and/or its supplementary documents.

If the amendments are likely to have a substantial impact on the safety of the trial participants, the physical or mental integrity of trial participants, the scientific value of the trial, the conduct of the trial, the quality or the safety of the investigational product(s), the sponsor shall submit an application in accordance with the regulatory requirements described in the guidelines for clinical trial applications.

It is mandatory to obtain ethical clearance from National Ethics Committee and approval from Authority before implementing such an amendment.

In case of substantial amendments, the Authority allows urgent safety measures to be taken, without prior approval, to protect trial participants from immediate hazards. However, the Authority should be notified about such measures as soon as possible in accordance with timelines set out in the relevant guidelines.

In case of non-substantial amendment (s), the Authority should be notified according to the timelines and regulatory requirements set out in the guidelines on clinical trials applications in Rwanda.

Article 13: Authenticity of clinical trial documents

All essential documents submitted to the Authority shall be authentic and approved by the sponsor, or principal investigator, or authorized agent. The investigator/institution should have full control of all essential documents and records generated by the investigator/institution before, during, and after the trial.

Article 14: Approval process of clinical trials

The Authority may accept pre-clinical and clinical data from other products using the same platform, provided the data must be relevant, scientifically sound, and meets regulatory standards for the new product. Additionally, the Authority may use reliance procedures and considers the safety and efficacy reports of the WLAs regulatory authorities and ML3 that have signed agreements with Rwanda FDA.

After scientific review of the submitted information and favourable opinion of the committee, the Authority issues approval certificate or rejection letter and updates the regulatory register according to the procedures in place.

Article 15: Validity of approval certificate

Approval certificate issued under Article 14 shall be valid for a period of one (1) year renewable based on the clinical trial duration.

Approval certificate unless previously renewed, suspended or revoked, shall expire at the end of the authorised period. The requirements for renewal or reinstatement of clinical trial approval shall be defined in the relevant guidelines.

Article 16: Disclosure of conflicts of interests in the conduct of clinical trial

All parties involved in the conduct and oversight of clinical trials in Rwanda shall disclose all potential conflicts of interest that may compromise the well-being of trial participants, lead to bias, and undermine the trust of trial results in order to guarantee independence and transparency.

A declaration of conflict of interests shall be signed by each party involved in the conduct of clinical trial according to the policy and procedures in place.

Article 17: Registration and publication of clinical trials

Prior to approval, the sponsor or investigator shall register the clinical trial in a relevant publicly accessible registry accepting international clinical trial information and which are recognized by the World Health Organisation (WHO).
The Authority shall publish and maintain a register of all clinical trials conducted in Rwanda according to these regulations and other international relevant guidelines.

The Authority shall record the following information required in the register of clinical trials:

a) Protocol title and version number;
b) Clinical trial certificate number;
c) Investigational product;
d) Principal investigators and co-investigators;
e) Sponsor;
f) Clinical trial site;
g) Clinical trial duration;
h) Clinical Trial Phase;
i) Status of the trial;
j) Targeted number of trial participants.

The Authority shall ensure that relevant information regarding decisions made (approvals and rejections) regarding clinical trial applications and their corresponding summarized evaluation reports shall be publicly available and updated regularly. The above shall be applied to suspended and/or terminated clinical trials as well.

Article 18: Conduct of clinical trial

All clinical trials shall be conducted in accordance with provisions of relevant laws, regulations, and guidelines issued by the Authority. All stakeholders involved in clinical trials shall strictly comply with approved protocol, the latest version of ICH Good Clinical Practices and Good Clinical Laboratory Practices.

Article 19: Responsibilities of principal investigator

The principal investigator shall be responsible for the conduct of the clinical trial at the clinical trial site. In case of multi-centre/site studies where the principal investigator is not a resident of Rwanda, a resident shall be appointed to assume full responsibilities of Principal investigator for all local trial sites.

He/she shall maintain a list of appropriately qualified persons to whom he has delegated significant trial-related duties. The principal investigator shall ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product, and their trial-related duties and functions.

The principal investigator shall ensure that adequate medical care is provided to a study participant for any adverse events, including clinically significant laboratory values, related to the trial. In particular, the principal investigator shall:

a) Comply with the protocol approved by the Authority.
b) Be responsible and accountable for the investigational product at the trial site.
c) Assign all duties for investigational product accountability at the trial site to an appropriate pharmacist, medical doctor or another qualified individual who shall be under the supervision of the investigator.
d) Follow the randomization procedures, if any, and shall ensure that the code is broken only in

accordance with the protocol.

Article 20: Qualifications of investigators and monitors

In any clinical trial, investigators shall be appropriately qualified to perform clinical trial investigation. Monitors shall be appointed by the sponsor and shall be appropriately trained, and have the scientific and, or clinical knowledge needed to monitor the trial adequately. The requirements are set out in the latest version of ICH-GCP guidelines.

Article 21: Ethical clearance

Applicant shall be required to submit a valid ethical clearance for the conduct of clinical trials issued by Rwanda National Ethics Committee.

Article 22: Responsibilities of sponsor

The sponsor shall implement and maintain quality assurance and quality control systems to ensure that trials are conducted and data are generated, documented, recorded and reported in compliance with provisions of these Regulations.

The sponsor shall ensure that agreements are made between parties involved and the Authority have direct access to all trial related sites, source data and documents and reports for the purpose of inspection or audit.

The sponsor shall ensure that all agreements made with the Principal Investigator and any other parties involved in a clinical trial are in writing, as part of the protocol or in a separate agreement.

Transfer of any or all of the sponsor's trial-related duties and functions to a third party shall not exonerate from liability to the sponsor.

The sponsor shall provide insurance for trial participants or indemnify the investigator against claims arising from the trial, except for claims that arise from malpractice or negligence.

The sponsor shall ensure that sufficient safety and efficacy data from pre-clinical studies and, or clinical trials are available to support human exposure by the route, at the dosages, for the duration, and in the trial population to be studied.

The sponsor shall update the investigator brochure at any time when new significant information becomes available.

The sponsor shall ensure that the trial is adequately monitored for the protection of the rights, safety and well-being of trial participants and for the collection and analysis of high-quality data.

Article 23: Protection of clinical trial participants

Prior to the involvement of a participant in a trial, the investigator shall fully inform the participant or his legally acceptable representative, of all pertinent aspects of the trial including the favorable opinion by the ethics committee in the language understandable by the participant or his/her legally acceptable representative.

The participant or his/her legally acceptable representative shall freely give a written informed consent which shall be dated and signed by the participant or his/her legally acceptable representative, and by the person who conducted the informed consent discussion;

Clinical trials using pregnant or breastfeeding women shall be conducted only where the trial has the potential to produce a direct benefit to the concerned women, embryo, foetus or child after birth or where the trial poses a minimal risk to, and imposes a minimal burden on the concerned women, embryo, foetus or child after birth;

The rights of each participant to physical and mental integrity, to privacy and to the protection of the data concerning him shall be safeguarded.

No incentives or financial inducements shall be given to a participant except for compensation for expenses and loss of earnings directly related to the participation in the clinical trial.

Article 24: Insurance of trial participants

All clinical trial conducted in Rwanda shall have and maintain a valid local insurance policy issued by competent Authority to grant specific cover in connection with the reimbursement of damages/injuries caused to the trial participants by the clinical trial activities throughout the entire duration;

The insurance shall cover death, all permanent and/or temporary impairment of health conditions, relevant financial consequential losses which are the direct consequence of the trial and which can be traced to the liability of all people operating for the performance of the trial;

The Authority shall ensure that all trial participants of the trial are satisfactorily insured against possible damages/injuries caused to the trial participants by the clinical trial activities throughout the entire duration;

In case of clinical trials involving gene therapy, cellular therapy, and radio-pharmaceuticals as investigational products, the insurance shall remain valid at least ten (10) years after the completion of the trial. The authority shall set out guidance on insurance and indemnities for in clinical trials in Rwanda.

If the term of validity of the insurance certificate is shorter than the actual term of the trial, the sponsor has to submit to the Authority, the relevant renewal of the insurance certificate.

The submission of the renewal certificate to the Authority is a non-substantial amendment. The Authority, after review and analysis of the design and interventions of clinical trials, may exempt participant insurance in case of the clinical trial with minimal risks to the trial participants.

Article 25: Reporting in clinical trial

The Principal Investigator shall submit the progress report (s) to the Authority during the conduct of the Clinical trials on monthly basis for the trials not exceeding six (6) months, on quarterly basis for trials from seven months to eleven months and on a six months' basis for one-year trial and above.

The principal investigator shall submit written clinical trial progress reports annually, or more frequently, as may be required by the Authority.

After the completion of the clinical trial, the principal investigator shall submit to the Authority a close out report within thirty (30) calendar days and final report within ninety (90) calendar days in accordance with the format provided by the Authority.

Article 26: Records and record keeping

Without prejudice to any regulation, the investigator and sponsor shall keep in safe custody all records, documents and information related to a clinical trial at the clinical trial site for a period of not less than twenty (20) years after completion of a trial.

Unless there are pending or contemplated marketing applications, essential documents used in clinical trials shall be retained for at least two (2) years after the last approval of a marketing application. The Authority may require the Principal investigator or sponsor to submit records, documents and information stored under paragraph 1 of this article when it may deem fit and just.

The principal investigator and sponsor shall maintain complete and accurate records to establish that the clinical trial is conducted in accordance with good clinical practices and provisions of these Regulations. Without prejudice to any other requirements, the sponsor shall, in respect of the use of an investigational product in a clinical trial, maintain records according to the relevant guidelines.

Article 27: Clinical trial authorization timelines

The Authority shall allocate sufficient time to review the application dossier for clinical trials without jeopardizing participant safety or public health while ensuring quick access to new and innovative treatments according to routine and non-routine circumstances such as public health emergencies.

The timelines of scientific review and approval shall not exceed sixty (60) working days for routine clinical trial application.
However, the review of the clinical trial application for amendment and renewal applications shall be completed as soon as possible but no later than thirty (30) working days from the date of receipt of the completed application for amendment.
The Authority may expedite or fast-track the review process and approve a clinical trial application

within thirty (30) working days. The modalities for fast-tracking or expeditions are specified in the relevant guidelines.
In the event of public health emergencies, the Authority shall expedite the clinical trial review process and shall approve a clinical trial application as soon as possible but not later than fifteen (15) working days in order to ensure quick access to lifesaving medical products.
The Authority shall put in place an internal tracking system to monitor compliance with above review timelines.

Article 28: Requirements related to the data and safety monitoring board/committee

In case of high-risk clinical trials and/or life-threatening diseases, the Authority reserves the discretion to impose the establishment of a Data and Safety Monitoring board/Committee (DSMB/C) depending on the design and scientific background, risk and benefit assessment of the clinical trial.

In any case, where clinical trials involve the Data and Safety Monitoring board/Committee to monitor clinical trials, the Authority may require the charter of the Data Safety Monitoring the terms of reference, responsibilities, composition and qualifications of members of the committee. It is required that for national clinical trials conducted in Rwanda, at least one member of the Data and Safety Monitoring Board (DSMB) be of Rwandan nationality. In the case of multi-country clinical trials, the DSMB shall include at least one member from the African region where the trial is taking place.

Article 29: Discontinuation of a clinical trial by a sponsor

In case of clinical trial discontinuation by a sponsor in its entirety or at a clinical trial site, the sponsor shall:

a) cause the information to reach the Authority not later than fifteen (15) calendar days after the date of the discontinuation;
b) provide the Authority with the reason for the discontinuation and its impact on the proposed or ongoing clinical trials in respect of the investigational product including issues related to accountability and disposal of the investigational product;
c) inform all investigators of the discontinuation and the reasons for the discontinuation, and advise them in writing of any potential risks to the health of clinical trial participants or other persons as soon as possible;
d) stop the use or importation of the investigational product from the date of the discontinuation and take all reasonable measures to ensure the recovery of all unused quantities of the investigational product in respect of each discontinued clinical trial site.

Article 30: Suspension or termination of a clinical trial

The Authority may suspend a clinical trial due to the serious safety issues related to the use of the investigational product or intervention that could harm trial participants, non-compliance with regulations or trial protocols, lack of efficacy, data integrity issues, concerns about welfare of trial participants and significant complaints or critical inspection findings related to the trial.

The Authority may terminate the clinical trial if the issues are severe enough that they cannot be

resolved through corrective action or if there is a significant risk of harm to the trial participants.

In case of suspension or termination for any reason, the Principal investigator and/or sponsor should promptly inform the trial participants and shall ensure that appropriate therapy and follow-up care are provided to the trial participants according to the guidelines set out in the protocol and applicable regulations.

The Authority may also warn, disqualify or blacklist an investigator if there is information indicating that the principal investigator has failed to comply with the requirements of these Regulations, or has submitted to the Authority or to the sponsor false information in any required report.

Article 31: Safety monitoring and reporting of SAEs and SUSARs

The principal investigator or sponsor shall monitor record and report to the Authority any serious adverse event (SAE) and any suspected unexpected serious adverse reaction (SUSAR) that are fatal or life threatening and occur during the course of a clinical trial conduct.

The Principal Investigator shall report immediately but not later within seven (7) calendar days to the Authority any serious adverse event (SAE) which occurs in a study participant at a clinical trial site at which she/he is responsible for the conduct of a clinical trial.

The Sponsor/Principal investigator shall make a detailed written report on the event within the next eight (8) calendar days after she/he has information that the case fulfilled the criteria for an SAE.

The principal investigator or sponsor shall report immediately but not later than seven (7) calendar days to the Authority any suspected unexpected serious adverse reaction (SUSAR) that is fatal or life-threatening which occurs during the course of a clinical trial and provide a detailed written report with any follow up information within next eight (8) days after she/he has information that the case fulfilled the criteria for a SUSAR.

All other SAEs or SUSARs shall be reported to the Authority within fifteen (15) calendar days after the sponsor/Principal Investigator has information that the case fulfilled the criteria for a SUSAR.

The principal investigator or sponsor of a clinical trial shall, within thirty (30) calendar days, report to the Authority, any serious adverse event (SAE) and Suspected Unexpected Serious Adverse Reactions (SUSARS), which occur in another country (s) for the same intervention that the sponsor has first knowledge.

The sponsor and/or investigator shall keep detailed records of all adverse events, which are reported from the clinical trials and shall evaluate the severity, causal relationship and expectedness of those adverse events according to the procedures in place.

The reported SAEs, SUSARs and other safety reports should be analysed by a technical committee established by the Authority according to the procedures in place and propose appropriate regulatory action.

In case the event reported consists of or results in the death of a trial participant, the Authority shall conduct a deep investigation.

Article 32: Quality of the investigational products

The sponsor and the Authority shall ensure that the investigational product(s) (including active comparator(s) and placebo, if applicable) is characterized as appropriate to the stage of development of the product(s), is manufactured in accordance with any applicable GMP standards, controlled, coded and labelled according to the procedures and relevant guidelines.

In the application for Clinical Trial Authorization, the sponsor shall specify the types, pharmaceutical forms of the investigational product and the site where the investigational products were manufactured.

Any application for the grant of a manufacturing, importation or exportation license or permit for an investigational product shall be made in accordance with the provisions of applicable regulations.

In the case of a locally manufactured investigational product, the content and format of GMP certificate shall comply with guidelines on Good Manufacturing Practices issued by the Authority.

In the event of imported investigational product, the Authority shall rely on the evidence of GMP compliance issued by the competent Authority of the country of origin. The Authority shall define the criteria for acceptance of GMP compliance in relevant guidelines.

The import or disposal of investigational products /placebo shall follow requirements as described in relevant guidelines issued by the Authority.

Article 33: Labelling of investigational product

An investigational product shall be labeled in at least one of the official languages used in Rwanda. The investigational product shall be labeled in a manner that protects the blinding where applicable. Re-labeling and shelf life extension of remaining investigational product from previously manufactured batches shall be performed in accordance with established written procedures and Good Manufacturing Practice principles upon the approval of the Authority.

Article 34: Inspection of clinical trial sites

The Authority shall inspect clinical trial sites to verify compliance with GCP standards, regulatory requirements and approved clinical trial protocol and its supplementary documents.

The Authority shall conduct inspections for any ongoing and completed clinical trial as per the procedures and frequency stipulated in the GCP inspection guidelines to determine if the investigators or sponsors are operating in compliance with GCP guidelines and the provisions of these Regulations. The Authority shall take regulatory action for any non-compliance to the provisions of the laws and

regulations. Investigators shall permit the Authority to access, copy, and verify any records or reports made with regard to the handling, storage, use, and disposal of the product and participants' medical records at the approved trial site(s) and all other facilities used or being used for the purpose of the clinical trial. The Authority may conduct either announced or unannounced inspections.

Article 35: Qualification of GCP inspectors

After fulfilling the requirements as per the training program and qualification of Rwanda FDA inspectors and the competence matrix of inspector's qualification; the Authority shall officially nominate a lead GCP inspector to assure expertise necessarily to lead the entire inspection process of authorized clinical trials. In case of complex clinical trials including Advanced therapy medicinal product (ATMP), vaccines and other biological products, radiopharmaceuticals, the Authority shall qualify and nominate the lead inspector as an expert.
The Authority shall maintain up-to-date records of training, qualifications and experience of the individuals entitled to conduct inspections. All qualified lead inspectors must be recognized and involved in clinical trials inspections when needed. The expertise of qualified GCP inspectors shall be recognized by other similar institutions as per the existing framework.

Article 36: Establishment of clinical trial technical committees

The Authority may establish Clinical Trial Technical Committees comprising of experts with knowledge and experience from different fields and scientific research to advise the Authority on clinical trial regulation matters. The composition and functioning of the Clinical Trial Technical Committees shall be defined in the terms of reference issued by the Authority.

Article 37: Post-trial access

The Sponsor and Principal Investigator shall ensure the post-trial access of the investigational product when revealed necessary and beneficial to the study participants.

Article 38: Clinical trial site

The Sponsor and Principal investigator shall ensure the clinical trial site is prepared, and equipped with all necessary requirements and staff to accommodate the planned clinical trial and achieve its objectives. They shall also have agreements with the manager of the clinical trial site to enable smooth implementation of the trial, where applicable.

Article 39: Implementation of these regulations

The Authority shall issue guidelines, standards operating Procedures (SOPs), forms, and checklists for better implementation of these Regulations.

Article 40: Clinical trials during public health emergencies or unmet medical needs

In case of public health emergencies, the clinical trial application shall follow non-routine procedures

set out in the relevant guidelines issued by the Authority.

The Authority shall fast-track or expedite the review and approval of clinical trials in the following circumstances:

a) products listed by WHO Emergency Use Assessment and Listing (EUAL) Procedure;
b) products listed on the African Vaccine Regulatory Forum (AVAREF) readiness plan;
c) accelerated development of medical products aiming at preventing or treating life-threatening diseases or targeting high priority diseases ensuring quick access to effective treatment;

The Authority shall establish the conditions for compliance and mechanisms to fast-track, expedite and rolling reviews for decision-making in public health emergencies or any other unmet medical.
In order to facilitate quick access to the treatment, the Authority shall review available data from pre-clinical studies, clinical studies, Real-World-Data(RWD) ensuring product benefit- risk profile to help an individual patient or a group of patients with life-threatening, long-lasting or seriously debilitating illnesses, which cannot be treated satisfactorily with any currently authorized medicine.
The regulatory requirements for compassionate use authorization shall be set out in relevant guidelines issued by the Authority.

Article 41: Reliance in clinical trials

The Authority shall apply reliance pathways as non-routine procedure for Clinical Trial Authorization. The Authority shall rely on clinical trial review reports and/or clinical trial decisions or information from other national regulatory Authorities, regional and international regulatory bodies when deemed necessary.

In the case of multi-center clinical trials carried out in more than one country including Rwanda, the Authority may rely on regulatory decision, information or report from other regulatory authorities in order to protect the trial participants in Rwanda.

The Authority shall also establish the procedures, circumstances, collaborative and/or mutual agreement for reliance. The Authority shall maintain its own regulatory responsibilities for decision-making.

Article 42: Good performance monitoring in clinical trials oversight

The Authority shall use key performance indicators to continuously monitor and maintain the good performance of clinical trials oversight activities

CHAPTER III: MISCELLANEOUS PROVISIONS

Article 43: Languages

All clinical trial applications and supporting documents shall be presented in at least one of the official languages used in Rwanda. This includes English, French and Kinyarwanda.

Article 44: Appeals to the authority

Any person aggrieved by a decision of the Authority may appeal to the Authority for review of the decision showing grounds for dissatisfaction within thirty (30) calendar days from the date of notice.

The Authority shall, within fifteen (15) calendar days from the date of receiving the application, review, reject or vary its own decision. In case the applicant is not satisfied by the decision of the Authority, he/she may appeal to the supervising Authority.

Article 45: Administrative sanctions

Anyone who violates the provisions of these regulations is subject to regulatory administrative sanctions under Annex-A, which comprises administrative fines, suspension, or termination of ongoing clinical trials. The termination shall lead to the immediate revocation of the Clinical Trial Approval Certificate.

Article 46: Repealing

All prior provisions contrary to these regulations are hereby repealed.

Article 47: Commencement

These regulations shall enter into force on date of its signature and publication.

End of Document

Annex-A: List of Faults, administrative sanctions, and fines

S/No	Faults	Administrative sanctions and fines
1.	Conducting clinical trials without prior authorization from the Authority	Termination of the trial + administrative fines of five million Rwandan Frw (5,000,000 Frw)
2.	Publishing findings of a clinical trial that were not previously authorized by the Authority	Forced retraction of the publications + an administrative fine of ten (10) millions Rwandan Francs (10,000,000 Frw)
3.	Implementation of substantial amendment to the approved clinical trial protocol without prior authorization from the Authority	A fine of one (1) million Rwandan Francs (1,000,000 Frw)
4.	In the case of recidivism, the same faults related to clinical	A suspension + administrative fine of two million Rwandan Francs (2,000,000 Frw)
5.	Failure to take out insurance coverage for clinical trial participants	Pay the required insurance premium and pay an administrative fine of two million Rwandan Francs (2,000,000 Frw)
6.	Publication of clinical trial findings which are different from authorization	Immediately delete the content published without authorization and pay an administrative fine of not less than five million Rwanda Francs (1,000,000 Frw)
7.	Failure to comply with eligibility criteria during the recruitment of trial participants	Suspension + a fine of one (1) million Rwandan francs (1,000,000 Frw)
8.	Enrolment of trial participants without signed informed consent	Suspension + Administrative fines of five hundred thousand Rwandan Frw (500,000 Frw)
9.	Failure to timely report the timelines for reporting Serious Adverse Events (SAEs)	Suspension + Administrative fines of five hundred thousand Rwandan Frw (500,000 Frw)
10.	Implementation of a clinical trial that has Serious Adverse Events (SAEs) or harmful effects on the clinical trial participants	Termination + administrative fine of five million Rwandan Francs (FRW 5,000,000 Frw)