REGULATIONS GOVERNING THE CONDUCT OF CLINICAL TRIALS IN RWANDA

(Rwanda FDA law N° 003/2018 of 09/02/2018, Article 8)

REGULATIONS DEVELOPMENT HISTORY

DRAFT ZERO BY CONSULTANTS	20th May 2018
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STAKEHOLDERS' CONSULTATION	14th October 2020
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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 and ISSUES these regulations N° CBD/TRG/015 Rev_0 governing the conduct and inspection of clinical trials, made this 31st day of December, 2020.

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Ag. Director General

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CHAPTER I: GENERAL PROVISIONS

Article 1: Purpose

The purpose of these regulations is to create a favourable environment 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 and inspection of clinical trials, Bioavailability and Bioequivalence studies for human participants and recommend approval of the conduct of clinical trials.

Article 2: Citation

These regulations may be cited as "*Regulations Governing the Conduct of Clinical Trials in Rwanda."*

Article 3: Application

These regulations shall apply to all clinical trials including Bioavailability and Bioequivalence studies involving Rwanda FDA regulated products to be conducted in Rwanda.

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 which 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 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 which 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 has 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 for the purpose of ascertaining 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 center or any other establishment involved in a clinical trial;

11. **"code"** means identification code assigned by the investigator to each clinical trial study participant to protect the study participant's identity and used in lieu of the study participant's name when the investigator reports adverse events or other trial related data;

12. **"confidentiality"** means maintenance of the privacy of trial participants including their personal identity and all personal medical information;

13. **"coordinating investigator"** means an investigator assigned the responsibility for the coordination of investigators at different centers participating in a multi-centre trial;

14. **"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;

15. **"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;

16. **"direct access"** means permission to examine, analyze, verify and reproduce any records and reports that are important to evaluation of a clinical trial;

17. **"essential documents"** means documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced;

18. **"ethical clearance"** means an authorization to conduct a clinical trial issued by an approved institute for medical research;

19. **"Fee"** means the fee prescribed in regulation N° CBD/TRG/004 related to regulatory Services tariff /fees and fines.

20. **"good clinical practice"** means 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 study participants are protected;

21. **"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;

22. **"herbal drug"** 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;

23. **"informed consent"** means participant voluntary confirmation of willingness to participate in a particular trial, and the documentation thereof;

24. **"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;

25. **"investigational medicinal 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;

26. **"investigator"** means a qualified persons(physician, dentist, Pharmacist, Anesthetists, Veterinary doctor and any other qualified persons)who conducts a clinical trial at a trial site;

27. **"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;

28. **"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;

29. **"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;

30. **"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;

31. **"national registry"** means a database created by the Authority that houses and manages information about a clinical trial submitted by an applicant;

32. **"pharmacovigilance"** means the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem;

33. **"pre-clinical studies"** means biomedical studies not performed on human study participants;

34. **"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;

35. **"product"** means investigational medicinal product;

36. **"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;

37. **"protocol amendment"** means a written description of changes to or formal clarification of a protocol;

38. **"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;

39. **"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;

40. **"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;

41. **"serious adverse event or serious adverse drug reactions"** means any untoward medical occurrence that at any dose may cause any of the following:
    (a) Death;
    (b) Life threatening;
    (c) Hospitalization or prolongation of existing hospitalization;
    (d) Persistent or significant disability or incapacity; or
    (e) Congenital anomaly or birth defect.

42. **"sponsor"** means an individual, company, institution or organization who takes responsibility for the initiation, management and, or financing of a clinical trial;

43. "**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

44. "**'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

45. **"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;

46. **"trial or study site"** means the location(s) where clinical trial-related activities are conducted;

47. **"unexpected adverse drug reaction"** means an adverse reaction with the nature or severity not consistent with the applicable product information;

CHAPTER II: APPLICATION, ASSESSMENT, INSPECTION AND REPORTING IN CLINICAL TRIALS

Article 5: General Principles

1. All clinical trials, including Bioavailability and Bioequivalence studies, shall be designed, conducted, recorded and reported in accordance with these Regulations.

2. All clinical trials must be conducted in accordance with Good Clinical Practices (GCP) principles.

3. Clinical trials shall be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP.

4. 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.

5. The rights, safety, and well-being of the trial subjects shall prevail over interests of science and society.

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

7. Clinical trials shall be scientifically sound, and described in a clear, detailed protocol. The trial shall be conducted according to the approved protocol.

8. A trial shall be conducted in compliance with the protocol that has received prior Ethics Committee (EC) favorable opinion.

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

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

11. Freely given informed consent shall be obtained from every subject prior to clinical trial participation

12. All clinical trial information shall be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.

13. The confidentiality of records that could identify subjects shall be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

14. Investigational medicinal 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.

15. Systems with procedures that assure the quality of every aspect of the trial shall be implemented.

16. Amendments relating to the conduct, design, methodology, investigational medicinal 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.

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

18. The sponsor or the investigator shall submit study reports as prescribed by the authority

19. The authority shall carry out inspection at the approved trial sites and all other facilities used or being used for the purpose of the clinical investigation to ensure compliance with provisions of these Regulations

Article 6: Application requirements for Authorization of a Clinical Trial

a) **Pre-clinical trial application (CTA) meeting**
b)

i. An application for a pre-CTA consultation meeting shall be made by the sponsor or Principal Investigator and submitted to the Authority;
ii. The pre-CTA meeting shall include the proposed date and time for the meeting and a brief synopsis (electronic copies) of the proposed study listing questions (if any) to be addressed by Authority,
iii. A confirmation of the date and time of the meeting shall be duly conveyed to the Sponsor within **fifteen (15) calendar days** after the receipt of meeting request

c) **Clinical Trial application**

1. A person who desires to conduct a clinical trial shall submit to the Authority an application in the prescribed form duly signed and dated;
2. An application to conduct a clinical trial shall be submitted both hard copy and electronically to the Authority;
3. All 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 (efficacy, performance and safety);
4. An application to conduct a clinical trial shall be made by a sponsor or the sponsor's agent who shall submit a power of attorney attesting that she/he is a duly appointed agent;
5. The application shall be accompanied by proof of payment of applicable fees

Article 7: Authorization to conduct clinical trials in Rwanda

a) Authorization for a clinical trial shall be granted to all categories of products and circumstances described in clinical trial application guidelines.

Article 8: Reasons for rejection of Clinical trial application

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

(a) the information and documents as set out in these regulations 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 medicinal product or clinical trial;

(d) queries raised by the Authority in relation to the application were not adequately responded to;

(e) the applicant has not submitted an ethical clearance from any approved institute for medical research;

(f) the use of the drug, medical device or herbal drug 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 9: Amendment to clinical trials application

(a) Any amendment to an approved clinical trial application shall be notified to the Authority.

(b) In case of non-substantial amendments, the authority should be notified via the annual progress report. In case of substantial amendments, it is mandatory to obtain an approval from authority before implementing such amendments, in accordance with the requirements described in relevant guidelines.

(c) The authority allows urgent safety measures to be taken, without prior approval, to protect trial participants from immediate hazards. However, the authority must be notified about such measures as soon as possible but not later than **seven (7) calendar days** after becoming aware of the information.

(d) An application for amendment to an approved clinical trial shall be made using the form provided by the Authority according to the relevant guidelines for implementation of these regulations.

(e) The amendment shall be accompanied by amendment prescribed fees.

An application for amendment to an approved clinical trial shall be accompanied by Ethical Clearance Certificate from the Ethics Committee.

Article 10: Authenticity of clinical trial documents

Any document submitted to the Authority shall be authentic when approved by the Principal investigator or by the sponsor.

Article 11: Assessment process for the clinical trial application

a)

b) The Authority shall, upon being satisfied by the application, conduct assessment to verify the compliance with safety, efficacy, and performance requirements through assessment procedures.

c) The authority shall set out guidelines, Standard operating Procedures (SOPs), forms, and tools for assessment procedures.
d) The Authority may, during the assessment of clinical trial, require the applicant to submit additional information, data or clarification to support the clinical trial application.
e) Where the Authority requires additional information, data or clarification pursuant to Article 12c, the processing of the application shall not proceed until when the applicant makes submission.
f) Where the applicant fails to submit requested information according to Article 12c, within the period of **thirty (30) calendar days** from the date of request letter, the application shall be considered as **withdrawn**.
g) Pursuant to the requirements of article 12e, the applicant may, by giving reasons in writing within **thirty (30) calendar days**, request for extension of time for submission of additional information, data or clarification requested by the Authority.
h) If the applicant fails to provide satisfactory responses two (2) times for the same requested information according to article 12c, the application shall be **rejected.**

Article 12: Approval of clinical trial application

Upon assessment and approval of clinical trial application, the Authority shall:
a) Issue clinical trial approval certificate ;
b) Allocate a clinical trial approval number.

Article 13: Validity of clinical trial certificate

A clinical trial approval certificate issued under Article 13 shall be valid for all the period of clinical trial when the trial duration is less than one (1) year or for one (1) year renewable.

Article 14: Renew of clinical trial approval

1) For the applicant conducting a clinical trial who fails to complete the trial within the planned period, shall apply for renew of clinical trial approval;
2) For clinical trial beyond one (1) year, the applicant shall submit the annual report and apply for renewal of clinical trial approval. The guidelines shall set out the requirements for renew of clinical trial approval.

Article 15: Register of Clinical trials

1. The Authority shall maintain a Register of all clinical trials conducted in Rwanda according to these regulations and other international relevant guidelines;
2. The Authority shall record the following information required in the Register of clinical trials:
   a) protocol title and 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)

j)

3. The Authority shall ensure that relevant information on Register of clinical trials is publicly available.

Article 16: Conduct of clinical trial

All clinical trials shall be conducted in accordance with provisions of relevant laws, regulations and guidelines issued by the Authority. It shall strictly comply with Good Clinical Practices (GCP) and Good Laboratory Practices (GLP).

Article 17: Responsibilities of Principal Investigator

1. The principal investigator shall be responsible for the conduct of the clinical trial at the clinical trial site.
2. 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.
3. The principal investigator shall maintain a list of appropriately qualified persons to whom he has delegated significant trial-related duties.
4. 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.
5. 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.

6. The principal investigator shall comply with the protocol approved by the Authority.
7. The principal investigator shall be responsible and accountable for the investigational product at the trial site.
8. The principal investigator may 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.
9. The principal investigator shall follow the randomization procedures, if any, and shall ensure that the code is broken only in accordance with the protocol.

Article 18: Qualifications of investigators and monitors

1. In any clinical trial, investigators shall be appropriately qualified to perform clinical trial investigation;
2. 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.

Article 19: Ethical clearance

Applicant shall be required to submit ethical clearance for the conduct of clinical trials issued by Rwanda National ethic committees or designated Institutional Review Boards.

Article 20: Responsibilities of sponsor

1. 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 these Regulations;
2. 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;
3. 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;
4. 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;
5. 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;

6. 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;
7. The sponsor shall update the investigator brochure at any time when new significant information becomes available.

Article 21: Protection of clinical trial participants

1. Prior to 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.
2. 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;
3. 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;
4. The rights of each participant to physical and mental integrity, to privacy and to the protection of the data concerning him shall be safeguarded;
5. 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 22: Insurance of trial participants

1. 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 subjects by the clinical trial activities throughout the entire duration;
2. 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;
3. The Authority shall ensure that all subjects of the trial are satisfactorily insured against possible damages/injuries caused to the subjects by the clinical trial activities throughout

the entire duration;

4. For clinical trials which involve gene therapy, cellular therapy and radio-pharmaceutical shall require minimum extended tail coverage for the risk of at least ten (10) years;
5. 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 insurance certificate. The submission of the renewal certificate to the Authority is a non-substantial amendment;
6. The Authority, after review and analysis of the design and interventions of clinical trials, may exempt participant insurance.

Article 23: Reporting in Clinical trial

1. The principal Investigator shall submit the report 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;
2. The principal investigator shall submit written clinical trial progress reports annually, or more frequently, as may be required by the Authority;
3. After the completion of the clinical trial, the principal investigator shall submit a final study report to the Authority within ninety (90) calendar days in accordance with the format provided by the Authority.

Article 24: Records and record keeping

1. 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.
2. 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;
3. The Authority may require the principal investigator or sponsor to submit records, documents and information stored under point (1) when it may deem fit and just;
4. 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 these Regulations;
5. 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 25: Clinical trial Authorization timelines

The review process of a clinical trial application by the Authority shall not exceed **sixty (60) working days** upon compliance with all requirements.

Article 26: Requirements related to Data and Safety Monitoring Committees

1. The Authority reserves discretion to impose a condition for establishment of a Data and Safety Monitoring Committee (DSMC) depending on the design and scientific background, risk and benefit assessment of the clinical trial;
2. In any case, where clinical trials involves Data and Safety Monitoring Committee to monitor clinical trials, the Authority may require the terms of reference, responsibilities, composition and qualifications of members of the committee.

Article 27: 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 investigational product;
(c) inform all investigators of the discontinuation and of 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; and
(d) stop the use or importation of the investigational product as 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 28: Suspension or termination of a clinical trial

1. The Authority may, by a notice in writing to the holder of authorization, suspend or terminate the authorization due to non-compliance with these Regulations;
2. The Authority may disqualify or blacklist an investigator if there is information indicating that an investigator (including a sponsor-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 29: Reporting of adverse events & suspected unexpected serious adverse reactions

1. 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;

2. The Sponsor/Principal investigator shall make a detailed written report on the event within fifteen (15) calendar days after she/he has information that the case fulfilled the criteria for a SAE.
3. The Authority may require additional information in case the event reported consists of, or results in the death of a participant;
4. The principal investigator or sponsor shall record and report 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, within **seven (7) calendar days** and provide detailed written report with any follow up information within **fifteen (15) days** after she/he has information that the case fulfilled the criteria for a SUSAR.
5. All other 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
6. The principal investigator or sponsor of a clinical trial shall, within **thirty (30) calendar days**, report to the Authority, Suspected Unexpected Serious Adverse Reactions which occur outside the concerned trial that the sponsor has first knowledge.

Article 30: Investigational products

1. The sponsor should 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, and is coded and labelled in a manner that protects the blinding, if applicable;
2. 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 these regulations.
3. The sponsor shall specify, in the application for authorization, the types and pharmaceutical forms of the investigational medicinal product manufactured or imported, the manufacturing or import operations, the manufacturing process where relevant, the site where the investigational medicinal products are to be manufactured. A Certificate of Good Manufacturing Practices (GMP) for manufacture of the trial product and/or placebo shall be provided.
4. The import and disposal of investigation products /placebo will follow requirements as described in relevant guidelines.
5. The manufacturing and import of investigational medicinal products in Rwanda shall be subject to the holding of an authorization for Clinical Trial.

Article 31: Labelling of investigational product

1. An investigational product shall be labelled in at least one of the official languages used in Rwanda. The investigational product shall be labelled in the manner that protects the blinding where applicable.

2. Re-labeling and shelf life extension of any investigational product shall be performed in accordance with established written procedures and Good Manufacturing Practice principles upon the approval of the Authority.

Article 32: Inspection of clinical trial Sites

1. The Authority shall verify the compliance with the standards of good clinical practices and the need to subject data, information and documents to inspection in order to confirm that they have been properly generated, recorded and reported are essential in order to justify the involvement of human subjects in clinical trials;
2. The Authority may at any time it deems necessary, conduct inspections for any ongoing clinical trial to determine if the investigators or sponsors are operating in compliance with the provisions of these Regulations and other regulatory requirements;
3. The Authority may take any legal action for any non-compliance in accordance with the provisions of the laws and regulations;
4. 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 investigation;
5. The Authority may conduct both announced and unannounced inspections.

Article 33: Establishment of Technical Committee

The Authority may establish a Technical committee comprising of experts from different fields and scientific research to advise the Authority on clinical trial regulation matters.

Article 34: Post-Trial access

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

Article 35: Clinical trial site

1. The Sponsor and Principal investigator shall ensure the clinical trial site is prepared, equipped with all necessary requirements and staff to accommodate the planned clinical trial and achieve its objectives;

2. The Sponsor or Principal Investigator shall have agreements with manager of the clinical trial site to enable smooth implementation of the trial.

Article 36: Implementation of these regulations

Guidelines, SOPs, forms and checklists shall be issued by the Authority for better implementation of these Regulations.

Article 37: Clinical Trials during Public Health Emergencies

1. In case of public health emergencies of the international concern, the Authority shall expedite the review of products listed on Emergency Use Assessment and Listing Procedure (EUAL) and African Vaccine Regulatory Forum (AVAREF) readiness plan;
2. The Authority shall establish the conditions for compliance and review mechanisms for expedited assessment in public health emergencies.

Article 38: Reliance in Clinical Trial

1. The Authority shall rely on clinical trial review reports from other national regulatory Authorities, regional and international regulatory bodies when deemed necessary;
2. The Authority shall establish the procedures, circumstances, collaborative and mutual agreement for reliance.
3. The authority shall maintain its own regulatory responsibilities for decision-making.

CHAPTER III: MISCELLANEOUS PROVISIONS

Article 39: Languages

All clinical trial applications and supporting documents shall be presented in at least one of the official languages used in Rwanda.

Article 40: Appeals to the Authority

1. Any person aggrieved by a decision of the Authority may apply to the Authority for review of the decision showing grounds for dissatisfaction within **thirty (30) calendar days** from the date of notice;
2. The Authority shall, within **fifteen (15) calendar days** from the date of receiving the application, review, reject or vary its own decision;
3. In case the applicant is not satisfied by the decision of the Authority, he/she may appeal to the supervising Authority.

Article 41: Administrative sanctions

Any person who conducts clinical trials in contravention with any provision of these Regulations shall be liable to administrative sanctions stipulated on the regulations N° CBD/TRG/004.

Article 42: Commencement

These regulations shall enter into force on date of its signature and publication. All prior provisions contrary to these regulations are hereby repealed.

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