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REGULATIONS ON CLINICAL TRIALS IN LIBERIA

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DECLARATION

This Regulation, made in fulfilment of PART V, Section 7 of the Liberia Medicines and Health Products Regulatory Authority Act of 2010, which confers upon the Authority the responsibility of regulating medicines and health products within the Republic of Liberia. The Management, with approval of the Board of Directors hereby promulgate this regulation designed for Clinical Trials of medicines and health products this 29th day of January, 2025

Part I: PRELIMINARY

Section 1: Title

Regulation on Clinical Trials in Liberia

Section 2:

Application and Scope

1. This Regulation outlines legal provisions for authorization and conduct of clinical trials as defined in Part V, Section 5 of the Liberia Medicines and Health Products Regulatory Authority Act of 2010.
2. This Regulation shall apply to clinical development of investigational medicinal products and health products falling under the mandate of the Authority as the competent Authority, responsible by Law to regulate such activities.
3. This Regulation shall be applied during all stages of clinical development of investigational medicines and health products and is addressed to investigators, the pharmaceutical industry, clinical research organizations and sponsors of clinical trials, whether for academic purposes or for generation of data, intended for inclusion in the regulatory submissions for medicines and health products.
4. This Regulation provides special provisions for non-interventional clinical studies
5. The Authority shall publish guidelines on provisions specified in this Regulation for the purpose of giving further clarifications to stakeholders involved in the conduct of clinical trials.

Section 3: Purpose

The purpose of this Regulation is to provide a legal framework for the effective and efficient regulation of Clinical Trials and to provide an open, transparent and nondiscriminatory process for generation of data, non-interventional clinical studies of medicines and health products and other products as required by the Act of 2010.

Section 4: Definitions

In this regulation, unless the context otherwise requires, the following words and phrases shall have the meanings as ascribed to them in this section.

Adverse Drug Reactions means the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established as all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase "responses to a medicinal product" means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

Adverse Event means any untoward medical occurrence in a patient or clinical investigation subject administered as pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. See Serious Adverse Event (SAEs).

Amendment means a written description of a change(s) to or formal clarification of a change to approved clinical trial or investigational product applied in the clinical trial.

Applicant means the sponsor, sponsor´s legal representative, principal investigator or sponsor-investigator applying for approval by the Authority and issuance of a written permission from the National Research Ethics Board (NREB) to conduct a clinical trial in Liberia or any other action as specified in this Regulation.

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

Clinical Trial/ Study Report means a written description of a trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the

clinical and statistical description, presentations, and analyses are fully integrated into a single report.

Contract Research Organization (CRO) means a person or an organisation (commercial, academic, or other) contracted by the sponsor to perform one or more of sponsor´s trial-related duties and functions.

Good Clinical Practice means a standard for the design, conduct, performance, monitoring, auditing, recording, analysing and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Legal Guardian (Legal Representative of a Minor) means the basis that a minor cannot grant consent or enter into an agreement. The law provides that the interest of a minor must be firstly protected by the parents (the father if the parents are married or the child is legitimized) or the mother of the child if the parents are not married. Where there is no parent alive, especially the mother if the child is not born out of wedlock or legitimized, any next of kin, preferably the grand-parents first, the siblings second, or any person with interest in the welfare of the child, may petition the Probate Court for Decree of Guardianship. Only then can such guardian be authorized to give consent for the minor child. NO INSTITUTION CAN SERVE AS GUARDIAN AND GIVE CONSENT FOR RESEARCH ON THE CHILD. A guardian must be a natural person, not an institution.

Independent 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.

Independent Ethics Committee means an independent body (a review board or a committee, institutional, regional or supranational), constituted of medical professionals and non-medical members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial and to

provide public assurance of that protection, by among other things, reviewing and approving/providing written permission on the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects. In Liberia this function is fulfilled by the National Research Ethics Board.

Informed Consent means a process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of the risk involved and other alternatives including all aspects of the trial that are relevant to the subject´s decision to participate Informed consent shall constitute the voluntary written consent of the person taking part in the clinical trial having been freely obtained by the person conducting the trial and for a person who cannot read and write, consent shall be obtained in a language that the person understands and given through video with the assistance of a psychosocial counsellor. Where the subject involved is a child or persons under legal disability, the voluntary written informed consent of their parents or legal guardians must be freely obtained by the person conducting the trial.

Inspection means the act by the regulatory authority of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority to be related to the clinical trial and that may be located at the site of the trial, at the sponsor´s and/or contract research organization´s facilities, or at other establishments deemed appropriate by the regulatory authority.

Investigational Product 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 authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

Investigator (Clinical Investigator) means a person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal

investigator. *In Liberia clinical investigator must hold a degree in healthcare Sciences.*

Investigator´s Brochure means a compilation of the clinical and nonclinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects.

Interim Clinical Trial/ Study Report means a report of intermediate results and their evaluation based on analyses performed during the course of the trial pending final reports.

International Non-Propriety Names (INN) means to facilitate the identification of pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognized and is public property.

ICH is the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)

Person Under Legal Disability means the same category as a minor as to his /her ability to grant consent, except that the person under disability may be above the age of consent (18yrs), even though he or she may lack the mental capacity to reason properly and grant consent, or may be too ill to participate in decisions on their own health. In this case, priority is not given to parents or next of kin to petition the Probate Court for Guardianship, but any natural person who demonstrate best interest in the welfare of the disabled.

Minor means a person of age below 18 years.

Monitoring

means the act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded and reported in accordance with the protocol, standard operating procedures, good clinical practice, and the applicable regulatory requirements.

Multicenter 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.

Non-interventional Clinical Study means a study in the context of which findings resulting from person´s treatment with medicinal products are analysed using epidemiological

methods; the treatment, including the diagnosis and monitoring, shall not follow a predetermined trial protocol but shall result exclusively from current medicinal practice according to the specifications regarding its use contained in the marketing authorisation (e.g. observational study).

Preclinical Studies (Nonclinical Studies) means biomedical studies not performed in human subjects.

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

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

Principal Investigator means holder of an independent grant and the lead researcher for the grant project, usually in the sciences, such as a laboratory study or a clinical trial. The phrase is also often used as a synonym for "head of the laboratory" or "research group leader".

Serious Adverse Event (Serious Adverse Drug Reaction) means any untoward medical occurrence that at any dose (i) results in death, (ii) is life-threatening, (iii) requires inpatient hospitalisation or prolongation of existing hospitalisation, (iv) results in persistent or significant disability/ incapacity, or (iv) is a congenital anomaly/birth defect. In the case of a Serious Adverse Drug Reaction it is to note that the causal relationship between the investigational medicinal product and the adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

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

Sponsor-investigator means an individual who both initiates and conduct, alone or with others, a clinical trial and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The term does not include any

person other than an individual (e.g. it does not include a corporation or an Authority). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.

Trial Participant means an individual who participates in a clinical trial, either as a recipient of the investigational product(s) or as a control.

Unexpected Adverse Drug Reaction means as adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g. Investigator´s Brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product).

CHAPTER II: CLINICAL TRIALS OVERSIGHT

Section 1: General Conditions for Clinical Trials

a. The sponsor, the investigator and all of the other persons involved in the clinical trials shall, in the conduct of the clinical trials of an investigational medicinal and health product on human beings, fulfil the requirements of good clinical practice as laid down in the ICH Guideline for Good Clinical Practice and WHO Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products as determined by the Authority.

b. The clinical trial of an investigational medicinal product on human beings may only be commenced by the applicant if the Ethics Committee has issued a written permission and the Authority has given its written approval based on the conclusion that the anticipated therapeutic and public health benefits justify the risks and may be continued only if compliance with this requirement is permanently monitored.

c. An application to conduct a clinical trial shall be submitted to the Authority consistent with law by the sponsor or its legal representative or the principal Investigator or the sponsor-investigator.

d. An application for a clinical trial shall be made to the National Research Ethics Board (NREB) and the Authority in parallel or sequential orders. The application to the Authority shall be made on an application form as prescribed by the Authority, accompanied by a prescribed fee and the following documents:

    1. Cover letter including list of documents submitted and their version numbers and date;
    2. Completed clinical trial application form including cover page;
    3. Clinical trial protocol ;
    4. A list of the planned clinical trial sites and the planned number of subjects at the sites located in Liberia;
    5. Details of the site(s) where the trial is to be conducted and a duly justified written statement on the suitability of the clinical trial sites adapted to the

nature and use of the investigational medicinal product and including a description of the suitability of facilities, equipment, human resources and description of expertise, issued by the head of the clinic/institution at the clinical trial site or by some other responsible person;

6. Participant information sheet, Informed consent form(s) or videos or, assent forms in case of minors or persons under legal disability are to participate in the clinical trial and informed consent procedure for human trials;
7. Insurance coverage for prospective participants.
8. Product information if the investigational medical product is registered: summary of product characteristics, patient information leaflet/package insert and labelling
9. Investigator's brochure containing relevant chemical, pharmaceutical, pre–clinical pharmacological and toxicological data and where applicable, human or animal pharmacological and safety and efficacy clinical data about the investigational medicinal product;
10. If applicable, synopsis of previous trials with the investigational medical product(s);
11. If applicable, electronic copies of key peer reviewed publications following (International Committee of Medical Journal Editors (ICMJE) recommendations to support the application;
12. Copy(ies) of recruitment advertisement(s) (if applicable) and questionnaires;
13. Investigational medical product dossier
14. Content of the labelling of the investigational medicinal products;
15. Product information and certificate of analysis for the concomitant and rescue medications;
16. GMP certificate issued from the National Regulatory Authority of the country where the investigational medicinal product is manufactured, translated into English language;
17. Certificate(s) of analysis of the investigational medical product(s);
18. Certificate(s) of accreditation for the central laboratories (if applicable);

19. Signed declaration by the applicant;
20. Signed declaration by the national principal investigator;
21. Workload forms for investigators;
22. Signed curriculum vitae for all key staff participating in the conduct of the clinical trial, e.g. national principal investigator, principal and/or co-investigators, study coordinator, regional and local monitor, contract research affiliate etc…
23. Signed declaration(s) by each investigator(s);
24. Signed joint financial declaration between the sponsor and the national principal investigator;
25. Signed declaration by the sub-investigators and key staff participating in the clinical trial;
26. Signed declaration by the regional monitor(s);
27. Signed declaration by the Sponsor/ Sponsor-Investigator of the trial referred to in these Regulations that they are familiar with and understand the protocol and will comply with Good Clinical Practice as determined by the Authority in the conduct of the trial;
28. Proof of registration on Pan African Clinical Trial Registry (PACTR) or other WHO primary accessible registry;
29. Active clinical trials insurance (Phase I, II, III);
30. Proof of sponsor indemnification for investigators and trial site;
31. GCP certificates for the investigators;
32. Proof of registration of the key investigators with a professional statutory body ~~.~~
33. Proof of residence in Liberia of the Principal investigator;
34. Proof of professional indemnity (malpractice insurance);
35. Study budget;
36. In case of parallel submission, proof of submission of the clinical trial application to the National Research Ethics Board;
37. The written permission of the National Research Ethics Board in case of sequential submission, and in case of parallel submission the updated

versions of documents or information as requested by the National Research Ethics Board, for the conduct of the clinical . Information on the composition of the Data and Safety Monitoring Board, including the list, terms of reference and curriculum vitae of its members justifying their expertise as members of the Data and Safety Monitoring
Board;

38. Summary of product characteristics or other professional information for all registered medicines used in the trial, or the international equivalent thereof if the medicines are not registered in Liberia;
39. Recruitment arrangements.

a. In the case of an application for a clinical trial in respect of a registered medicine, a registered indication or registered dosage regimen of a registered medicine or substance, as referred to in these Regulations shall apply accordingly.

b. Any substantial amendment to the approved clinical trial documentation, trial arrangements and investigational medicinal product referred to in this document shall be submitted by the applicant to the Authority and the National Research Ethics Board together with the prescribed fee for the evaluation and authorization related to such amendment.

- Amendments shall be classified and processed as determined by the Authority in corresponding guidelines.

c. The clinical trial of an investigational medicinal product may only be conducted on human beings if and as long as:

- the foreseeable risks and inconveniences are medically justifiable, compared with the benefit for the person on whom the clinical trial is to be conducted (trial participant), and the anticipated significance of the investigational medicinal product for medical science,

d. according to the state of scientific knowledge in relation to the purpose of the clinical trial of an investigational medicinal product consisting of a genetically modified organism or a combination of genetically modified organisms or containing such organisms, unjustifiable harmful effects on: a) the health of third persons and b) the environment, are not to be expected

e. The trial participant:

1) if an adult has been informed of the nature, significance and implications of the clinical trial and has given a voluntary written informed consent;
2) if a minor or a person under legal disability, their parents or guardians/legal representatives have been informed of the nature, significance and implications of the clinical trial and have given a written voluntary informed consent. In addition, an assent form shall be signed and if possible dated by the minor. If the informed implication is grave it may be necessary for the Guardian to secure the permission from the Probate Court before granting consent, for the simple reason that the Decree of Guardianship has a clause that the Court appointed Guardian shall not release the minor or disable to any other body in which case their welfare will be put at peril. If otherwise, it can be argued that the appointed Guardian breach his or her fiduciary duty to the Court by releasing the minor or disabled to peril.
3) If a person under legal disability, their parents or guardians/ legal representatives have been informed of the nature, significance and implications of the clinical trial and have given a written voluntary informed consent.
4) If the trial participant is unable to read or write English, the informed consent shall be obtained in the language he or she understands and in presence of at least one witness. The witness, who shall be able to read and write English and understand the local language in which the trial participant is informed, shall not be a member of the investigating team. The consent given by the trial subject shall be documented in writing, dated and signed by the witness and thumb printed by the trial participant.
5) Instance where participants can read and write his or her language, inform consent should be written in his/her language
6) The trial participant or witness, if applicable, shall be informed by an investigator, who is a healthcare personnel, or a person designated by the investigator, who is knowledgeable about the nature, significance, risks and implications of the clinical trial as well as about his/her right to withdraw from the clinical trial at any time. A generally comprehensible information sheet is to

be handed out to him/her. Furthermore, the trial participant is to be given the opportunity to have a counselling session with an investigator or a person designated by the investigator about the other conditions surrounding the conduct of the clinical trial.

7) The trial participant shall be informed of the purpose and scope of the collection and use of personal data, especially medical data. The trial participant shall be informed especially of the fact that where necessary, the collected data:
   a. shall be kept available for inspection by the Authority or for monitoring or auditing by the sponsor in order to verify the proper conduct of the clinical trial,
   b. shall be passed on to the sponsor and Authority without disclosing the identity of the trial participant;

8) A declaration of consent to participate in a clinical trial, can be revoked at any time in presence of the investigator or a member of the investigating team, orally or in writing, without disadvantage to the trial participant. In the case of a revocation of a consent, the study participant shall decide whether his/her stored data may continue to be used.

9) It is conducted in an appropriate facility by a suitably qualified investigator in a responsible manner and the trial is managed by an investigator who can provide evidence of sufficient experience in the conduct of clinical trials as determined by the Authority,

10) In the event that a trial participant suffers injury or death related to the clinical trial, an insurance which provides benefits, exists,

11) Sign an indemnity in the form determined by the Authority protecting the Authority from liability in respect of an injury or an adverse event which may be sustained by a person, directly or indirectly, as a result of the conduct of the trial and which occurs or reveals itself at the time of trial or subsequently.

12) A medical doctor is responsible for the medical care of the trial subject.

13) In case of emergency situations the Authority may:

   a. Apply expedited application and review process for clinical trials;
   b. Make exemptions to the documentation requirements for submission of clinical trial applications.

Section 2: Special Preconditions for Clinical Trials

1. In the case of a clinical trial on a person of legal age who is suffering from a disease which is to be treated by the investigational medicinal product, Section 1 shall apply with the following provisions when applicable:
   a. The use of the investigational medicinal product is indicated according to the findings of medical science in order to save the person's life, or
   b. Must be of direct benefit to the group of patients who are suffering from the same disease as this person.
2. In an emergency situation where consent cannot be obtained, treatment which is necessary without delay to save the life of the trial participant, can be started immediately. Such situations shall be defined by the Authority and consent for continued participation must be obtained as soon as possible and not later than as defined by the National Research Ethics Board for a given clinical trial.
3. Section 1 when indicated shall apply with the following provisions to the conduct of a clinical trial on a minor who suffers or may suffer from a disease for which the investigational medicinal product is to be used:
   a. the use of the investigational medicinal product must be indicated according to the findings of medical science in order to save the life of the trial participant, to restore him or her to health, to alleviate suffering, or to prevent a disease:
      i. The clinical trial must be of direct benefit to the group of patients suffering from the same disease as the trial participant,
      ii. The research must be absolutely necessary in order to confirm data obtained in clinical trials on other persons or by means of other research methods,
      iii. The research must relate to a clinical condition from which the minor concerned is suffering or may suffer, and
      iv. The research may cause only minimal risk and minimal burden to the trial participant.
4. Section 1 when indicated shall apply under the following provisions to the conduct of a clinical trial on a person of legal age who is incapable of comprehending the nature, significance and implications of the clinical trial and of determining his/her

will in the light of these facts and who is suffering from a disease in the treatment of which the investigational medicinal product is to be used:

a. The use of the investigational medicinal product must be indicated, according to the findings of medical science, in order to save the life of the trial participant, to restore him or her to health or to alleviate suffering; furthermore, such research must relate directly to a life-threatening or highly debilitating clinical condition suffered by the trial participant and the clinical trial may involve as little burden and other foreseeable risks as possible for the trial participant. Both the degree of burden and the risk threshold must be defined specifically in the trial protocol and monitored constantly by the investigator. The clinical trial may only be conducted if there is a justified expectation that the benefits of using the investigational medicinal product for the trial participant outweigh the risks;
b. Consent shall be given by the authorized representative after participant has been duly informed pursuant to Section 1;
c. The research must be absolutely necessary for the confirmation of data obtained from clinical trials conducted on persons capable of granting informed consent or by means of other research methods;
d. With the exception of adequate compensation, no advantages may be granted.

Section 3: Investigational Medicinal Product(s)

1. Investigational medicinal product(s) for clinical trials must be manufactured according to internationally accepted good manufacturing practice (GMP) principles.
2. It is the responsibility of the sponsor to supply investigational medicinal product(s) produced in compliance with internationally accepted GMP principles.
3. Investigational medicinal product(s) for clinical trials center must be properly labelled and the package must sufficiently identify the –
   a. Clinical trial to be carried out;
   b. Medicine(s) to be used;
   c. Trial subject identification number to whom the medicine is to be administered;

d. Name and address of the site where the clinical trial is conducted;
e. The directions in regard to the manner in which such medicine should be used;
f. Date of dispensing, if applicable;
g. The storage conditions;
h. Use-by or expiry or re-test date, as applicable
i. Reference number, as applicable; and
j. Any other information as may be required by the Authority.

4. An application letter to the Managing Director for a permit to import investigational medicinal product(s) must contain the following information and documentation:-
   a. Name and address (both physical and postal) of the sponsor, sponsor´s legal representative or sponsor-investigator of the clinical trial;
   b. Name, address (both physical and postal) and contact details of the Principal Investigator including the -
      i. Telephone number; and

ii. Email address;

iii. The clinical trial for which the application is made;

iv. The planned clinical trial sites and the planned number of subjects at the sites;

v. Description of the investigational medicinal product(s) by name or code, strength and dosage form;

vi. Unit of issue, total quantity, batch number, manufacture and expiry dates of the product(s);

vii. Sample of the labels of the primary and secondary containers;

viii.. Planned return of unused investigational medicinal product(s) to sponsor or destruction at the clinical trial site;

ix. Name and address of manufacturer.

5. Destruction operations for investigational medicinal products should be carried out in such a manner that all operations may be accounted for. These documents should clearly identify, or allow traceability to, the batches and/or trial participant numbers involved and the actual quantities destroyed.
6. In case the sponsor/ sponsor- investigator would like to export the investigational medicinal product(s) remaining after the clinical trial has been stopped or completed, the sponsor, sponsor´s legal representative or/ sponsor- investigator must obtain an export authorization from the Authority.

Section 4: Management of Biological Samples

1. The applicant must obtain an authorization from the Authority in case biological samples are to be exported out of Liberia.
2. A material transfer agreement must be provided by the applicant to the Authority.
3. The applicant must provide annual update on the use and results obtained from biological samples exported out of Liberia.
4. A none refundable fees shall apply

Section 5: Procedures for Authorization of Clinical Trials by the NREB and the Authority

1. Upon the submission of application to the National Research Ethics Board

(NREB) pursuant to Section 1, the applicant must submit to the said National Research Ethics Board all of the information and documents as required for its opinion. A written permission may only be refused if:

a. The documents submitted are incomplete up to the expiry of an appropriate deadline given to the applicant for their supplementation;
b. The documents submitted, including the trial protocol, the investigator's brochure, the modalities for selecting trial participants and informed consent/ assent, do not correspond to the current state of scientific knowledge, and especially, the clinical trial is unsuitable for providing proof of the safety or efficacy of an investigational medicinal product(s), or
c. The requirements specified in Section 1, as applicable are not fulfilled.

2. The National Research Ethics Board provides its opinion on the application for a clinical trial in line with its written standard operating procedures.
3. An application for the authorization by the Authority required pursuant to Section 1 must be made by the applicant to the Authority. In this regard, the applicant must submit all the information and documents necessary for the assessment especially the results of the analytical and pharmacological-toxicological tests as well as the trial protocol and the clinical data on the investigational medicinal product(s) including the investigator's brochure as outlined in Section 1 subsection **(3). The authorization may only be refused if:**

a. The documents submitted are incomplete up to the expiry of an appropriate deadline given to the applicant for their supplementation,
b. The documents submitted, especially the data on the investigational medicinal product(s) and the trial protocol including the investigator's brochure do not comply with the current state of scientific knowledge, and especially, the clinical trial is unsuitable for providing proof of the safety or efficacy of an investigational medicinal product(s), or
c. In the case of trials involving human participants the requirements stipulated in Section 1 in particular regarding the insurance of trial participants, are not fulfilled,

d. The Authority is in possession of findings which indicate that the testing facility is not suitable to conduct the clinical trial
e. The Authority is of the opinion that the number of clinical trial participants to be recruited in the trial is not scientifically justified, or
f. The requirements provided for in Section 1 or Section 2 are not fulfilled.

4. Upon the review of the application package, the Authority shall inform the applicant in writing about the receipt of a valid clinical trial application or the formal grounds for non-acceptance within 10 working days from the receipt of the clinical trial application. The applicant must address formal grounds for nonacceptance within 10 working days. The Authority shall inform the applicant in writing about the outcome of the assessment of the clinical trial application within a maximum of 45 working days for pharmaceuticals, 60 working days Biological and biotechnology medicinal products and 90 working days for Genetically modified organisms, after validation of a formally complete clinical trial application, or as stipulated by the Authority in the respective clinical trial guidelines. This excludes time taken for applicant to respond to queries from the Authority. If changes are required and the applicant fails to modify the application correspondingly within a maximum of 30 working days, or as stipulated in the clinical trial guidelines, following the reasoned objections, the application shall be deemed to be rejected.
5. The Authority shall inform the National Research Ethics Board if it is in possession of information bearing on other clinical trials which is of significance to the National Research Ethics Board's assessment of the clinical trial on which it is to issue an expert opinion; this applies especially to information on aborted or otherwise prematurely discontinued investigations. In such instances, business and company secrets shall remain confidential.
6. The Authority can in the assessment of a clinical trial application recognize/ rely on relevant clinical trial decisions, reports or information from other National Regulatory Authorities, regional or international bodies. The scope/extent of utilization of relevant clinical trial decisions, reports or information from other National Regulatory Authorities, or regional and international bodies will be at the

sole discretion of the Authority. In such instances, business and company secrets must remain confidential.

7. The Authority can establish advisory committees for the review of clinical trial applications and for post approval safety and compliance issues, if needed, especially in the event of new/ emerging technologies.
8. All clinical trials must be registered with a public international database by the Sponsor/ Sponsor-investigator as determined by the Authority.
9. The Authority shall ensure that the list of approved and rejected clinical trial applications as well as summary of evaluation reports and status of approved clinical trials are publicly available and periodically updated.

Section 6: Suspension and Withdrawal of the Clinical Trial Authorization or of the Written Permission

1. A clinical trial authorization shall be suspended by the Authority for a limited period of time if:
   a. It becomes known that one of the grounds for refusal as referred to in Section 5 existed at the time of issuance of the clinical trial authorization; or
   b. The conditions surrounding the clinical trial do not correspond to the information contained in the authorization application; or
   c. If facts presented give reason to doubt the safety or the scientific basis of the clinical trial.
2. The clinical trial authorization shall be withdrawn by the Applicant in cases under (a)-(c) where scientific justification for resuming the clinical trial is not provided to the Authority.
3. The Authority shall immediately inform the National Research Ethics Board through a written communication stating the grounds for its action.
4. Before a decision pursuant to sub-sections (1) and (2) is taken, the applicant shall be allowed a deadline of 10 working days to submit a statement, unless the Authority orders the immediate interruption of the clinical trial. The lodging of an objection and action to rescind the suspension or the order to suspend the authorization as well as against orders pursuant to sub-section (5) shall have no suspensive effect.

5. If the authorization to conduct a clinical trial is withdrawn or suspended, the clinical trial may not be continued.
6. The written permission by the National Research Ethics Board shall be withdrawn if the National Research Ethics Board subsequently becomes aware that grounds for a refusal pursuant to Section 5 existed at the time; it shall be withdrawn if the National Research Ethics Board becomes aware of the fact that subsequently:
    a. The requirements regarding the suitability of the investigator, his or her deputy or the trial site are no longer fulfilled,
    b. In case of trials on human beings the clinical trial participants are no longer properly insured or the prerequisites for an exception to the insurance obligation no longer exist,
    c. The modalities for selecting trial participants no longer correspond to the current state of medical knowledge and, especially, the clinical trial is unsuitable for providing proof of the safety or the efficacy of the investigational medicinal product(s), or
    d. The prerequisites for the inclusion of persons pursuant to Section 1 and 2 are no longer fulfilled. The NREB shall inform the Authority through a written communication.
7. If the Authority, in the context of its activities, becomes aware of facts which justify the assumption that one or any of the investigators or the sponsor or a sponsor's representative no longer fulfils his/her obligations with regard to the proper conduct of the clinical trial, the Authority shall immediately inform said person thereof. The Authority shall order remedial measures to be taken by this person.

Section 7: Inspection of Clinical Trials

1. The Authority shall inspect a clinical trial to ensure that:
    a. Adequate protection of the general public against the risks of adverse events related to the clinical trial of an investigational medicinal product(s) is ensured; and
    b. That the specific and general conditions subject to which the trial was authorized are being strictly adhered to by the Principal Investigator and

Sponsor, including sponsor's representatives.

2. The Authority may:
   a. Request additional information;
   b. Inspect any resources that are deemed by the Authority to be related to the clinical trial and that may be located at the site of the trial, at the sponsor´s and/or contract research organization´s facilities, or at other establishments deemed appropriate by the Authority;
   c. Suspend or stop a clinical trial; or
   d. Withdraw the authorization to conduct a clinical trial, if the Authority is of the opinion that the safety of the trial participants in the trial may be compromised, that the scientific reasons for conducting the trial have changed, or if the integrity of the data is compromised.
3. The National Research Ethics Board representatives may accompany the Authority in the conduct of inspections of clinical trial sites or may choose to do it independently.

Inspection of CRO

Section 8:

Notification of Serious Adverse Events

1. The Principal Investigator/ Sponsor must report any serious adverse events/ serious adverse drug reactions which occurred in Liberia to the Authority and National Research Ethics Board as soon as possible but not later than 3 calendar days of occurrence of the said event, to the Authority and the National Research Ethics Board. See definitions of serious adverse events supra. However, in the case of death, all SAEs must be reported within 24hrs.
2. The Principal Investigator must inform the Authority and the National Research Ethics Board of any adverse events as part of the end of study report.
3. The Principal Investigator must submit to the Authority and the National Research Ethics Board all safety updates as determined by the Authority and the National Research Ethics Board.
4. In case of multi center trials (In and out of Liberia) the PI must submit all serious adverse events/ serious adverse drug reactions as well as safety update report to the Authority and the NREB.

Section 9: Clinical Trial Reports

1. The Authority must be informed in writing on the exact date of commencement of a clinical trial, i.e. first patient first visit, by the applicant.
2. If the trial does not begin within 90 calendar days from issuance of the Clinical Trial Certificate, the applicant must show cause for the failure to commence as scheduled and solicit issuance of a new Clinical Trial Certificate.
3. Failure to inform the Authority of the commencement or not starting the clinical trial within this period shall have regulatory implications including but not limited to the payment of administrative charges for the re-issuance of the clinical trial certificate on its expiration.
4. The applicant must submit to the Authority and NREB progress reports containing safety updates and duly signed and authenticated Data and Safety Monitoring Board reports, as specified in the corresponding clinical trial guidelines.
5. The applicant must submit to the Authority and NREB a final clinical trial summary report as required by the Authority and the National Research Ethics Board.

6. If the trial is suspended or terminated before its purpose is achieved, the applicant must convey the reason(s) in writing to the Authority and the National Research Ethics Board within 10 working days and all information shall be provided as determined by the Authority.
7. The applicant must notify the Authority and the National Research Ethics Board in writing, not later than 30 calendar days after the completion of a clinical trial.
8. A close-out report on the clinical trial including a copy of the disposal certificate issued by the Authority must be submitted to the Authority after study completion in the recommended format as required by the Authority.
9. The applicant must, not later than 1 year after the completion of the trial, compile and submit to the Authority and the National Research and Ethics Board a comprehensive end-of-study report conforming to the ICH E3 Guideline as revised and other requirements as determined by the Authority.

CHAPTER III OFFENSES AND PENALTIES

ADMINISTRATIVE SANCTIONS

1. Any person(s), institution(s), Corporate Entity(ies), their Designees or legal representatives who cause or takes any action or any failure to act that violates Chapter II Sections 5 and 8 of this regulation, shall be liable to pay a fine of not less than Five Thousand United States Dollars (US $ 5,000) and not more than Ten Thousand United States Dollars (US $10,000) or be subjected to other administrative actions such as revocation or suspension of study until all procedures and processes as required by sections 5 and 8 are fully complied with.

2. Failure to inform the Authority of the commencement of a clinical trial and failure to act within the specified period approved shall have regulatory implications including but not limited to the payment of administrative charges for the re-issuance of the clinical trial certificate on its expiration.

3. Any person(s), institution(s), Corporate Entity(ies), their Designees or legal representatives who in wanton disregard of the provisions of section 6, violates section 6 count 5, shall be liable to pay a fine of ten Thousand United States Dollars (US $10,000)

4. Any person(s), institution(s), Corporate Entity(ies), their Designees or legal representatives who is found in violation of any provision of section 4 shall be liable to fines as prescribes by the Authority at the time of commission.

CIVIL LIABILITY

1. **Any Serious Adverse Event/Serious Adverse Drug Reaction** that is life-threatening or results in persistent or significant disability/ incapacity, congenital anomaly/birth defect during the conduct of a clinical trial, subjects the principal investigator or organization to an action of damages.

CRIMINAL PENALTY

1. Any person(s), institution(s), Corporate Entity(ies), their Designees or legal representatives who contravenes Chapter II Section 1(7) c commits a misdemeanour of the first degree.

2. Any serious adverse events that results in the death of a participant during the conduct of a clinical trial shall constitute negligent homicide consistent with **section 14.3 of the Penal Law of Liberia which provides that "**A person is guilty of negligent homicide if he causes the death of another human being negligently. Negligent homicide is a felony of the third degree."

CHAPTER IV: FEES

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The following Non-Refundable fees shall apply for Clinical Trials Applications:

S/N	Category	Rates (US$)
1	Industry Funded (Phase I)	25,000.00
2	Industry Funded (Phase II)	20,000.00
3	Industry Funded (Phase III)	15,000.00
4	Clinical Research Organization (CRO) Funded Phase I	10,000.00
5	Clinical Research Organization (CRO) Funded Phase II	8,000.00
6	Clinical Research Organization (CRO) Funded Phase III	6,000.00
7	Investigator/Local Phases 3&4	2,500.00
8	Academic Research Trial (Individual)	2,000.00
9	Amendment (Substantial) to Clinical Trial Protocol	1,000.00
	administrative charges	500.00
	MTA fees	1,500.00
	GCP Inspections	1,000.00

Section 12: Miscellaneous

The Authority shall develop guidelines on special provisions for non-interventional clinical studies, as applicable.

This Regulation shall take effect immediately upon the approval of the chairman of the Board of Directors.

A Regulation for Clinical Trials in Liberia is Hereby Promulgated and Submitted for Approval to the Board of Directors on This 29th Day of January A. D. 2025 by the Managing Director of the Authority.

Hon. Luke L. Bawo
Managing Director / LMHRA

A Regulation for Clinical Trials in Liberia is Hereby Submitted to the Chairman of the Board of Directors for Approval.

Approved This 29th Day of January A. D. 2025

Dr. David Sumo
Chairman / Board of Directors