	TITLE: GUIDELINES FOR APPLICATION AND AUTHORISATION OF CLINICAL TRIALS OF MEDICINES, VACCINES, MEDICAL DEVICES AND FOOD SUPPLEMENTS IN SIERRA LEONE	
Rev No: 01	**Doc No: PBSL/GL/002**	Version: 02
Issue date: 15 Feb 2021	**Effective date: 17 Feb 2021**	Approved by: Registrar

PHARMACY BOARD OF SIERRA LEONE
PMB 322
CENTRAL MEDICAL STORES COMPOUND
NEW ENGLAND VILLE
FREETOWN

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1.0 INTRODUCTION

In pursuance of Pharmacy Board of Sierra Leone Regulation on Clinical Trials in humans, these Guidelines are hereby made by the Pharmacy Board of Sierra Leone (PBSL) to define the general norms and scientific principles and to set applicable standards for the conduct, performance and control of clinical trials in human beings in Sierra Leone particularly in relation to granting of marketing authorization. It applies to clinical development of investigational medical products and health products falling under the mandate of the Pharmacy Board of Sierra Leone as the competent Authority in charge of clinical trials. They do not cover veterinary trials.

2.0 OBJECTIVES

These guidelines seek to ensure that clinical trials conducted in Sierra Leone are designed and conducted according to sound scientific principles and ethical standards within the framework of good clinical practice. Compliance with this guideline provides the public with assurance that the rights, safety and wellbeing of trial participants are protected.

3.0 SCOPE

These Guidelines cover the regulatory requirements for authorization of clinical trials in Sierra Leone. It also covers all stages of clinical development of investigational medical products and compassionate use of investigational medical products whether as an interventional or non-interventional study 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 medicinal products.

4.0 ABBREVIATIONS AND GLOSSARY

The definitions below apply specifically to the terms used in this guideline:

"Adult" A person who is eighteen (18) years of age or over that age.

"Adverse Drug Reaction (ADR)" 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.
Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function (see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

"Adverse Event (AE)" Any undesirable experience occurring to a subject during a clinical trial, whether or not considered related to the investigational product(s). An unexpected AE is an experience not reported in the current Investigators Brochure or elsewhere.

"Amendment" is 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, e.g: Protocol amendment is a written description of a change(s) to or formal clarification of a protocol.

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

"Approval(s)" The affirmative decision of the appropriate institutions (Regulatory authority(ies), IRB/IEC) that the clinical trial has been reviewed and may be conducted at the institution site within the constraints set forth by the appropriate institutions, Good Clinical Practice (GCP), and the applicable regulatory requirements.

"Assent" A process by which a child, who is capable of understanding voluntarily, confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the child's decision to participate. Assent is documented by means of a written, signed and dated assent form from the child. As part of the assent process, parents and guardians must give informed consent.

Assisted review – The same approach may be used on a case by case basis to assist a single country in the review of a CTA that complies with the criteria under Section 6.

"Audit" A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analyzed and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

"Auditor" A person who carries out an audit.

"Audit Certificate" A declaration of confirmation by the auditor that an audit has taken place.

"Audit Report" A written evaluation by the sponsor's auditor of the results of the audit.

"Audit Trail" Documentation that allows reconstruction of the course of events.

"Biological Specimen/Sample" means materials derived from various animal and human sources (ranging from fluids like blood, tissues and cells) used to treat and prevent diseases.

"Blinding/Masking" A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the subject(s) being unaware, and double-blinding usually
refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

"Case Report Form" A printed, optical or electronic document designed to record all of the protocol required information. There should be assurance of accurate input and presentation and it should allow verification.

"Certificate of Analysis (COA)" An authenticated document issued by an appropriate authority that certifies the quality and purity of pharmaceuticals, and animal and plant products.

"Child/Minor" A person who is below eighteen (18) years of age.

"Clinical Trial Site" The location(s) where trial-related activities are actually conducted.

"Clinical Study" is medical research involving people. There are two types: non-interventional clinical studies (e.g. observational studies) and clinical trials.

"Clinical Trial" Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic 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" is 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 (see the International Council on Harmonization E3 Guideline for Structure and Content of Clinical Study Reports).

"Clinical Trials Technical Advisory Committee (CT-TAC)" As established by the clinical trial regulation 2019.

"Compassionate use" means access to unregistered medical products in special or emergency situations. In general, either the patient has a severe or life-threatening illness and existing therapy has failed, or the disease is a rare one for which specialist medicines do not have a local marketing authorization. The medical products are still experimental, or at any rate unproven, and the government is not obliged to fund their supply.

"Contract Research Organization (CRO)" A scientific body (commercial or academic) contracted by a Sponsor to perform some of the Sponsors trial related duties and function

"Data Safety Monitoring Board (DSMB)" An independent data-monitoring committee that may be established by the Sponsor to assess at intervals the progress of a clinical, the safety data, and the critical efficacy endpoints, and to recommend to the Sponsor whether to continue, modify, or stop a trial.

"Date of Commencement" For the purpose of the Clinical Trial Certificate and Quarterly Progress Report Form, this is defined as the date when the clinical trial site shall start to enroll participants in the clinical trial.

"Drug/Medicine" includes as per the Pharmacy and Drugs Act 2001 means any substance or preparation used or intended to be used for internal or external application to the human or animal body either in the treatment or prevention of disease or for improving physiological functions and it includes nutritional agents and cosmetics.

"PBSL" means Pharmacy Board of Sierra Leone

"Good Clinical Practice (GCP)" is a standard for the design, conduct, performance, monitoring, auditing, recording, analyses, 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 participants are protected.

"Good Clinical Practice (GCP) Inspection" The act by regulatory authority(ies) or PBSL of conducting an official review of documents, facilities, records and any other resources that are deemed 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 (CRO's) facilities, or at other establishments deemed appropriate.

"Good Manufacturing Practice (GMP)" The part of pharmaceutical quality assurance which ensures that products are consistently produced and controlled to quality standards appropriate to their intended use and as required by the marketing authorization.

"Herbal Medicinal Product" Includes plant-derived material preparations with therapeutic or any other human health benefits which contain raw or processed ingredients from one or more plants and materials or organic or animal origin.

"Independent ethics Committee"An independent body (a review board or a committee, institutional, regional, national, or supranational), constituted of medical professionals and non-medical members, whose responsibility it is to ensure the protection of the rights, safety and well-being of human participants involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving / providing favourable opinion 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 participants. In Sierra Leone this function is fulfilled by the Sierra Leone Ethics and Scientific Review Committee

"Investigational Medical Product" A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial including a product with a marketing authorization when used or assembled 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's Brochure" is 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 participants.

Joint review – The AVAREF joint review process brings experts from the NRAs and ECs of two or more countries, together with the sponsor, as well as external experts that serve to guide and support the NRAs and ECs of the target countries of the CTAs to review a common CTA submitted by a sponsor. Countries may also be invited as

observers to benefit from the knowledge and experience of other regulators and ECs towards building their capacity.

"Legal representative" The name given to describe the executor, administrator or the person who looks after another person's affairs.

"Local Monitor" A person appointed by the Sponsor or CRO to oversee the progress of a clinical trial and of ensuring that it is conducted, recorded and reported in accordance with the SOPs, GCP and the applicable regulatory requirements.

"Lot Release Certificate (LRC)" An official document that authorizes the manufacturer to release a specific lot of a product.

"Medical products" include medicines, vaccines, diagnostics and medical devices.

"Medical Device" An instrument, apparatus, implement, a medical equipment, machine, contrivance, implant, in vitro reagent or any other similar or related article, including a component, part or an accessory which is:

a. recognized in the official natural formulary or pharmacopoeia or a supplement to them, or
b. intended for use in the diagnosis of a disease or any other condition, or in the cure, mitigation, treatment or prevention of disease in humans and animals, or
c. intended to affect the structure or a function of the body of the human being or other animal and which does not achieve any of its principal intended purposes through chemical action within the body of the human being or any other animal and which is not dependent on being metabolized for the achievement of any of its principal intended purposes.

"Medicine" means any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in: -

a) the diagnosis, treatment, mitigation, modification or prevention of disease, abnormal physical or mental state or the symptoms thereof in humans; or

b) restoring, correcting or modifying any somatic or psychic or organic function in humans, and includes any veterinary medicine;

"NMRA" means National Medicines Regulatory Authority

"PBSL" means Pharmacy Board of Sierra Leone

"Placebo" A medication with no active ingredients or a procedure without any medical benefit.

"Investigator" is 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.

"Protocol Amendment/ Clinical Trial Application" A written description of a change(s) to or formal clarification of a clinical trial application/protocol.

"Protocol" is a document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guideline the term protocol refers to protocol and protocol amendments.

"Research Institution" Any public or private entity, agency, medical or dental facility where clinical trials are conducted.

"Serious Adverse Event (SAE)" means any untoward medical occurrence that at any dose results in death, is life threatening, requires inpatient hospitalization or

prolongation of existing hospitalization, results in persistent or significant disability/incapacity or is a congenital anomaly/birth defect.

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

"Sponsor's Medical Expert (Medical Monitor)" An Employee of the sponsor (or CRO) who is readily available to advise on trial-related medical questions or problems. If necessary, outside consultant(s) may be appointed for this person.

"Study Pharmacist" A registered pharmacist appointed by the Sponsor/Principal Investigator to ensure the proper management of pharmaceutical investigational products to be used in the study.

"Sub investigator" Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows). See also Investigator.

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

"Vaccine" A biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism, and is often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins. The agent
stimulates the body's immune system to recognize agent as foreign, destroy it, and the "remember" it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters.

"Vulnerable population" An individual whose willingness to volunteer in a clinical trial may be unduly influenced by the expectations, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are pregnant women, cognitively impaired subjects, children and prisoners. Research concerning vulnerable population should be conducted in line with applicable regulatory requirement(s).

5.0 REQUIREMENTS

5.1 Clinical Trial Application

A Clinical Trial Application made to the PBSL for the conduct of a clinical trial shall be accompanied by the following and contains the following information:

1. Covering Letter
2. A non-refundable Application Fee prescribed by the PBSL (see appendix I)
3. A Clinical Trial Protocol
4. Completed Application Forms for Conducting Clinical Trials signed by authorized persons (see appendix II)
5. A proof of registration with PACTR or an internationally recognized online registry approved by the Agency as in the case of non-interventional clinical studies;
6. Investigator's Brochure
7. 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 Sierra Leone;
8. A list of the planned clinical trial sites and the planned number of trial participants at the sites
9. The name and position of the principal investigators who will be responsible for the sites where the trial is to be conducted and who shall be-

- Registered with the relevant statutory health council, where applicable; and
- Resident in Sierra Leone;

10. Description of the qualification of all investigators and pharmacists in current curriculum vitae and other relevant documents;
11. Proof of current training in Good Clinical Practice of all investigators, pharmacists and monitors.
12. Any previous training in the principles of good clinical practice or experience obtained from work with clinical trials and patient care;
13. Any conditions, such as economic interests and institutional affiliations that might influence the impartiality of the investigators:
14. In the case of trials involving human participants, proof of current, relevant and appropriate study insurance for all participants undertaken by the sponsor; or
15. Proof of Sponsor Indemnification for Investigators and trial sites
16. Professional indemnity insurance for investigators and other trial staff;
17. 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 medical 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;
18. The favourable opinion of the Sierra Leone Ethics and Scientific Review Committee (SLESRC) and in case of parallel submission proof of submission of the clinical trial application to the Sierra Leone Ethics and Scientific Review Committee and the updated versions of documents or information as requested by the Sierra Leone Ethics and Scientific Review Committee;
19. Recruitment arrangements;
20. Financial Declaration of the Trial

21. DSMB membership, CVs and signed charter
22. Investigational Medicinal Product (IMP) dossier
23. Label of the investigational medical products (IMPs);
24. Current GMP certificate issued from the National Regulatory Authority of the country where the investigational medical product is manufacture
25. Certificate(s) of Analysis
26. Participant information sheet, informed consent form, and informed consent procedure for human trials
27. Sponsor/PI Contractual Agreement including the study budget
28. Signed declaration by the Principal Investigator and the Sponsor of the trial that they are familiar with and understand the protocol and will comply with Good Clinical Practice as determined by the Agency in the conduct of the trial;
29. CVs and signed Declaration by local Monitors
30. Workload Forms for Investigators

Forms on declaration of PI and sub-investigator as well as the form on joint financial declaration by sponsor and PI can be found in appendix IIIa – IIIc. All clinical trial application documents shall be submitted in hard and soft copies (15 hard copies and 1 soft each; format of soft copy of documents submitted should be in MS-word which is usually the acceptable format, although Acrobat PDF files are also acceptable).

a) **N.B. PBSL does not screen for the following:**

- Insurance certificate
- Financial declaration
- GMP Certificate
- Drug product labels

b) Failure of applicant to address all outstanding issues related to an application within a year renders an application null and void

c) The application shall indicate the phase of clinical trial that is intended; see Appendix IV of these Guidelines.

5.1.1 Cover Letter

Application should be addressed to the Registrar, Pharmacy Board of Sierra Leone

5.1.2 Application Fees

An application shall be accompanied by a non-refundable application fee as specified in the PBSL fee schedule.

5.1.3 Application Form to Conduct a Clinical Trial

Two (2) copies of completed application forms (Appendix II) signed by all sponsor or sponsor's authorized person shall contain at least the following as stipulated in the application form:

5.1.3.1. General information
5.1.3.2. Trial details
5.1.3.3 Regulatory details
5.1.3.4 Sponsor details
5.1.3.5 Applicant's details
5.1.3.6 Investigator's details
5.1.3.7 Study pharmacist details
5.1.3.8 Monitor's details
5.1.3.9 Study manager/coordinator details
5.1.3.10 Trial site details
5.1.3.11. Investigational product details
5.1.3.12. Medical condition or disease under investigation details

5.1.3.13. Type of trial
5.1.3.14. Scope of trial
5.1.3.15. Recruitment and duration of trial
5.1.3.16. Current workload of investigator(s).

The annexes to the application form can be obtained on PBSL website.

5.1.4 Clinical Trial Protocol and Trial Amendment

For the content and structure of the clinical trial protocol and clinical trial protocol amendment please refer to PBSL GCP section 6 and ICH-GCP E6 section 6: clinical trial protocol and trial amendment, as revised.

5.1.5 Clinical Trial Application/Protocol amendments

5.1.5.1 Any proposed amendment to the trial application, trial arrangements and investigational product shall be submitted to the SLESRC that originally approved the protocol and the PBSL for approval by these bodies before such amendments are carried out.

5.1.5.2 The amendments shall be described in a completed CT Amendment Form (Appendix V).

5.1.5.3. All amendments shall attract a fee which shall be determined by PBSL (Appendix I).

5.1.5.4 The sponsor may make amendments to the application after the commencement of the clinical trial. If those amendments are substantial and are likely to have an impact on the safety of the trial participants or to change the interpretation of the scientific documents in support of the conduct of the trial, the sponsor shall notify PBSL of the reasons for, and content of, these amendments.

5.1.5.5 The notion of "amendment"

The following changes do not count as an 'amendment':

i. A change to the documentation submitted to PBSL during the ongoing assessment of the request for authorization, and

ii. A change to the documentation submitted to the SLESRC during the ongoing assessment of the request for authorization.

iii. Safety report (SR) is not per se an amendment and thus does not have to be notified as a substantial amendment. However, the sponsor has to verify whether the data presented in the SR requires a change to the documentation submitted with the request for authorization of a clinical trial. If this amendment is

substantial, the rules for notification of substantial amendments apply to these changes.

iv. A change of the contact person or in the contact details of the contact person (e.g. a change of e-mail or postal address) is not considered as an amendment, if the sponsor and legal representative remain identical. However, the sponsor should ensure that the PBSL is aware of this change as soon as possible, in order to allow its supervisory function.

5.1.5.6. The notion of "substantial"

i. Amendments to the trial are regarded as 'substantial' where they are likely to have a significant impact on:

a. the safety or physical or mental integrity of the clinical trial participants, or

b. the scientific value of the trial.

ii. In all cases, an amendment is only to be regarded as 'substantial' when one or both of the above criteria are met.

iii. The responsibility of assessing whether an amendment is regarded as substantial or not lies with the sponsor.

iv. The PBSL shall however recommend a reassessment of a Sponsor's classification of an amendment when necessary.

v. The annual update of the IB is not per se a substantial amendment. However, the sponsor has to verify whether the update relates to changes which are to be considered as substantial. In that case, the rules for notification of substantial amendments apply to the change.

vi. The sponsor should assess also whether the combination of substantial amendments lead to changes of the clinical trial to an extent that it has to be considered as a completely new clinical trial, which would then be subject to a new authorization procedure.

vii. Substantial amendments may relate to information relevant for assessment by the PBSL, the SLESRC, or both.

viii. Without prejudice to the above points, the PBSL reserves the right to direct for an amendment to the protocol.

5.1.5.7 Format and content of notification

The notification of a substantial amendment should include the following:

i. A signed cover letter, including a highlighted indication of any special issues related to the amendment and indication where the relevant information or text is in the original application dossier and rationale for the amendment

ii. A description of the amendment:

a. an extract from the amended documents showing previous and new wording in track changes, as well as the extract only showing the new wording;

b. notwithstanding the previous point, if the changes are so widespread or far-reaching that they justify an entire new version of the document should be

provided. In this case, an additional table should list the amendments to the documents. In this list, identical changes can be grouped.

c. The new version should be identified with the date and an updated version number.

iii. Supporting information including, where applicable:

a. summaries of data,
b. an updated overall risk/benefit assessment,
c. possible consequences for participants already included in the trial,
d. possible consequences for the evaluation of the results.

5.1.6 Investigator's Brochure

For the content and structure of the Investigator brochure, please refer to PBSL GCP section 7 and ICH-GCP E6 section 7: investigator brochure, as revised.

An updated investigator's brochure should be submitted at least once a year, or whenever it is updated within this period. Additional information and any changes that have been incorporated in the updated investigator's brochure should be highlighted for ease of review and evaluation.

5.1.7 Sierra Leone Ethics and Scientific Review Approval

5.1.7.1. Ethical Clearance for all phases of clinical trials in humans shall be sought from the SLESRC in the conduct of clinical trials in Sierra Leone.
5.1.7.2. Submissions to the PBSL and the SLESRC can be done in parallel in case of a public health emergency or as deemed fit by PBSL.
5.1.7.3. Original copy of approval letter/certificate from SLESRC shall be required.

5.1.8 Insurance Cover

5.1.8.1. All subjects must be satisfactorily insured against possible injuries that might arise during the conduct of the clinical trial.
5.1.8.2. For all Sponsor-initiated trials, a valid insurance certificate for the duration of the study must be provided prior to study initiation.
5.1.8.3. The sponsor shall provide insurance or should indemnify (legal and financial coverage) the investigator/the institution and trial site against claims arising from the trial, except for claims that arise from malpractice and/or negligence.

5.1.8.4. Sponsors and Principal Investigators shall ensure insurance cover for clinical trial participants and shall submit as evidence a Certificate of insurance cover for participants. The certificate shall at least contain:
1. Insurance company
2. Policy number
3. Initial Date
4. Expiry Date
5. Insured (Policy Holder/Sponsor)
6. Description of activity (purpose of the policy)

5.1.9 Financial Declaration

5.1.9.1. The financial aspects of the trial shall be documented in an agreement between the Sponsor and the Principal Investigator/Contracted Research Organization/Institution.
5.1.9.2. A declaration must be signed by both the Sponsor and the Principal Investigator which states that there are sufficient funds available to complete the study.

5.1.10 Data Safety Monitoring Board/Committee (DSMB/C) or Independent Data-Monitoring Committee (IDMC) or Data Monitoring Committee (DMC)

5.1.10.1. An independent data-monitoring committee (IDMC) shall 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.
5.1.10.2. For trials conducted in Sierra Leone, at least one member of the IDMC must be a Sierra Leonean.
5.1.10.3. The Sponsor shall include charter of work, membership and curriculum vitae of the IDMC member.
5.1.10.4. All members of the DSMB/IDMC/DMC shall sign the charter
5.1.10.5. A DSMB/IDMC/DMC Charter shall include:
1. Terms of Reference
2. Membership and their CVs
3. Proof of Independence of the Committee
4. Scope of work for Members/responsibilities of the Committee which is to assess the progress of a clinical trial including safety data and the critical efficacy endpoints at intervals, and to recommend to the sponsor whether to continue, modify, or stop a trial.
5. Meeting schedules
6. Standard Operating Procedures of the Committee

5.1.11 Investigational Medicinal Product Dossier (IMPD)/ Chemistry Manufacturing and Control (CMC) Dosssier

The IMPD gives information related to the quality of any IMP (i.e. including reference product and placebo), chemistry, manufacture and control of the IMP, and data from nonclinical studies and from its clinical use. However, in

many cases where the IP has a marketing authorization, an IMPD is not required. However, a detailed monograph of the product is required when a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorization but:

1. used or assembled (formulated or packaged) in a way different from the authorised form, or
2. when used for an unauthorised indication, or
3. when used to gain further information about the authorised form.

Refer to Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials (EMA/CHMP/QWP/834816/2015) for more details.

5.1.12 Proof of Registration of the Clinical Trial

Proof of registration of the trial with the Pan African Clinical Trials Registry (PACTR) shall be submitted as part of a Clinical Trial application. However, in the case of non-interventional clinical studies registration in another internationally recognized online registry might be acceptable as approved by the Agency.

5.1.13 Sponsor/PI Contractual Agreement

The Sponsor/PI Contractual Agreement shall indicate;

5.1.13.1. The study title
5.1.13.2. Protocol version and date
5.1.13.3. Trial site
5.1.13.4. Investigational Product

5.1.13.5. Definitions of all terms
5.1.13.6. Effective date of agreement
5.1.13.7. Outline of the Sponsor's responsibilities which shall include
1. General management of the trial
2. Provision of adequate funding, resources/logistics and Investigational Products for the study
3. Insurance for the study participants
5.1.13.8. Outline of the PI's responsibilities which shall include
1. conduct the trial in compliance with GCP, with the applicable regulatory requirement(s), and with the protocol agreed to by the sponsor and given approval/favourable opinion by the SLESRC and The Board
2. comply with procedures for data recording/reporting
3. permit monitoring, auditing and inspection
4. retain all trial related essential documents until the sponsor informs the PI these documents are no longer needed
5.1.13.9. Term (period of study duration) and Termination of agreement (conditions for this)
5.1.13.10. Confidentiality
5.1.13.11. The Sponsor and the PI shall sign this agreement and the protocol.

5.1.14 Informed Consent and Assent

5.1.14.1. The informed consent discussion and the written informed consent form and any other written information to be provided to participants shall include explanations of the following;
1. That the trial involves research
2. The purpose of the trial
3. The trial treatment(s) and the probability for random assignment to each treatment
4. The trial procedures to be followed, including all invasive procedures.

5. The participant's responsibilities.
6. Those aspects of the trial that are experimental, etc
7. Signature and date of participant, participant's legal representative, impartial witness (where applicable) and person administering Informed Consent

Refer to section 4.8.10 of the PBSL GCP Guidelines for more details

5.1.14.2. In trials involving minors, parents/guardians of a minor shall be required to sign an Informed Consent form as above. In addition, an assent form similar to the Informed Consent Form shall also be signed and dated by a minor who is capable of understanding as a confirmation of his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the minor's decision to participate.

5.1.15 Statistical Analysis Plan (SAP)

A SAP for the study shall be submitted with the Clinical Trial Application or before datalock.

5.1.16 GMP Certificate

A current GMP certificate from the national competent authority of the country of origin shall be required when the IMP has no marketing authorization in Sierra Leone or has marketing authorization but its original indication is modified for the purpose of the trial. GMP certificate should conform to WHO format.

5.2 Responsibilities of Sponsors and Investigators

Sponsors and Principal Investigators shall have as their primary concern the protection of the life, health, privacy and dignity of the patients or healthy volunteers who participate in such trials.

5.2.1 Sponsor

Submission to PBSL for approval: Before initiating a clinical trial(s) in Sierra Leone, the Sponsor and the Principal Investigator must obtain approval from PBSL before commencement of the trial(s). The responsibility of the sponsor is specified in section 5 of the PBSL and the ICH GCP guidelines as revised

5.2.2 Investigator

A qualified medical or pharmaceutical practitioner (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions. The responsibilities of the investigator are specified in section 4 of the PBSL and the ICH GCP guideline as revised.

5.2.3 Qualification of Principal Investigators

Principal Investigator(s) directly in charge of a trial and at each site in a multi-centre trial shall be in good standing with the Pharmacy Board of Sierra Leone and the Sierra Leone Medical and Dental Council, conform with all applicable regulatory requirements and should be responsible for the proper conduct of the trial and must;

5.2.3.1. Be a Scientist and domicile in Sierra Leone in the country where the trial will be conducted.
5.2.3.2. The Principal Investigator must be an appropriately qualified and competent person having practical experience within the relevant professional area
5.2.3.3. Be sufficiently experienced in clinical and pharmaceutical evaluation of medicinal products and must have had previous experience as a co-investigator in at least two trials in the relevant professional area.
5.2.3.4. Have evidence of Good Clinical Practice training not less than 2 years
5.2.3.5. Provide evidence of such qualifications specified by the applicable regulatory requirement(s) .
5.2.3.7. A Veterinary Surgeon may be the Principal Investigator or clinician for veterinary studies.

5.3 Qualifications of Study Pharmacist

5.3.1. Must be a registered pharmacist in Sierra Leone where the clinical trial will be conducted.
5.3.2. Must be in good standing with the Pharmaceutical Society of Sierra Leone.
5.3.3. Have adequate knowledge in use of the Investigational Medicinal Product(s)
5.3.4. Must have evidence of Good Clinical Practice training within the last 2 years.

5.4 Qualifications of Local Monitor

5.4.1. Must be a scientist qualified by education, training and experience
5.4.2. Excellent knowledge in PBSL local regulatory requirements
5.4.3. Must have evidence of Good Clinical Practice training within the last 2 years

5.4.4. Must be a resident professional in Sierra Leone where the clinical trial is will be conducted

5.5 Qualifications of Study physician, Study Coordinator/Manager, Laboratory Manager, Data Manager, Regulatory Affairs Lead

5.5.1. Must be a scientist qualified by education, training and experience
5.5.2. Excellent knowledge in PBSL local regulatory requirements
5.5.3. Must have evidence of Good Clinical Practice training within the last 2 years.
5.5.4. Must be a resident professional in Sierra Leone where the clinical trial is will be conducted

5.6 Responsibilities of Pharmacy Board of Sierra Leone

5.6.1. PBSL shall approve a clinical trial by issuing a Clinical Trial Certificate in a format as may be prescribed for the initiation and conduct of clinical trials in Sierra Leone. The approval process shall involve establishing adequate procedures and / or requirement for review of the clinical trial application. Protocol revisions whenever it deems necessary.

5.6.2. Application may be withdrawn at the discretion of the sponsor

5.6.3. A Clinical Trial Certificate shall be renewed annually. An application for renewal shall be submitted to PBSL and should include the documents listed in section 3.1 of this guideline. A Clinical Trial Certificate issued shall be revoked if conditions for which the certificate was issued are violated.

5.6.4 A person conducting the clinical trial shall be ordered to stop or suspend the trial immediately if at any stage during the conduct of a clinical trial the PBSL is satisfied that it is in the public interest to do so.

5.6.5. PBSL shall monitor a clinical trial from the beginning to the end in order to ensure adequate protection of the general public against the risk or adverse events from authorized clinical trials. This is to satisfy itself that the specific and general conditions to which the trial was authorized are being strictly adhered to by the person(s) conducting the trial and that the trial will achieve its objectives.

5.6.6. The PBSL shall conduct on-site inspections of clinical trial site, sponsor or manufacturing facilities to ensure:
5.5.6.1. the safety of clinical trial participants,
5.5.6.2. the quality and reliability of data obtained in a trial, and
5.5.6.3. the facilities used continue to be acceptable throughout the clinical investigation

5.6.7. The PBSL shall establish an Expert Committee on Pharmacovigilance and Clinical Trials of the Board to provide support in reviewing and authorizing clinical trials applications and give medical and scientific opinion on issues related to clinical trials and medicines safety.

5.6.8. PBSL shall act as a Secretariat for the Expert Committee on Pharmacovigilance and Clinical Trials that has been established in section 12 of the CT regulation. The Expert Committee on Drug Safety and Clinical Trials shall carry out safety assessment of medicinal products among others things such as providing scientific opinion for clinical trials monitoring by the Board and whose terms of reference shall be:

- ✓ The committee shall review pharmacovigilance or medicine safety information and related data on all pharmaceuticals, biologicals and other regulated products on the Sierra Leone market;
- ✓ upon request, the expert committee will make recommendations to the Board regarding actions the Board may take to resolve issues or concerns related to post-approval product safety, quality and efficacy;
- ✓ the committee will also recommend to the Board appropriate product information labelling update; recall or withdrawal products as may be necessary;
- ✓ regularly review and advise the Board on the clinical trials structure in the country and make recommendations regarding its maintenance and enhancement;
- ✓ perform causality assessment and issue reports on adverse event in relation to clinical trials and also for adverse drug reaction reports from routine clinical care;
- ✓ make recommendations to the Board regarding actions the Board may take to resolve issues or concerns related to the conduct of clinical trials including the need to halt or suspend a clinical trial;
- ✓ recommend publication of case reports, as well as its risk or benefit assessments in medical and scientific journals with prior consent of the sponsor;
- ✓ recommend educational programmes and topics for pharmacovigilance and also for investigators aimed at enhancing reporting of adverse effect or event and improving compliance with Good Clinical Practice as recommended by the International Conference on Harmonization Guidelines and Helsinki Declaration;
- ✓ advise the Board periodically on the review of applications and guidelines for clinical trials, Good Clinical Practice and pharmacovigilance issued by the Board;
- ✓ recommend to the Board approval of clinical trials;
- ✓ evaluate final reports of clinical trials that have been approved by the Board;
- ✓ advise the Board on matters relating to Good Clinical and Laboratory Practice (GCLP) inspections; and
- ✓ perform any other functions that are supplementary to the attainment of the objectives of the Committee.

The membership of the Expert Committee should reflect areas of expertise and specialisation as the case maybe, such as:
1. General Medicine 2. Clinical Pharmacy 3. Clinical Pharmacology 4. Pharmacology/Toxicology 5. Epidemiology 6. Herbal Medicine 7. Pathology 8. Industrial Pharmacy/Quality Control/Quality Assurance 9. Biostatistics 10. Paediatrics/Child Health 11. Public Health

5.7 Reporting and Managing Adverse Events

The Sponsor of a clinical trial and Principal Investigators participating in a clinical trial are responsible for proper reporting of Serious Adverse Events (SAEs) and Adverse Events (AE). The Sponsor should expedite the reporting of all adverse drug events (AEs) that are both serious and unexpected. Reporting should occur within the timeframe and format specified by PBSL (Refer to Appendix VIa).

5.7.1. Any serious adverse event to the investigational product shall receive immediate medical attention and reported to PBSL within forty-eight (48) hours.
5.7.2. The SAE report form (Appendix VIa) shall be completed and detailed information such as laboratory results submitted to enable causality assessment report by the Expert Committee on drug safety and clinical trials of the Board.
5.7.3. All fatal cases shall be accompanied by a formal autopsy report.
5.7.4. In exceptional circumstances where a formal autopsy is not practicable, provision of a verbal autopsy report shall be prior approved by PBSL and shall be given with ample reasons.

Verbal autopsy shall be conducted in line with the World Health Organisation guideline for verbal autopsy. The cause of death shall be classified according to current ICD guideline.

5.7.5. Any adverse event to the investigational product shall receive immediate medical attention and reported to The PBSL within specified timelines.

5.7.6. The Principal Investigator is required to submit follow-up information as soon as it becomes available. Additional information may include copies of diagnostic test results, laboratory reports, or medical record progress notes. All additional information should be clearly marked as update information and should include the Protocol Number and Participant Number.

5.7.7. The Development Safety Update Report (DSUR) shall be submitted annually to PBSL. See PBSL DSUR guideline for more details.

5.7.8. Safety report from foreign sites and other reporting requirements shall be submitted according to appendix VIa - VIc.

5.7.9 All SAEs/SUSARs and AEs/ADRs shall be reported used CIOM 1 form format and also electronically through PBSL Web-based online platform on the PBSL website (Report an adverse reaction-www.pharmacyboard.gov.sl).

5.8 Clinical Trial Reports

5.8.1. Progress Report

5.8.1.1. The PBSL should be informed in writing on the exact date of commencement of the study.

5.8.1.2. Quarterly reports of the progress of a clinical trial starting from the date of issuance of the clinical trial certificate shall be submitted to PBSL within

the recommended timeframe and in the recommended format. (Refer to Appendix VIIa and VIIb).

5.8.1.3. Quarterly progress reports must be submitted to PBSL within 21 days after the end of the previous quarter. A quarter shall be considered as three months beginning from the date of initiation of a specific clinical trial.

5.8.1.4. If the trial does not begin or is delayed as per the date of commencement on the Clinical Trial Certificate issued, The PBSL shall be informed of the new date of commencement within ninety (90) days of issuance of the Clinical Trial Certificate.

5.8.1.5. If the trial is interrupted before its purpose is achieved, the reason shall be conveyed in writing to The PBSL within ten (10) working days. This shall include:

5.8.1.5.1. Justification for the premature ending or of the temporary halt of the trial;

5.8.1.5.2. Number of patients receiving treatment at the time of the study termination;

5.8.1.5.3. Proposed management of patients receiving treatment at the time of halt or study termination;

5.8.1.5.4. Consequences of the evaluation of the results.

5.8.1.6. **An interim report** shall be submitted to PBSL within 21 days after the end of the first half of the trial period and as stipulated in the protocol. An interim period shall be considered as half of the trial period beginning from the date of initiation of a specific clinical trial.

5.8.2. DSMB Report

Duly signed and authenticated DSMB reports and / or minutes shall be forwarded to PBSL upon request.

5.8.3 Close-out report

5.8.3.1. The Principal Investigator/Sponsor shall notify PBSL in writing, not later than 30 days after the completion of a clinical trial

5.8.3.2. A close-out report on the study shall be submitted to PBSL after study completion in the recommended format as per Appendix VIII

5.8.4 Final Report

5.8.4.1. In addition to the report referred to above, the PI/Sponsor shall, not later than 90 days after the completion of the trial, compile and submit to PBSL a comprehensive formal report conforming to the ICH E3 Guideline for the Structure and Content of Clinical Study Reports.

5.8.4.2. The report shall include a short but comprehensive summary of the essential findings of the trial and of its methodology and course.

5.8.4.3. The Final report shall be submitted in hard and soft copies.

5.8.4.4. Publication(s) of the study in a scientific journal or other medium for the purpose of disseminating the information obtained to stakeholders shall be done only after notification of the PBSL.

5.9 Procedure for Importing and handling of Investigational medical products

5.9.1. Approval to import products for clinical trials shall only be granted to recognized clinical research entity whose protocol has been approved by PBSL to conduct clinical trial in accordance with this guideline.

5.9.2. An application for importation of investigational products, placebo, comparator, auxiliary medicinal products shall receive prior approval from the PBSL.

5.9.3. Application to import investigational product and placebo shall be made to PBSL by submitting:

5.9.3.1. Letter stating the quantities of each investigational product, placebo and trial related products to be imported and also details of the location where the product is coming from and details of the recipient in Sierra Leone

5.9.3.2. Certificate of analysis of investigational product and placebo for all batches to be imported

5.9.3.3. Lot Release certificate (where applicable) for all batches to be imported

5.9.4. An application for import and clearance permit shall be processed by the PBSL.

5.9.5. All import permit applications shall bear the full name and address of the investigator, the Sponsor and the recognized clinical research entity, the name/description of the investigational product, placebo, active control and quantities to be imported.

5.9.6. Both the investigational medicinal product, active control and the placebo shall be appropriately labelled with the approved labels to indicate they are samples for the conduct of clinical trials only. Please see appendix IX for more details. The label shall bear the following as the basic information:

- 5.9.6.1. For Clinical Trial purposes ONLY
- 5.9.6.2. Trial name
- 5.9.6.3. Expiry date (if applicable)
- 5.9.6.4. Dosage (if applicable)
- 5.9.8.5. Investigational Product identity number

5.9.7. Products imported may be inspected by officials of PBSL at the port of entry before they are released to the recognized clinical research entity.

5.9.8. The PBSL shall order for destruction or re-exportation of the products intended for clinical trials if it has any reason to believe that there is a protocol violation resulting in the termination of the study.

5.9.9. The above notwithstanding, all other statutes governing importation procedures and tax liabilities in Sierra Leone shall apply to imported products regulated by the PBSL.

5.9.10. The Principal Investigator shall notify PBSL of each consignment of investigational product batches received on site. The notification shall include the following details:

- Name of product(s),
- Quantities received and
- Batches received

5.9.11. PBSL shall approve destruction of investigational medical products that 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 participant numbers involved and the actual quantities destroyed. A destruction certificate shall be issued by the Agency.

5.9.12. In case the Sponsor would like to export the investigational medical product remaining after the clinical trial has been stopped or completed, the sponsor shall obtain an export authorization from the Agency.

5.9.13. For investigational products purchased locally, the Principal Investigator shall document the source, proof of purchase, quantities purchased and Certificate of Analysis for each batch of Investigational Products.

5.9.14. Copies of all documents on investigational products, whether purchased locally or imported shall be kept on site for verification and accountability during GCP inspections.

5.10 Good Clinical Practice Inspections

In accordance with section 7 of the clinical trial regulation PBSL shall conduct GCP inspections. Details on GCP inspection are outlined in the PBSL GCP inspection guideline and PBSL and ICH GCP guidelines as revised.

5.11 Biological specimen/samples

5.11.1. Consent forms for the research protocol should include a separate section for clinical-trial participants who are requested to provide their consent for the use of their biological specimens for research. Separate consent may be appropriate in some cases (e.g., if investigators are requesting permission to conduct basic research which is not a necessary part of the clinical trial), but not in others (e.g., the clinical trial requires the use of subjects' biological materials).

5.11.2. Use of medical records and biological specimens. Medical records and biological specimens taken in the course of clinical care may be used for research without the consent of the patients/subjects only if an ethical review committee has determined that the research poses minimal risk, that the rights or interests of the patients will not be violated, that their privacy and confidentiality or anonymity are assured, and that the research is designed to answer an important question and would be impracticable if the requirement for informed consent were to be imposed. Patients have a right to know that their records or specimens may be used for research. Refusal or reluctance of individuals to agree to participate would not be evidence of impracticability sufficient to warrant waiving informed consent. Records and specimens of individuals who have specifically rejected such uses in the past may be used only in the case of public health emergencies.

5.11.3. Secondary use of research records or biological specimens. Investigators may want to use records or biological specimens that another investigator has used or collected for use, in another institution in the same or another country. This raises the issue of whether the records or specimens contain personal identifiers, or can be linked to such identifiers, and by whom. If informed consent or permission was required to authorize the original collection or use of such records or specimens for research purposes, secondary uses are generally constrained by the conditions specified in the original consent. Consequently, it is essential that the original consent process anticipate, to the extent that this is feasible, any foreseeable plans for future use of the records or specimens for research. Thus, in the original process of seeking informed consent a member of the research team should discuss with, and, when indicated, request the permission of, prospective subjects as to:

i) whether there will or could be any secondary use and, if so, whether such secondary use will be limited with regard to the type of study that may be performed on such materials;

ii) the conditions under which investigators will be required to contact the research subjects for additional authorization for secondary use;

iii) the investigators' plans, if any, to destroy or to strip of personal identifiers the records or specimens; and

iv) the rights of subjects to request destruction or anonymization of biological specimens or of records or parts of records that they might consider particularly sensitive, such as photographs, videotapes or audiotapes.

5.11.4 Requirements for material transfer authorization: All institution or individuals that wants to transport and use any clinical information, medical records and biological samples from Sierra Leone to an institution outside of Sierra Leone fulfill PBSL's requirement for material transfer authorization. All applications shall be authorized and submitted by the local principal

investigator or study lead. See Appendix X for more details and PBSL material transfer agreement template on PBSL's website at www.pharmacyboard.gov.sl

5.11.5 The Sponsor shall provide annual update on the use and results obtained from biological samples exported out of Sierra Leone.

5.12 Phases of Clinical Trials

The application shall indicate the phase of clinical trial that is intended; see Appendix IV of this Guideline.

5.13 Recognition of clinical trials decision or scientific opinion from other NRAs, regional and international bodies

This will be permitted and considered by the Agency, if the investigational medicinal product (IMP) or trial has been authorised by:

(i) ICH founding regulatory members
(ii) ICH standing regulatory members
(iii) ICH regulatory members
(iv) ICH legislative and administrative authorities
(v) the African Vaccine Regulatory Forum (AVAREF) at a joint review meeting facilitated
by the World Health Organization with the provision of a favourable scientific opinion.
(vi) Any other regulatory decision deemed appropriate by the Board

5.14 Regulatory and Scientific considerations for the application and authorization of clinical trials during a public health emergency

A public health emergency may constitute a case of an emerging infection or a request from the President of the Nation or the Minister of Health and Sanitation or a declaration of public health emergency of international concern by the WHO to name but a few.

The Agency can employ regulatory pathways such as (Rolling submission, Expand Access Programme etc) to address issues of accelerating the development of medicinal products needed for life-threatening illnesses, to fill unmet medical needs, and/or for "orphan" indications by permitting special procedures for investigating new medical products. Access to investigational medical products to be used in public health emergencies depend on ensuring the flexibility of the regulatory system to enable rapid review of incoming data as well as a framework for approval for which there may be only limited safety and efficacy data at the time of approval.

5.14.1 Agreeing to Undertake an Expedited Review

If an expedited review of a clinical trial is anticipated, an applicant should inform the Agency in writing, so that a review team may be assembled and plans made to manage the workload as well as interactions with other oversight bodies such as the SLESRC.

5.14.2. Expediting Review Times and Procedures for Regulatory Review of Clinical Trial Applications

Considerations of clinical trial applications under these circumstances shall be in relation with the underlisted PBSL guidelines with some exceptions stated below:

i. Guidelines for Application and Authorization of Clinical Trials of Medical Products (Medicines, Vaccines, Medical Devices and Food Supplements)
ii. Guidelines on Good Clinical Practice
iii. Guideline on Good Clinical Practice Inspection

5.14.2.1. Requirements for submitting a clinical trial application during a public health emergency shall be same as required by PBSL Guideline for application and authorization of clinical trials of medical products
5.14.2.2. To ensure a rapid start of the clinical study, PBSL will conduct simultaneous review, rather than sequential review of the application with the SLESRC.
5.14.2.3. The timelines for processing such applications shall be shortened to 10-20 working days.
5.14.2.4. The Sponsor as part of the application may request a joint review of the application which will be considered by the Agency
5.14.2.5. Applications for the joint review process shall be submitted at least 14 working days before the proposed date of the joint review.
5.14.2.6. The applicant should ensure that the staff involved in this expedited review is devoted entirely to the project covered by the application (during the time of the expedited review) and readily available to rapidly and reliably address all concerns of the regulators, including product, nonclinical, and clinical issues.
5.14.2.7. The Agency shall also request for joint reviews on a case by case basis or request for support from a well-resourced NRA to provide technical support in reviewing the application in agreement with the Sponsor.

5.15. Joint and Assisted Review of Clinical Trial Applications

Joint and assisted reviews by multiple National Regulatory Authorities (NRAs) and Ethics Committees (ECs) are increasingly being used as a platform for accelerating review of clinical trial applications (CTAs).

The Agency can consider an application for joint or assisted review if a candidate medical product of high public health value to countries on the African continent will be considered based on one or more of the following criteria:

- Addresses a neglected tropical disease or other highly prevalent and serious disease (e.g., non-communicable disease - NCD) on the continent
- Addresses an unmet medical need or a significant improvement over available intervention
- Involves a novel technology
- Product that addresses a disease for which the Director General of the World Health Organization has declared a Public Health Emergency of International Concern (PHEIC)
- Responds to request from one or more countries for assistance

Refer to African Vaccine Regulatory Forum (AVAREF) Guideline for joint and assisted reviews of clinical trial applications for information.

5.16 Appeals

5.16.1. Any person or institution who is aggrieved by a regulatory decision of PBSL of not granting authorisation for the conduct of clinical trials may appeal in writing within sixty days to the Agency after receipt of the decision for PBSL to review or reconsider the initial decision.

5.16.2. The affected person or institution shall ensure that the appeal includes the following:

- an appeal letter, dated and signed by the affected person or institution requesting the review
- a copy of the initial decision letter

- any documentation supporting the request and why review is requested

5.16.3. The applicant shall do so by giving grounds for review for each reason given for the rejection of a clinical trial. The grounds for the request shall be based on the information that was submitted in the application.

5.16.4. Upon review of the appeal application, PBSL shall give response in writing of the outcome of the appeal application, which shall include a statement of reasons (i.e. findings, references to evidence and reasons for the decision). The response shall be addressed to the affected person or institution within 90 days after submitting an appeal application.

5.16.5. An affected person or institution may withdraw their request at any time before PBSL convenes and reviews the appeal. Withdrawal of an appeal application should be made in writing to the Agency within ten working days of the initial appeal submission.

5.16.6. If the CT application was rejected, the applicant can appeal which shall be made in writing to the Registrar within sixty (60) days of receipt of the rejection notice.

5.16.7. No information given in a CTA shall be disclosed by the PBSL to a third party except with the written consent of the applicant.

5.17 Clinical Trial Application review and decision process

5.17.1 Timelines as defined per CT Regulation 2019 apply (Please refer to Appendix XI for an overview). During the assessment process, the PBSL may consult international bodies or other Agencies who already assessed the particular CT.

5.17.2The PBSL 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 CTA.

5.17.3 The applicant shall address formal grounds for non-acceptance within 10 working days.

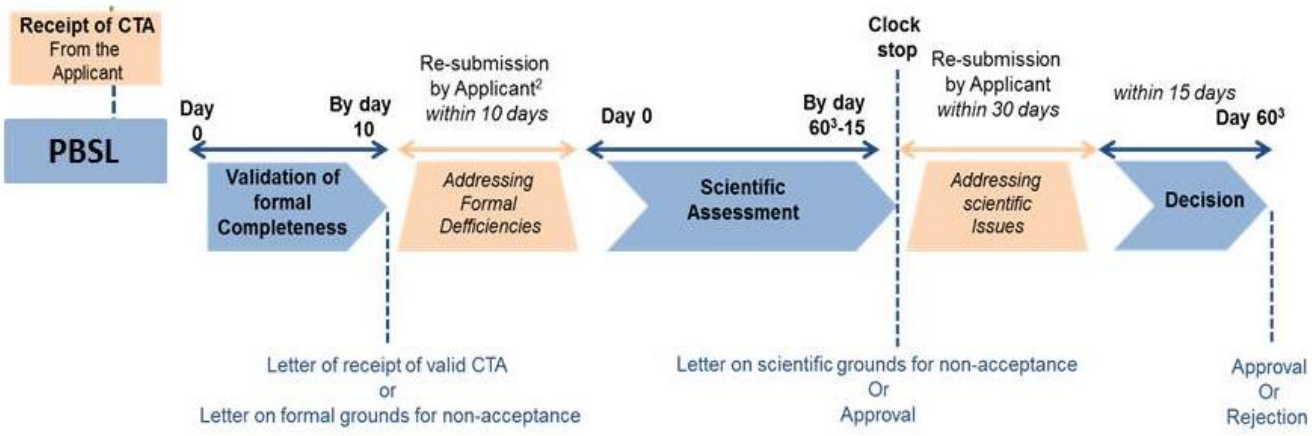
5.17.4 The PBSL shall inform the applicant in writing about the outcome of the assessment of the clinical trial application within a maximum of 60 working days after validation of a formally complete clinical trial application or as defined in Table 1. This excludes time taken for applicant to respond to queries from the Agency.

5.17.5 If changes are required and the applicant fails to modify the application correspondingly within a maximum of 30 working days, following the reasoned objections, the application shall be deemed to be rejected.

5.17.6 During evaluation, additional documents or changes may be requested through a query letter. Once a query has been raised and issued to the applicant, the process stops until when PBSL receives a written response to the query.

5.17.7 If PBSL requires changes to the application and the applicant fails to modify the application correspondingly within a maximum of ninety (90) days following the reasoned objections, the application shall be deemed to be rejected.

5.17.8 In general, CT applications should be processed as per the prescribed timelines presented in Figure 1



[1]CTA submission to the PBSL and SLESRC can be done in parallel or sequentially. [2]Appplicant: Sponsor/ Legal representative of Sponsor or PI or Sponsor-investigator who submitted CTA.
[3]Day 60- Different timelines may apply for specific types of investigational medicinal products (see Table 1)

Figure 1: Graphic display of the periods (counted as working days) and process of Clinical Trial Authorization (CTA) in Sierra Leone by the PBSL

Table 1: Timelines for the evaluation of the scientific content of CTA by PBSL for different types of IMPs, unless otherwise specified by the PBSL on case-by-case basis.

Type of IMP	Period for the evaluation of the scientific content of CTA
Medical devices	40 working days
Pharmaceuticals	50 working days
Biological and biotechnology medicinal products	60 working days
Genetically modified organisms	120 working days or extended on case-by-case basis

5.18 Pre-Investigational New Drug Application (INDA) Meetings

5.18.1 A sponsor/PI who desires to meet with PBSL prior to INDA or during the course of the trial shall send a request to the Agency indicating:

- Purpose for the meeting
- Agenda for the meeting
- Names of study team members expected to meet with PBSL

5.1.18.2 The Board shall consider the request and respond aptly.

5.19 **Sanctions**

A person who contravenes these Guidelines or sections is liable to regulatory sanctions. These sanctions may include but not limited to any of the under-listed:

5.19.1. Suspension of an on-going clinical trial.
5.19.2 Revocation of a clinical trial certificate issued (stopping of a trial/recall of all investigational products).
5.19.3Fines.
5.19.4 Caution statement to the appropriate person or institution.
5.19.5 Rejection of trial data.
5.19.6Imposition of a timeline to address deviations / violations.

6. **REFERENCES**

1. Council for International Organisations in Medical Science (CIOMS) Standards and Operational Guidance for Ethics Review of Health-related Research with Human participants 2011
2. International Conference on Harmonisation (ICH) Guidelines- ICH-GCP E6
3. African Vaccine Regulatory Forum (AVAREF) Guideline for Joint and Assisted Review of Clinical Trial Applications
4. African Vaccine Regulatory Forum (AVAREF) Guideline for Good Clinical Practice Inspection
5. Food and Drug Authority Ghana, 2020. Guidelines for Authorization of Clinical Trials of Medicines, Food Supplements, Vaccines and Medical Devices in Ghana

6. Pharmacy Board of Sierra Leone, 2020. Development and Safety Update Report
7. ICH Guidelines on Development Safety Update Report 2010

7.0 APPENDICES

APPENDIX I: PBSL Clinical Trial Application and Authorisation Fee Schedule

Types of Clinical Trial	**USD (Leone equivalent)**
Foreign sponsored clinical trials	
Industry funded (Phase I) for therapeutics, vaccines and other biological products	4,500
Industry funded (Phase II) for therapeutics, vaccines and other biological products	4,500
Industry funded (Phase III) for therapeutics, vaccines and other biological products	5,000
Research Institution funded (therapeutics, vaccines and other biologics)	4,000
Research institution funded for medical devices such as in-vitro diagnostics and other products	2,000
Research institution funded for validation studies for example for medical devices or other in-vitro diagnostics	1,500
Protocol amendment	1000
Expedited protocol review	1200
Renewal of clinical trial certificate (yearly)	100

Locally sponsored clinical trials	
Investigator/local phases for therapeutics and vaccines and other biologics	2,000
Medical devices and other products	1,500
Validation studies for example for medical devices such as invitro diagnostics	1,000
Protocol amendment	750
Expedited protocol review	900
Renewal of clinical trial certificate (yearly)	50

APPENDIX IIa: Checklist for submission of Clinical Trial Application (CTA)

Trials full title:	
Short title:	
Protocol no.	
Version no.	
Investigational product	
Sponsor:	
Contact person:	
Address:	
Telephone no.	
Fax no.	
Cell no.	
Email address:	
Date of application:	

Checklist for submission of CTA

Please tick (√) all documents submitted under applicant check list

Applicant's checklist	CTA Documents	PBSL checklist
	Cover Letter including list of documents submitted and their version number and date	
	Completed clinical trial application form including cover page	
	Application fee	
	Clinical trial protocol with all the relevant sections including site-specific addendums.	
	Informed consent information and form(s)	
	Product information if the investigational medical product is registered: summary of product characteristics, patient information leaflet/package insert and labelling	
	Investigator's brochure	
	If applicable, synopsis of previous trials with the investigational medical product(s)	
	If applicable, electronic copies of key peer reviewed publications following ICMJE recommendations to support the application	
	Copy/ies of recruitment advertisement(s) (if applicable)	

	and questionnaires	
	Investigational medical product dossier[1] (If applicable)	
	Product information and certificate of analysis for the concomitant and rescue medications	
	GMP certificate for the site(s) producing the IP(s)[2]	
	Certificate(s) of analysis of the investigational medical product(s)	
	Certificate(s) of accreditation for the central laboratories	
	Signed declaration by the applicant	
	Signed declaration by the local principal investigator	
	Workload forms for investigators	
	Signed curriculum vitae[3] for all key staff participating in the conduct of the clinical trial, eg local principal investigator, international principal, co-investigators, study coordinator/manager, local and regional monitors, contract research affiliate etc	
	Signed declaration(s) by each investigator(s)[4]	

	Signed joint financial declaration between the sponsor and the national principal investigator	
	Sponsor/PI Contractual Agreement	
	Signed declaration by the sub-investigators and key staff participating in the clinical trial	
	Signed declaration by the regional monitor(s)	
	Proof of registration on PACTR or any PBSL approved Clinical Trial registry	
	Active clinical trials insurance (Phase I, II, III)	
	Proof of sponsor indemnification for investigators and other key study staff	
	GCP certificates for the investigators	
	Proof of registration of the key investigators with a professional statutory body (if applicable)	
	Proof of professional indemnity (malpractice insurance) for key study staff (MD, Pharmacist, Nurse etc)	
	Study budget contract	
	Favourable opinion of the Sierra Leone Ethics and scientific review Committee	

	Data Safety Monitoring Board charter and composition (where applicable) and CVs	
	Labelled CD-ROM (List of files submitted on CD-ROM)	

1 This is not required if the investigational medical product was granted registration by a mature national regulatory authority and will be used as defined therein, or if the investigational product is prequalified by the WHO

2 Investigational medical product comparator and placebo

3 Curriculum vitae to be submitted in the format provided in Annex 8

4 They could include the national principal investigator, or principal investigator and co-investigator as applicable. Each investigator is expected to sign and date one form. The form is provided in Annex

Submitted by	Received by
Name	Name
Signature	Signature
Date	Date

APPENDIX IIb; APPLICATION FORM TO CONDUCT A CLINICAL TRIAL IN SIERRA LEONE

SECTION 1: GENERAL INFORMATION

Trial's full title	
Short title	
Protocol No.	
Version No.	
Investigational medical product	
Sponsor:	
Contact person:	
Address:	
Telephone No.	
Fax No.	
Cell No.	
E-mail address:	
Date of application:	

SECTION 2: TRIAL DETAILS[2]

SLERSC No (Date & Number)	
Countries to which the application is submitted	
PACTR[3] number or any other PBSL approved Registry	
Trial's title	
Trial's short title where available	
Protocol number, date, and version[4]	
Phase of the trial	
If applicable: additional international trial identifiers: WHO, clinicaltrials.gov, EudraCT, etc	
SECTION 3: REGULATORY DETAILS	
Name of other Regulatory Authorities or Ethics Committees to which this application has been submitted, and/or approved	
If applicable, explain why the trial is not going to be conducted in the host country of the applicant/sponsor	
If applicable, name other Regulatory Authorities or Ethics Committees that have rejected this trial and explain	

If applicable, provide details and explain why this trial was halted at any stage by other Regulatory Authorities or Ethics Committees	
SECTION 4: DETAILS OF THE SPONSOR RESPONSIBLE FOR THE APPLICATION	
Sponsor	
1.Name of the organization	
Name of the contact person	
Address	
Telephone number	
Fax number	
E-mail	
Sponsor's legal representative in the country where approval is sought	
2. Name of the organization	
Name of the contact person	
Address	
Telephone number	

Fax number	
E-mail	
Sponsor status	
Commercial	

Non-commercial	
SECTION 5: APPLICANT DETAILS	
State who is submitting the application: sponsor, sponsor's legal representative or person/organization authorized by the sponsor to submit the application	
Name of the organization	
Name of the contact person	
Address	
Telephone number	
Fax number	
E-mail	
SECTION 6: INVESTIGATORS' DETAILS	
1. Local Principal investigator (if applicable)	
Name	
Qualification (PHD, PharmD[5], MD[6], Dentist, other)	
Professional address[6]	
Telephone number	

Fax number	
E-mail	
2. Local principal investigator (if applicable)	
Name	
Qualification (PHD, PharmD, MD, Dentist, other)	
Professional address[7]	
Telephone number	
Fax number	
E-mail	
3. International principal investigator (if applicable)	
Name	
Qualification (PHD, PharmD, MD, dentist, other)	
Professional address[7]	
Telephone number	
Fax number	
E-mail	
4. Sub-investigator (if applicable)	
Name	
Qualification (PHD,PharmD,MD, dentist, other)	

Professional address[7]	
Telephone number	
Fax number	
E-mail	
SECTION 7: STUDY PHARMACIST DETAILS	
Name	
Qualification (PharmD, Bpharm, MPharm)	
Professional address[7]	
Telephone number	
Fax number	
Email	
SECTION 8: MONITOR (LOCAL) DETAILS	
Name	
Qualification	
Professional address[7]	
Telephone number	
Fax number	
E-mail	
Details of Regional monitor where applicable	
SECTION 9: STUDY MANAGER/COORDINATOR DETAILS	

Name	
Qualification	
Professional address[7]	
Telephone number	
Fax number	
E-mail	
SECTION 10: DETAILS OF TRIALISTS AND SITES	
Details of the site(s): name, physical address, contact details, contact person including telephone and email contacts	
Details on the staff including number, names, qualifications, and experience	
Details and evidence of the labs competences: • Collection and processing of samples for shipment to centralized testing facilities • Bedside/point-of-contact testing and details of staff training • Screening and safety	

testing of clinical samples during the trial • Specialized end-point testing, ie virology, immunology, cytokine analysis • Name of the organization • Department • Name of the contact person • Address • Telephone number • Fax number • E-mail	
SECTION 11: INFORMATION[8] ON THE IMP(S)[9]	
Indicate if the information refers to the IMP being tested or to the IMP used as a comparator[10], repeat as necessary	
Status of the IMP	
Does the IMP for the trial have a registration in an African country or elsewhere?	
If yes, provide the trade name, name of the marketing	

authorization holder and the country that granted registration	
Is registration[11] in Africa envisioned?	
For the purpose of this trial, is the IMP modified in relation to its registration?	
IMPD[12] submitted: • Full IMPD[13] • Summary of product characteristics (SmPC) only[14]	
Has this IMP been previously authorized in a clinical trial conducted by the sponsor in Africa? If so, provide the Authority's name, date and approval number, trial title, protocol number, [national] principal investigator, and date of the final report	
Description of the IMP	
Product name[15] if applicable	

ATC[16] code if officially registered[17]	
Pharmaceutical form	
Paediatric formulation? Y/N	

Maximum duration of treatment of a patient/participant according to the protocol	
Dose allowed: • First dose for first-in-human trials, specify per day or total dose; units and route of administration • Maximum dose allowed, specify per day or total dose; units and route of administration	
Estimated quantity of IMP required for the trial (including overage[18])	
Route of administration	
Name of each active substance (INN[19] or	

proposed INN if available)	
Strength (specify all strengths to be used): • Concentration unit • Concentration type (exact number, range, more than, or up to) • Concentration (number)	
Type of IMP	
Does the IMP contain an active substance of chemical origin or of biological/biotechnological origin?	
Is the IMP a: • Immunological product (vaccine, allergen, immune serum) • Plasma derived product • Recombinant product • Radiopharmaceutical product • Herbal product Other, specify	
SECTION 12: MEDICAL CONDITION OR DISEASE UNDER INVESTIGATION	

Medical condition/disease to be investigated; summarize the local epidemiology (up to 100 words)	
Therapeutic area	

SECTION 13: SCOPE OF THE TRIAL	
Diagnosis	
Prophylaxis	
Therapy	
Safety	
Efficacy	
Other, explain	
SECTION 14: TRIAL TYPE	
Human pharmacology (Phase I) First-in-humans Bioequivalence Other, specify	
Therapeutic exploratory (Phase II)	
Therapeutic confirmatory (Phase III)	
Therapeutic use (Phase IV)	
SECTION 15: TRIAL DURATION AND RECRUITMENT	
Total duration of the study including follow-up	
Envisioned globally	
Envisioned nationally	

Envisioned number of participants per site in the country to which the application is being submitted	

Section 16 Current workload of the investigator(s)

Provide the number of studies currently undertaken by the trialist(s) as principal and/or co-investigators, and the total number of patients participating in these studies. Present the commitments of the researcher(s) in relation to the work related to clinical trials and to other activities.

Recommended format for response:

Investigator (Name and designation)			
Total number of trials currently undertaken by the Investigator	Number	Date of commencement: Expected date of completion of study:	
Total number of patients/participants for which the principal investigator is responsible on specified date	Number	Date	
Estimated time per week [168 hours denominator]		**Hours**	**%**
Clinical trials	Clinical work (patient contact)		
	Administrative		

	work		
Organization	Clinical work		
(Practice/University/employer)			
	Administrative work		
Teaching	Preparation/evaluation		
	Lectures/tutorials		
Writing up work for:			
Publication/presentation			
Reading /sourcing information			
Other (specify)			

Write N/A if an item is not applicable

[2] This form is meant only for new submissions of clinical trial applications

[3] Pan African clinical trials registry

[4] Any translation of the protocol should be assigned the same date and version as those in the original document

[5]Doctor of Pharmacy

[6]Medical doctor

[7] If applicable, include the institution's name and department

8 Please present this information for each and all investigational medical products to be used in the trial

9 Investigational medical products

10 Include a justification for choosing this comparator

11 If more than one IMP is being tested, indicate for which IMP registration is envisioned

12 Investigational medical product dossier

13 The IMPD gives information related to the quality of any IMP, i.e. including reference product and placebo, manufacture and control of the IMP, and data from nonclinical studies and from its clinical use. Details on the content and structure are provided in: Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials

(EMA/CHMP/QWP/834816/2015)

14 An SmPC can be submitted instead of the IMPD if the IMP was granted registration by a stringent regulatory authority and will be used as defined therein, or if the IMP is prequalified by the WHO. Provide the corresponding evidence if the product is prequalified. Of note, the WHO is leading a process to change the term stringent reference authority to WHO-listed authorities. This term will be added to this application form once the WHO completes the process

15 To be provided only when there is no trade name. This is the name routinely used by a sponsor to identify the IMP in the CT documentation (protocol, IB)

16 Anatomical Therapeutic Chemical Classification is an internationally accepted classification system for medicines maintained by the WHO

17 Available from the summary of product characteristics

18 Provide a justification if the overage is higher than 20%

19 International Non-proprietary Names

APPENDIX IIIa: DECLARATION BY PRINCIPAL INVESTIGATORS(S)

Declaration by the principal investigator

Name:
Title of the trial:
Protocol No:
Version No:
Date of the protocol:
Investigational medical product: Site:

1. I have read and understood the duties and responsibilities of the investigator as outlined in the guidelines for good clinical practice guideline ICHE6R2 or as last amended
2. I have notified the Regulatory Authority of any aspects of the above guideline with which I do not / am unable to comply. If applicable, attach it to this declaration
3. I have thoroughly read, understood, and critically analysed the protocol and all applicable documentation, including the investigator's brochure, patient information leaflet(s)/package insert and the informed consent form(s)
4. I will conduct the trial as specified in the protocol
5. To the best of my knowledge, I have the potential at the site(s) I am responsible for, to recruit the required number of suitable participants within the stipulated time period
6. I will not commence with the trial before the relevant ethics committee(s) and the Regulatory Authority provide written authorization
7. I will obtain informed consent from all participants or from their legal representatives if they are not legally competent
8. I will ensure that every participant shall at all times be treated in a dignified manner and with respect including relatives
9. Using the broad definition of conflict of interest below, I declare that I have no financial or personal relationship(s) which may inappropriately influence me during the conduct of this clinical trial
   *[Conflict of interest exists when an investigator (or the investigator's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her actions.]**
   *Modified from: Davidoff F, *et al.* Sponsorship, Authorship, and Accountability. (Editorial) JAMA Volume 286 number 10 (September 12, 2001)
10. I have* / have not (delete as applicable) previously been the principal investigator at a site which has been closed due to failure to comply with Good Clinical Practice *attach details
11. I have* / have not (delete as applicable) previously been involved in a

trial which has been closed as a result of unethical practices
*attach details

12. I will submit all required reports within the stipulated timeframes

Signature:	Date:
Witness:	Date

APPENDIX IIIb: DECLARATION BY SUB-INVESTIGATORS

Declaration by sub-investigators and other staff involved in the clinical trial
Name: **Title of trial:** **Protocol:** **Version No:** **Date of protocol:** **Study investigational medical product:** **Principal investigator's name:** **Site:** **Designation:**

1. I will carry out my role in the trial as specified in the protocol
2. I will not commence with my role in the trial before written authorizations from the relevant ethics committee(s) as well as from the Regulatory Authority) have been obtained
3. If applicable to my role in the trial, I will ensure that informed consent has been obtained from all participants, or from their legal representatives if they are not legally competent
4. I will ensure that every participant shall at all times be treated in a dignified manner and with respect including relatives
5. Using the broad definition of conflict of interest below, I declare that I have no financial or personal relationship(s) which may inappropriately influence me in carrying out this clinical trial.
   *[Conflict of interest exists when an investigator (or the investigator's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her actions.]**
   *Modified from: Davidoff F, *et al.* Sponsorship, Authorship, and Accountability. (Editorial) JAMA Volume 286 number 10 (September 12, 2001)
6. I have* /have not (delete as applicable) previously been involved in a trial which has been closed due to failure to comply with Good Clinical Practice
   **attach details*
7. I will submit all required reports within the stipulated timeframes

Signature: Date:

APPENDIX IIIc: JOINT FINANCIAL DECLARATION BY SPONSOR (OR REPRESENTATIVE) AND PRINCIPAL INVESTIGATOR CONCERNING SUFFICIENT FUNDS TO COMPLETE STUDY

Joint declaration by the sponsor (or representative) and the national principal investigator (or principal investigator) concerning sufficient funds to complete the trial
Title of the trial: **Protocol No:** **Version No:** **Date of the protocol:** **Investigational medical product:**

I, <full name>, representing <sponsor or representative) And
I, <full name>, national principal investigator/principal investigator

Hereby declare that sufficient funds have been made available to complete the above-identified trial.

Signed: Date:
Sponsor (or representative)
Name:
Address:
Contact details:

Signed: Date:
National/Local principal investigator (or principal investigator) Name:
Address:
Contact details:

APPENDIX IV:Phases of Clinical Trials in vaccines and medicines

VACCINE DEVELOPMENT

Phase I refers to the first introduction of a candidate vaccine into a human population
for initial determination of its safety and biological effects, including immunogenicity.
This phase may include studies of dose and route of administration, and usually involves fewer than 100 volunteers.

Phase II refers to the initial trials examining effectiveness in a limited number of volunteers (usually between 200 and 500); the focus of this phase is

immunogenicity.

Phase III trials are intended for a more complete assessment of safety and effectiveness
in the prevention of disease, involving a larger number of volunteers in a multicentre
adequately controlled study.

MEDICINE DEVELOPMENT

Phase I refers to the first introduction of a drug into humans. Normal volunteer subjects
are usually studied to determine levels of drugs at which toxicity is observed. Such studies are followed by dose-ranging studies in patients for safety and, in some cases,
early evidence of effectiveness.

Phase II investigation consists of controlled clinical trials designed to demonstrate effectiveness and relative safety. Normally, these are performed on a limited number of
closely monitored patients.

Phase III trials are performed after a reasonable probability of effectiveness of a drug
has been established and are intended to gather additional evidence of effectiveness for
specific indications and more precise definition of drug-related adverse effects. This phase includes both controlled and uncontrolled studies.

Phase IV trials are conducted after the national drug registration authority has

approved
a drug for distribution or marketing. These trials may include research designed to explore a specific pharmacological effect, to establish the incidence of adverse reactions, or to determine the effects of long-term administration of a drug. Phase IV
trials may also be designed to evaluate a drug in a population not studied adequately in
the pre-marketing phases (such as children or the elderly) or to establish a new clinical
indication for a drug. Such research is to be distinguished from marketing research,
sales promotion studies, and routine post-marketing surveillance for adverse drug reactions in that these categories ordinarily need not be reviewed by ethical review committees (see Guideline 2 of CIOMS guideline.

APPENDIX V: Clinical Trial Amendment Form

APPLICATION FORM FOR CLINICAL TRIAL AMENDMENT IN SIERRA LEONE

1. ADMINISTRATIVE DETAILS

Particulars of applicant

If an individual:

Full name ……

Qualifications ……..
Postal Address ……

Telephone number……
Fax……..

E-mail ……..

If an institution:
Name of institution ……
Postal Address ……
Telephone Number ……
Fax ……

Email……
Name and status of person in the company making the application on behalf of the company……
……

Name of Sponsor: ……

Address: ……
Phone ……Fax ……

E-mail ……..

Name of Contact Person(s) ……

Postal Address:

……

……

Telephone Number ……

Fax ……

E-mail ……

Name of Principal Investigator: ……

Address: ……

Phone …….

Fax.....

E-mail ……

Name of Principal Investigator: ……

Address: ……..

Phone …….. Fax.....

E-mail ……

Name of Study pharmacist(s): ……
Address: ……

Phone……
Fax……

E-mail ……

Name of Local Monitor: ……
Address: ……

Phone ……
Fax……
e-mail ……

2. TRIAL DETAILS

Study title and Acronym

……
……
……

Clinical Trial Registration Number (PACTR)……

SLESRC No (Date & Number)……

PBSL Authorization number……

Name(s) of Trial Centre(s):

……

……

Premises Address (es): ……

Phone …… Fax ……

E-mail ……

Proposed date of Implementation of the Amendment

……

…….

Type of Trial: ……

……

Number of participants enrolled in the study so far……

3. INVESTIGATIONAL MEDICINAL PRODUCT DETAILS

Proprietary Name of Product:

……

……

Approved Name of Product:

……

Dosage Form: ……

Route of Administration:

……

Dosing:……

……

Details of control (Name, dosage form, route of administration, dosing etc):

……

……

……

Indicate whether any other drug(s) will be given concomitantly. YES/NO*

If YES, state the name of the drug(s)……

State the total quantities of all investigational products including products for control group(s) that would be required for the full conduct of the study……..

……

……

Attach the label and package insert of investigational product if product has already been registered for use in Sierra Leone.

State any adverse or possible reactions to the product

……

……

……

……

……

……

4. DETAILS OF AMENDMENT

NO	AMENDMET	RATIONALE FOR AMENDMET	PAGE NUMBER & NAME OF DOCUMENT IN AMENDED VERSION

APPENDIX VI:Serious Adverse Events (SAE) Reporting Timelines

APPENDIX VIa: REPORTS FROM CLINICAL TRIAL SITES IN SIERRA LEONE

Type of ADR Report	Time Frame for Reporting	Format
Serious Adverse Events	Immediately where possible and in any event, within 48 hours after becoming aware of the information but no later than 15 calendar days	A Serious Adverse Events form conforming to the CIOMS format or previously approved by PBSL must be completed and submitted after the site becomes aware of an event. Electronic submissions must be E2B compliant.
☐ Follow-up reports	Immediately when any of the under-listed occurs: i. Change in the severity of SAE initially reported. ii. Whenever there is any new development on an initially reported SAE. iii. When the SAE resolves.	Follow-up reports should include an assessment of the importance and implication of any findings. All fatal cases must be followed up with formal autopsy report.
☐ Frequent adverse events (greater than or equal to 1% but less than or equal to 10%)	Immediately where possible and in any event, within 7 days	Line listing and through PBSL web-based online reporting platform on its website (www.pharmacyboard.gov.sl)

	after becoming aware of the information	
Non-Serious Adverse Events	On request and where applicable, submitted as part of an application for registration	Individual reporting in accordance with the data elements specified in the ICH guidance Document E2A

APPENDIX VIb: REPORTS FROM FOREIGN SITES (For multicenter studies with Sierra Leone as a participating country)

Serious Events	Immediately where possible and in any event, within 7 days after becoming aware of the information.	Line listing Reports should include an assessment of the importance and implication of any findings.
Foreign regulatory decisions that affect the safety or use of the product	7 days	Detailed report Records with respect to all adverse events in respect of the drug that have occurred inside or outside the country, including information that specifies the indication for use and the dosage form of the drug at the time of the

		adverse event may be added.

APPENDIX VIc: OTHER REQUIREMENTS

Literature reports that affect the safety of the product	7 days	Detailed report and / or copy of the publication Records with respect to the enrollment of clinical trial subjects including information sufficient to enable all clinical trial subjects to be identified and contacted in the event that the sale of the drug may endanger the health of the clinical trial subjects or other persons may be added.
Notification of change in nature, severity or frequency of risk factors	28 days	Complete and accurate records with respect to each change made to the Investigator's Brochure, including the rationale for each change and documentation that supports each change

New information impacting on risk benefit profile of product or conduct of trial	7 days	Communicate with appropriate scientific and medical judgments being applied to each situation. Additional information may include copies of diagnostic test results, laboratory reports or medical record progress notes
Development Safety Update Reports (DSUR)	Annually and on request by PBSL	As a Follow Up Report including copies of diagnostic test results, laboratory reports or medical record progress notes

APPENDIX VIIa: Clinical Trial Report timeline

ACTION	REFERENCE	TIMELINE
Quarterly progress reports	3.7.1	Within 21 days after the end of the previous quarter. A quarter in this instance is considered as three months beginning from the date of initiation of a specific clinical trial.

Notification of Trial initiation	3.7.1.1	Immediately trial commences or within ninety (90) days of issuance of the Clinical Trial Certificate if the trial does not begin or is delayed as per the date of commencement on the Clinical Trial Certificate issued
Notification of interruption of an approved trial before achievement of its purpose.	3.7.1.5	Within ten (10) working days
Interim report Close out report	3.7.1.6 3.7.3	Within 21 days after the end of the first half of the trial period Not later than 30 days after the completion of a clinical trial
Final Report of Clinical Trial as per the current ICH E3 guidelines.	3.7.4	Not later than 90 days after the completion of the trial

APPENDIX VIIb: Clinical Trials Quarterly Progress Report Form

SECTION A: ADMINISTRATIVE INFORMATION

Clinical Trial Certificate Number: …… …… …… ……	Expected Date of Commencement (as indicated on the certificate):……./……/……	Actual Date(s) of Commencement (at the Study Centre(s): ……/…… …./…… .	Protocol Number: …… …… …… …… …… …… …… ……

Study Title: …….

Reporting Period — From…… ……..to…… ……..

Principal Investigator (Name, Address, Phone, Email):

Co-Investigators: (Name, Address, Phone, Email)

Study pharmacist (Name, Address, Phone, Email):
:

Other Study Contact (if applicable): (Name, Address, Phone, Email):

:

SECTION B: STUDY STATUS (Check one category only)

□Enrollment has not begun

□Actively enrolling subjects

□Enrollment closed on: ..... (insert date): subjects are receiving treatment/intervention

□Enrollment closed on: ..... (insert date): subjects are in follow-up only.

□Analyzing data

- Data analysis completed

SECTION C: INFORMATION ON SUBJECTS & STUDY ACTIVITIES

a. Number of subjects consented and screened.....
b. Total number of subjects consented and screened who are eligible for the study.....
c. Number of subjects to which the investigational product(s) has been administered.....
d. Number of subjects left to be enrolled in the coming months (years).....

e. Number of participants who have discontinued the study:

- by Investigator:
- voluntarily:
- due to SAE:

f. Have there been any Serious Adverse Events (SAEs)?	□Yes	□ No
g. Total number of SAEs: ..... (attach line list of SAEs documented for the quarter)	□Yes	□ No
h. Have these SAEs been reported to PBSL	□Yes	□ No
i.If No, explain…… …… ……..	□Yes	□ No
j. Have there been any changes to the protocol since PBSL approved?		
k. Was this amendment submitted to the PBSL?		
l. If No, explain…… …… ……..		
m. Date for the end of the study.....		

n. Date for the final study report.....

SECTION D: COMMENTS (if any)

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SECTION E: SIGNATURE

Signature of Principal Investigator:..... Date: .....

Return this form and all supporting documentation to PBS

APPENDIX VIII: CLINICAL SITE CLOSE- OUT REPORT

SECTION A: ADMINISTRATIVE INFORMATION

SITE INFORMATION

Protocol Title:

Protocol Identification number:

Clinical Trial Certificate number:

Name and address of Clinical Site:

Name, address, telephone number and e-mail address of Principal Investigator:

Name, address, telephone number and e- mail address of Sponsor:

Date of last recruitment:

Reason for closure:

Date(s) of Report:

Clinical Site Personnel Involved with the Study:

OBJECTIVE	COMMENTS
1. All regulatory and other essential documents as stipulated in PBSL GCP guideline are up- to- date and on file	*Provide list of documents on file at the site*
2. Notification of all relevant oversight bodies oof closure of study	
3. Signed, informed consent is on file for each sstudyparticipant	*Provide list of participants (use codes/ study IDs)*

II **CLINICAL SITE CLOSE- OUT CHECKLIST**

Instructions: Please provide comment (s) for each of the items listed below. Additional sheets may be attached if necessary.

OBJECTIVE	**COMMENTS**
4. Documentation of all protocol violations/ deviations and/ or appropriate note- to-	*Provide list*
5. Appropriate follow- up and reporting of all SAEs to PBSL	*Provide number of SAEs reported. Summary of outcome for SAEs listed*
6. Completion of all Case Report forms for each participant	
7. Entry/ submission of all relevant data into database/ to sponsor/ coordination center. If not complete, indicate the timeline fo	
8. Status of all outstanding data edits, queries or delinquent forms and timeline for their resolution	
9. Tentative date for submission of full Clinical Study Report	
10. Requirements for retention of study records. Indicate if requirements have been met	
11. Drug accountability • Quantity of IPs received • Quantity of IPs utilized in the study • Quantity of IPs destroyed (attach copy of destruction certificate (s))	

12. Status/ shipment/ analyses of all p articipant specimen according to protocol requirements (inc luding plans for	
13. If blinded study drug was used, co nfirm that the tear- off labels were not opened. For any that w ere opened,	

CLINICAL SITE CLOSE- OUT REPORT

Additional comments:

STATUS OF PAST OBSERVATIONS/RECOMMENDATION MADE DURING MONITORING/ GCP INSPECTIONS: (Have corrective measures been implemented for all observations and recommendations?), Provide summary of measures implemented for each point)

OUTSTANDING ISSUES OR ACTIVITIES TO BE IMPLEMENTED: (Include problems identified, if any, and recommendations/ action items for corrections)

_____

_____

Prepared by:

Date:

(Signature)

APPENDIX IX: Packaging and Labeling requirements for investigational medicinal products (IMP)

(A). Packaging requirements

1. The container in which the product is contained should be of good quality
2. The container and closure should be properly sealed so as to protect the product from the influence of outside environmental factors
3. Each sample should have an insert

(B). Labelling requirements

All information should be in English and the print should be clear, legible and indelible. The following information should be included on labels.

(a) details of sponsor.
(b) pharmaceutical dosage form, route of administration, quantity of dosage units, and in the case of open trials, the name/identifier and strength/potency;
(c) the batch number
(d) a trial reference number
(e) the trial subject identification number
(f) the name and address of the site where the clinical trial is conducted as well as the name and address of the principal investigator
(g) directions for use and any warnings or precautions that may be necessary
(h) "For clinical trial/research use only"
(i) storage conditions;
(j) period of use (use-by date, expiry date or re-test date as applicable), in month/year format and in a manner that avoids any ambiguity as well as date of dispensing, if applicable;
(k) "keep out of reach of children" except when the product is for use in trials where the product is not taken home by subjects.

APPENDIX X: Requirements for material transfer authorization

All institution or individuals that wants to transport and use any clinical information, medical records and biological samples from Sierra Leone to an institution outside of the region, must submit the following:

1. An application for export permit should be made through the Ministry of Health and Sanitation (MOHS) to PBSL by the local principal investigator or study lead.

2. All applications must be accompanied by the following documents:

a. Evidence of informed consent for use of medical records, clinical information and biological samples from patients who are alive.
b. Authorisation from the MOHS for deceased patients
c. Memorandum of understanding (MOU) between MOHS and applicant
d. Signed and dated Material Transfer Agreement (MTA).

3. Payment of prescribed export permit fee.

APPENDIX XI: PROCESSING OF SUBMITTED DOCUMENTS BY THE PBSL

ACTIVITY	TIMELINE****
Processing of Clinical Trial Applications	40-120 days
Processing of import permits for Investigational Products	10 days
Processing of quarterly progress and safety reports	15 days
Notification of receipt of electronic submissions including SAE reports	5 days
Communicating GCP Inspection findings	21 days
Processing of application for protocol amendment	30 days
Processing of application for renewal of Clinical Trial Certificate	15 days
Processing of final Clinical Trial reports	30 days

The days refer to working days * * *

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