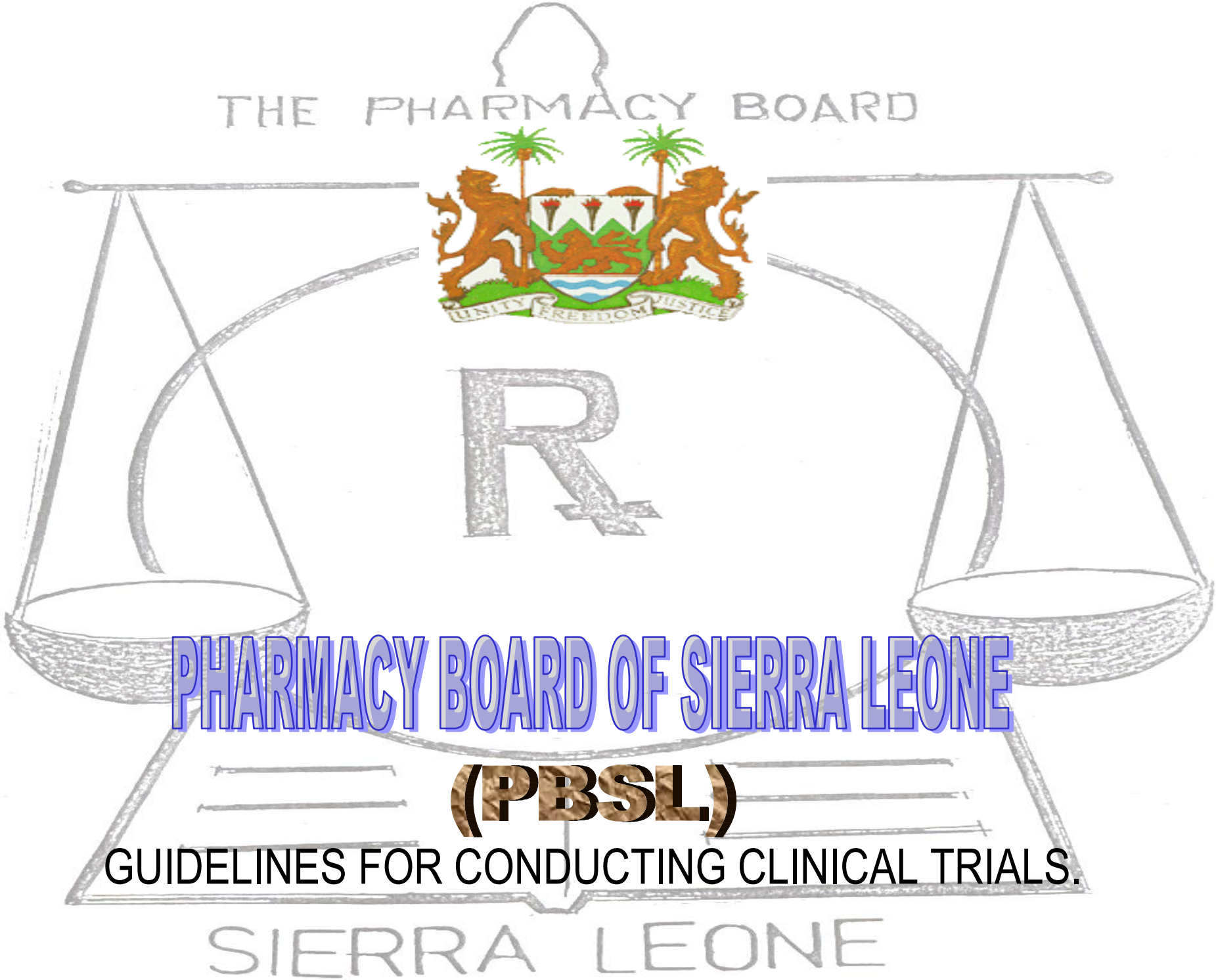

PHARMACY BOARD OF SIERRA LEONE

(PBSL)

GUIDELINES FOR CONDUCTING CLINICAL TRIALS.

FOREWORD

The purpose of Drug Registration is to ensure that a pharmaceutical product has been adequately tested and evaluated for safety, efficacy and quality, and that the product information provided by the manufacturer is accurate. It also allows the pharmaceutical product to be placed on the market until the registration period for the product has expired.
The Pharmacy Board of Sierra Leone has developed and adopted the following guidelines on:

I) Guidelines for conducting clinical trials of medicinal products and vaccines.**(Please note that this guideline is only applicable for new drug entity)**

These guidelines are intended to facilitate the registration process of Pharmaceutical products, and are meant to be adopted and implemented by all stakeholders intending to market Pharmaceutical products in Sierra Leone.

The overall goal of these guidelines is to achieve the highest practicable standards of the quality of products imported into Sierra Leone and in addition to ensure the safety, quality and efficacy for these products including manufactured, imported, exported and distributed to ensure the protection of the public health as envisaged by the Pharmacy and Drugs Act.

It should be noted however, that these guidelines are subject to review as and when necessary by the Pharmacy Board of Sierra Leone.

PHARMACY BOARD OF SIERRA LEONE

GUIDELINES FOR CONDUCTING CLINICAL TRIALS OF MEDICINAL PRODUCTS AND VACCINES,

In pursuance of Section 55 of the Pharmacy and Drugs Acts, these guidelines are hereby made to define the general norms and scientific principles for the conduct, performance and control of clinical trials particularly in the context of registration of drugs in Sierra Leone.

1 DEFINITION OF TERMS

1.1 Board means Pharmacy of Sierra Leone (PBSL**)**

1.2 In these Guidelines, unless the context otherwise states

"**Clinical trial**" means systematic studies in humans and/or animals in order to discover or verify the pharmacokinetics(absorption, distribution, metabolism and excretion), as well as the pharmacodynamics (therapeutic effects or adverse effects) of drugs. Clinical trials may also be aimed at identifying other indications for use of the drug not previously approved.

2 REQUIREMENTS

2.1 An application for the conduct of a Clinical Trial shall be made in writing.

2.2 The application shall be accompanied by:

a) A covering letter

b) Two (2) copies of completed application forms signed by all participating investigators

c) Good Manufacturing Practice (GMP) certificate/statement in the country of manufacture for the product/ placebo.

d) Chemistry, Manufacturing and Control Data (CMC) for the product. For a new chemical entity (NCE), pre-clinical data shall be included.

e) A comprehensive trial protocol.

f) Original copy of approval letter/certificate by the applicant's Institutional Research and Ethics Review Board or recognised independent ethics committee. In the case of multicentre studies, an approval from each institution's review board will be required.

g) Non-refundable application fee as specified in the Board's fee schedule.

3 TYPES OF CLINICAL TRIALS

3.1 Clinical trials shall be categorized as follows;

a) Trials initiated by the Pharmacy Board of Sierra Leone.

b) Trials initiated by pharmaceutical companies or agencies for newly developed substances.

c) Trials initiated by the PBSL / Ministry of Health and Sanitation and Pharmaceutical Companies / NGO's (Non Governmental Organisation) to be carried out locally for pharmacogenetic or other reasons peculiar to the population in Sierra Leone.

d) Trials initiated by academic and research institutions either locally or as part of an international multi-centre study.

3.2 In all the categories above (section 3.1), the primary end-point of the trial shall be clearly specified.

3.3 The application shall indicate the phase of clinical trial that is intended. (See appendix).

4 QUALIFICATIONS OF INVESTIGATORS

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

4.2 Principal investigator(s) directly in charge of a trial (at each site of a multi-centre trial) must be

a) Medically qualified and clinically competent

b) In good standing with the Sierra Leone Medical and Dental Council, Pharmacy Board of Sierra Leone and Nursing Board.

c) Sufficiently experienced in clinical evaluation of medicinal products

d) Experts in the pathology and the clinical handling of the particular disease or condition under study

4.3 Non-medically qualified scientists may participate only as co- investigators or in other roles, but not as Principal Investigators.

5. ETHICAL CLEARANCES

5.1 Ethical Clearance for all phases of clinical trials in humans shall be sought from the Institutional Research and Ethical Review Board or a recognized, independent ethics committee of each of the proposed Institution(s) or centre(s) where the trial is to be conducted.

6. TRIAL PROTOCOL

The protocol shall contain, but not be limited to, the following

6.1 Explanation for the trial being conducted in Sierra Leone and not in the host country of applicant or sponsor

6.2 Aim of the trial and the reasons for its execution

6.3 The essentials of the problem to be studied and its background

6.4 General ethical considerations relating to the trial and informed consent sheet or form or otherwise to be given to patients or volunteers

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6.5 Description of the type of trial, trial design, blinding technique, randomization specification and other bias reducing factors to be implemented.

6.6 Number of patients expected to take part in the trial and the statistical Justification

6.7 Route of administration, dosage and dosing schedules and treatment period for the drug being tested and the drug or placebo being used as control

6.8 Storage of drug before administration.

6.9 Description of treatment applied to control group(s) or control period(s), placebo, and other therapy and any other treatment that may be given concomitantly including measures to be implemented to ensure the safe

handling of the products.

6.10 Procedures for handling and processing records of effects, side-effects and adverse reactions to the product(s) under study

6.11 Description of special analyses and/or tests or procedures to be carried out.

6.12 Specific plan for effective control and monitoring of the trial.

6.13 Specifications and instructions for anticipated deviations from the Protocol.

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6.14 Procedure for keeping a list of participating volunteers/patients and records for each individual taking part in the trial.

6.15 Measures to ensure the safe handling of drugs.

6.16 Inclusion and exclusion criteria should be well defined as specified in the World Medical Association Declaration of Helsinki- Ethical Principles for Medical Research Involving Human Subjects. (download from www.wma.net/e/policy/pdf/17c.pdf)

6.17 Evaluation of results, description of statistical methodology and a specified account for how the response is to be evaluated, methods of computation and calculation of effects.

6.18 Provisions for dealing with complications.

6.19 Clear procedures for interim assessment of trial.

6.20 Procedures for aborting trial.

6.21 Certificates of insurance cover for participants should be well defined as specified in the World Medical Association Declaration of Helsinki- Ethical Principles for Medical Research Involving Human Subjects.

7 Protocol Amendments.

7.1 Any amendment to the trial protocol, the trial arrangements and the investigational medicinal product should be reported to the independent ethics committee, and simultaneously to the Board, before such amendments are carried out.

7.2 If such amendments are necessary to protect the life of subjects, an urgent amendment may be carried out but the investigator should inform the independent ethics committee and the Board of such amendments with a phone call, followed by a written document within 48 hours.

7.3 Reports of all amendments shall include:

a) Reasons for the amendments

b) Possible consequences for subjects already included in the trial

c) Possible consequences for the evaluation of the report

8 REPORTING OF ADVERSE EVENTS

8.1 Any serious and or frequent adverse reaction to the product shall receive immediate medical attention and reported to the Board within forty eight(48) hours

8.2 All cases that are fatal shall be accompanied by a formal autopsy report

9 REPORTING RESULTS OF CLINICAL TRIALS

9.1 The method and other modalities of reporting the outcome of a clinical trial must be agreed upon by all participants

9.2 A formal report conforming to the consolidated system of reporting trials (CONSORT) shall be required in all cases to be submitted to the Board.

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

9.4 If the trial does not begin, or is interrupted before its purpose is achieved, the reason shall be conveyed in writing to the Board.

9.5 The Board reserves the right to audit and interrupt any trial for which authorization has been given, as and when necessary, on advice of its appointed Technical Committee.

9.6 After a report is sent to the Board, a publication in a scientific journal or other medium, for the purpose of disseminating the information obtained to stakeholders, will be encouraged.

9.7 All clinical and experimental data shall be kept safely for a period of 5 years after completion of the trial and be readily available for review upon request by the Board.

9.8 If the trial does not begin, or is interrupted before its purpose is achieved, the reason shall be conveyed in writing to the Board within ten (10) working days. This shall include:

a) Justification for the premature ending or of the temporary halt of the trial;

b) Number of patients receiving treatment at the end of the study termination;

c) Proposed management of patients receiving treatment at the time of halt or study termination;

d) Consequences of the evaluation of the results.

10 PROCEDURE FOR IMPORTING CLINICAL TRIAL BATCHES

10.1 Permit to import clinical trial batches shall only be granted to duly recognized clinical research organizations (CROs) that have protocols approved by the Board to conduct clinical trial in accordance with these guidelines

10.2 Application to import samples for clinical trials shall be made to the Board in writing accompanied by a import permit application letter.

10.3 All import permits shall bear the full name and address of the innovator, the sponsor and the clinical research organization, the name/description of the investigational medical product, placebo and quantity.

10.4 Permit to import clinical trial batches shall be signed and dated by the principal investigator.

10.5 Both the investigational medicinal product and the placebo shall be labeled to indicate they are samples for the conduct of clinical trials only.

10.6 Products imported shall be inspected by officials of the Pharmacy Board at the port of entry before they are released to the CRO.

10.7 The Board may order the re-exportation of the products intended for clinical trials if the Board has any reason to believe that there is a protocol violation or any of provisions in these guidelines have been violated.

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

10.9 Permit to import investigational medicinal product and placebo shall be accompanied by the certificates of analysis.

11 GOOD CLINICAL PRACTICE INSPECTIONS

11.1 The Board shall periodically conduct Good Clinical Practice (GCP) Inspections of the trial sites in accordance with these guidelines.

11.2 These inspections shall be conducted to ensure that the facilities used continue to be acceptable throughout the clinical investigation.

11.3 During the inspection the Board shall assure itself that:

a) The facilities used by the investigator continue to be acceptable for the purposes of the study.

b) The study protocol for the investigation is being followed.

c) Any changes to the protocol have been approved by Ethics Committee and the Board.

d) Accurate, complete and current records are being maintained.

e) Accurate, complete, and serious adverse events (SAEs) are timely reported to the sponsor and to the Board.

f) The investigator is carrying out the agreed-upon activities, and has not delegated them to other previously unspecified staff.

11.4 Before such inspection, the principal investigator (or the co-investigator) shall be informed of the impending inspection either in writing, by phone or electronically

11.5 An unannounced inspection may however be conducted, if the Board has reasonable cause to believe that the approved protocol is being violated.

APPENDIX

PHASE I

- Studies preceding this phase would have established the effect and safety of the product in animals. The purpose of this phase is to establish a preliminary evaluation of safety, tolerance and a first outline of how the drug is metabolized and excreted in humans.

- Phase I trials, being the first trials of a new drug in humans, shall be conducted in healthy volunteers, with their informed consent, who shall.

  □ be aged between 18 and 65 years and in good mental health and not pregnant or lactating

  □ not have any illness which could potentially affect the results of the trial, or which could create special conditions for unfavorable effects of the drug

- The number of volunteers participating in this phase of clinicaltrials shall not be less than twenty-four (24).

PHASE II

- The purpose of a phase II trial is to demonstrate activity of the drug and to obtain further safety data. It also aims at the determination of effective dose ranges and regimens and provides an optimal background for the design of future therapeutic trials.
- This phase may be an open trial in a small number of informed consenting patients suffering from the disease or condition which the product potentially can treat.
- This phase of clinical trials is performed with no less than 100 (one hundred) subjects. Chronic toxicity studies may be conducted in laboratory animals at this stage over a period of not less than 24 months.
- If the drug is found to be effective at this stage, and the risks considered acceptable, then it progresses to phase 3 trials.

PHASE III

- This phase consists of wider trials with 1,000 – 3,000 participants to further determine the therapeutic effects of the drug and possibly the short and long-term safety and efficacy balance of formulations of the drug

- The effect of treatment with the drug may be compared in this phase with established methods of treatment, if any, or with other control procedures.

- The pattern and profile of less common side-effects become more evident as more and more participants are tested with the drug over long periods.

- The design of trials in this phase shall, preferably, be randomized, double-blind and crossed-over. Other designs may be acceptable for long-term safety studies.

- Generally, the conditions of the trial shall be as close as possible to the normal clinical setting in which the disease for which the drug is intended occurs.

PHASE IV

- Phase IV trails shall be conducted on an approved product already on the market to find out more about the long-term risks, benefits, and optimal use, or to test the product in different populations of people, such as children

- The trial shall include post-market surveillance.

Pharmacy Board of Sierra Leone

Clinical Trial Certificate

Name of Product:
Protocol Code No.:

Study Title:

Type of Study (e.g. Single centre, open label, phase I):

Name and Address of Sponsor:

Name and Address of Principal Investigator:

Name and Address of Study Centre:

Expected Date of Commencement:

Duration of Investigation:

Please note that any amendment(s) to the original protocol on which this certificate is being issued would render the certificate invalid. Adverse reactions observed during the study must be **immediately** reported to the Pharmacy Board of Sierra Leone.

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REGISTRAR

PHARMACY BOARD OF SIERRA LEONE