



---

# GUIDELINES FOR THE CONDUCT OF CLINICAL TRIALS IN SRI LANKA

---

OCTOBER 15, 2019

NATIONAL MEDICINE REGULATORY AUTHORITY  
No.120, Norris Canal Rd, Colombo 01000, Sri Lanka

# GUIDELINES FOR THE CONDUCT OF CLINICAL TRIALS IN SRI LANKA

## CONTENTS

1	PURPOSE.....	3
2	SCOPE.....	3
3	PROCEDURE/S .....	3
	3.1 Approvals required to conduct a clinical trial .....	3
	3.2 Ethics Review committees recognized by NMRA.....	3
	3.3 Categories of clinical trials requiring Clinical Trials Evaluation Committee (CTEC) approval .....	4
	3.4 Phases of clinical trials permitted to be conducted in Sri Lanka .....	4
	3.5 Application for approval to conduct a clinical trial.....	4
	3.6 priority review of a clinical trial .....	5
	3.7 Timelines for related processes.....	5
	3.8 Periodic Reports to CTEC.....	5
	3.9 Safety reporting requirements for Clinical Trials .....	5
	Annex I - CIOM-I format .....	10
	Annex II- Data Elements for Inclusion In Expedited Reports Of Serious Adverse Drug Reactions.. ..	11
	Annex III - Clinical trials safety reporting requirements and timelines to the CTEC .....	12
4	DEFINITIONS .....	14
5	RELATED LEGISLATION AND DOCUMENTS .....	14
6	FEEDBACK .....	18
7	APPROVAL AND REVIEW .....	18

## 1. PURPOSE

The aim of this guideline is to provide comprehensive guidance to assist clinicians, scientists, sponsors and research organizations to become familiar with the existing procedures and requirements for the conduct of clinical trials in Sri Lanka.

Also, one of the principal objectives of this guideline is to help investigators better understand their responsibilities with respect to protecting human research participants and ensuring the integrity of the data from clinical investigations.

## 2. SCOPE

These guidelines indicate the order of the material to be submitted and the minimum requirements for conducting clinical trials. These guidelines are not intended as a comprehensive guide on Good Clinical Practice (GCP), and should be read in conjunction with local regulations and ICH GCP guidelines.

## 3. PROCEDURE/S

### Approvals required to conduct a clinical trial

1. A clinical trial shall be initiated in Sri Lanka only after:
  - a) Obtaining approval from the Clinical Trials Evaluation Committee (CTEC), National Medicines Regulatory Authority (NMRA), Ministry of Health.
  - b) Obtaining clearance from an Ethics Review Committee (ERC), which have been recognized by the Clinical Trials Evaluation Committee, NMRA, Ministry of Health
  - c) Obtaining approval or a no-objections certificate from the head(s) of the institution(s) of the trial site(s) (e.g. Director of a hospital).
  - d) Registering the study in the Sri Lanka Clinical Trials Registry.

Parallel submissions can be made to both the CTEC and to the relevant ERC. However, CTEC approval to conduct a clinical trial will be granted only after clearance from one of the ethics review committees listed below has been obtained for the trial.

### Ethics Review Committees (ERC) recognized by the NMRA

2. For the purpose of granting ethical clearance for trials requiring regulatory approval following Ethics Review Committees have been recognized by the CTEC :
  - ERC, Faculty of Medicine, University of Colombo
  - ERC, Faculty of Medical Sciences, University of Sri Jaewardenepura
  - ERC, Faculty of Medicine, University of Peradeniya
  - ERC, Faculty of Medicine, University of Kelaniya
  - ERC, Faculty of Medicine, University of Ruhuna
  - ERC, Faculty of Medicine, University of Jaffna
  - ERC, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka
  - ERC, Medical Research Institute, Colombo
  - ERC, Sri Lanka Medical Association, Colombo

## Categories of clinical trials requiring Clinical Trials Evaluation Committee (CTEC) approval

3. Approval from the CTEC is required to conduct a clinical trial for the following categories of medicines;
  - a) Unregistered medicines, and
  - b) Registered medicines where the proposed clinical trial is outside of the conditions of registration. These may include changes to:
    - (i) indication(s) and clinical use
    - (ii) target patient population(s)
    - (iii) route(s) of administration
    - (iv) dosage regimen(s)

Clinical trials for other categories of medicines sponsored by non-commercial sponsors such as investigators either as individuals or collaborative groups, academic institutions, healthcare institutions and cooperative establishments are not subject to regulatory review and do not require approval from the CTEC. Such clinical trials require only ethics approval and registration with the Sri Lanka Clinical Trials Registry.

## Phases of clinical trials permitted to be conducted in Sri Lanka

4. Phase I / first-in-man clinical trials are not allowed in Sri Lanka at present.

Phase II trials are allowed provided the same study protocol is approved in countries with reference regulatory authorities – USA, Canada, European countries governed by EMA, UK, Japan, Australia, New Zealand, and Singapore.

Phase III and IV trials are allowed to be conducted in Sri Lanka.

## Application for approval to conduct a clinical trial

5. An application for permission to conduct a clinical trial should be made by logging into eNMRA portal at [www.http://enmra.nmra.gov.lk](http://enmra.nmra.gov.lk) and furnishing the requested details and documents. NMRA would charge a processing fee for industry sponsored trials as specified in the gazette extraordinary No. 2052/33 of 05.01.2018. In addition, NMRA may require the applicant to submit manually (one hardcopy and softcopy in compact disc) the stipulated Application Form accompanied by a covering letter and the following essential documents:

- Clinical trial protocol
- Investigator's brochure – containing chemical and pharmaceutical information, animal pharmacology & toxicology data, specific pharmacological actions, pharmacokinetic data, and available human clinical pharmacology data related to the investigational product(s)
- Informed consent document(s) with Sinhala and Sri Lankan Tamil translations
- Curriculum vitae of principal investigators
- Undertaking by the principal investigators
- Ethics review committee clearance, if clearance has already been granted

- Regulatory status in other countries, if available, in case of international multi-centre studies
- Current copy of certificate of Good Manufacturing Practices (GMP) & complete certificate of analysis
- Valid insurance certificate with insurance cover in Sri Lanka
- Any other information as the CTEC may require

### **Priority review of a clinical trial**

6. The applicant may request for priority review for an investigational product if there are unmet medical needs. The request for priority review should be made at the point of the application submission and should be accompanied by justifications for requesting for a priority review and how the investigational product is expected to benefit patients.

The Authority reserves the right to deny a request for priority review if it is deemed inappropriate. The decision for the granting of priority review would be conveyed to the applicant at the point of acceptance of the application for evaluation.

### **Timelines for related processes, excluding stop-clocks**

7. The following timelines will be applicable for the below mentioned regulatory activities;

Processing of a clinical trial application	– 75 days
Processing of a variation (i.e. for amendments requiring NMRA approval)	– 35 days
Issuing of sample import licences of investigational and non-investigational products	- 7 days

### **Periodic reports to the CTEC**

8. The CTEC may require the holder of an approval during a clinical trial to provide any information or report at such times and in such manner as the CTEC may require.

The holder of an approval should submit to the CTEC a notification of trial initiation, progress reports during the conduct of trial as well as final report of the clinical trial within six (06) months after the completion of the trial or such longer period as the CTEC may allow.

This summary reports should provide a brief description of the study, number of participants exposed to the drug, dose and duration of such exposure, details of adverse reactions, if any, and reason(s) for discontinuation in case of a prematurely discontinued clinical trial.

### **Safety reporting requirements for clinical trials in Sri Lanka**

#### **9. Serious Adverse Event or Adverse Drug Reaction**

During clinical investigations, adverse events may occur which, if suspected to be medicinal product-related (adverse drug reactions), might be significant enough to lead to important changes in the way the medicinal product is developed (e.g. change in dose, population, needed monitoring, consent forms). This is particularly true for reactions, which, in their most severe

forms, threaten life or function. Such reactions should be reported promptly to the Clinical Trials Evaluation Committee (CTEC).

Therefore, special medical or administrative criteria are needed to define reactions that, either due to their nature ("serious") or due to significant, unexpected information they provide, justify expedited reporting.

To ensure no confusion or misunderstanding of the difference between the terms "serious" and "severe," which are not synonymous, the following note of clarification is provided:

The term "severe" is often used to describe the intensity (severity) of a specific event (as in mild, moderate, or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache). This is not the same as "serious," which is based on patient/event outcome or action criteria usually associated with events that pose a threat to a patient's life or functioning. Seriousness (not severity) serves as a guide for defining regulatory reporting obligations.

A serious adverse event (experience) or reaction is any untoward medical occurrence that at any dose:

- results in death,
- is life-threatening,
- requires inpatient hospitalisation or prolongation of existing hospitalisation,
- results in persistent or significant disability/incapacity, or
- results in a congenital anomaly/birth defect.

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event, which hypothetically might have caused death if it were more severe.

The investigator(s) shall report all serious adverse events which occur in a study participant at a trial site at which he is responsible immediately to the sponsor for the conduct of a clinical trial. The investigator(s) shall report all serious adverse events and serious and unexpected adverse drug reactions (SUSARs) to the sponsor within twenty four hours after he was first aware of the event or reaction.

In general, serious adverse events or reactions observed during the conduct of a study should be considered an unanticipated problem involving risk to human participants and reported to the relevant ethics review committee and the CTEC as per required timelines.

## **10. Expectedness of an Adverse Drug Reaction**

The purpose of expedited reporting is to make regulators, investigators, and other appropriate people aware of new, important information on serious reactions. Therefore, such reporting will generally involve events previously unobserved or undocumented, and a guideline is needed on how to define an event as "unexpected" or "expected" (expected/unexpected from the perspective of previously observed, not on the basis of what might be anticipated from the pharmacological properties of a medicinal product).

As stated in the definition, an "unexpected" adverse reaction is one where the nature or severity of which is not consistent with information in the relevant source document(s). Until source documents are amended, expedited reporting is required for additional occurrences of the reaction.

The following documents or circumstances will be used to determine whether an adverse event/reaction is expected:

- a. The Investigator's Brochure will serve as the source document for a medicinal product that is not yet approved for marketing;
- b. The local product information leaflet for a medicinal product that has been approved for marketing;
- c. Reports which add significant information on specificity or severity of a known, already documented serious ADR constitute unexpected events. For example, an event more specific or more severe than described in the Investigator's Brochure would be considered "unexpected".

## 11. Standards for Expedited Reporting

### a. What Should Be Reported

All adverse drug reactions (ADRs) that are both serious and unexpected (suspected unexpected serious adverse reactions; SUSARs) arising from ongoing clinical trials in Sri Lanka on pre-marketed and marketed products are subjected to expedited reporting.

These include reports of the following:

- SUSARs originating in Sri Lanka
- SUSARs originating outside Sri Lanka where the sponsor has an ongoing trial in Sri Lanka involving the same Investigational Medicinal Product (IMP)

The holder of a letter of authorization should send such expedited safety reports to CTEC when the minimum criteria for expedited reporting are met. The source of these expedited safety reports should always be specified.

Expedited reporting of reactions, which are serious but expected, will ordinarily be *inappropriate*. Expedited reporting is also *inappropriate* for serious events from clinical investigations that are considered not related to study product, whether the event is expected or not. Similarly, non-serious adverse reactions, whether expected or not, will ordinarily *not* be subjected to expedited reporting. Figure 1 is a flow chart of the safety reporting decision process for clinical drug trials.

### b. Reporting Time Frames

#### i. Fatal or life-threatening unexpected ADRs

Certain ADRs may be sufficiently alarming so as to require very rapid notification to regulators in countries where the medicinal product or indication, formulation, or population for the medicinal product are still not approved for marketing, because such reports may lead to consideration of suspension of, or other limitations to, a clinical investigation programme. The sponsor shall ensure that all relevant information about a **SUSAR** which occurs during the course of a clinical trial in Sri Lanka and is **fatal or life-threatening** is reported as soon as possible to the CTEC, the relevant ethics committee(s), and the investigator(s) participating in the study. This needs to be done **not later than seven (07) calendar days** after the sponsor was first aware of the reaction. This report may include an assessment of the importance and implication of the findings, including relevant previous experience with the same or similar medicinal products. This report shall be communicated to the relevant authorities in Sri Lanka through the holder of a letter of authorization.

*ii. All other serious unexpected ADRs*

Serious, unexpected reactions (ADRs) that are **not fatal or life-threatening** must be reported to the CTEC, the relevant ethics committee(s) as soon as possible but **no later than 15 calendar days** after the sponsor is first aware of the reaction. Follow-up information should be actively sought and submitted as it becomes available.

*iii. Minimum criteria for reporting*

Information for final description and evaluation of a case report may not be available within the required time frames for reporting outlined above.

Nevertheless, for regulatory purposes, initial reports should be submitted within the prescribed time as long as the following minimum criteria are met:

- An identifiable study participant;
- A suspect medicinal product;
- An identifiable reporting source;
- Event or outcome that can be identified as serious and unexpected;
- In clinical investigation cases, there is a reasonable suspected causal relationship.

Where incomplete information is available at the time of initial reporting, all the appropriate information for an adequate analysis of causality should be provided as follow-up reports as it becomes available.

*iv. Investigator responsibilities*

The investigator shall report any serious adverse event (SAE) which occurs in a participant immediately to the sponsor.

The immediate report may be made orally or in writing and shall be followed by a detailed written report on the event. Where the event reported consists of, or results in, the death of a study participant, the investigator shall supply the sponsor with any additional information requested by the sponsor. Where the death has been reported to the relevant ethics review committee, the investigator shall supply any additional information requested by that committee.

*v. Sponsor responsibilities*

The sponsor shall keep detailed records of all adverse events relating to a clinical trial which are reported to him by the investigators for that trial. The Regulatory Authority may require the sponsor to send those records, or copies of such records, to the CTEC.

A sponsor shall ensure that all relevant information about a suspected unexpected serious adverse reaction (SUSAR) which occurs during the course of a clinical trial in Sri Lanka and is fatal or life-threatening is reported as soon as possible to the CTEC, the relevant ethics committee(s), and the investigator(s) participating in the study through the holder of a letter of authorization. This needs to be done not later than **seven days** calendar after the sponsor was first aware of the reaction.

A sponsor shall ensure that a suspected unexpected serious adverse reaction (SUSAR) which is not fatal or life-threatening is reported as soon as possible, and in any event not later than **15 calendar days** after the sponsor is first aware of the reaction, to the CTEC, the relevant ethics committee(s), and the investigator(s) participating in the study through



the holder of a letter of authorization. These reports or information may be provided on paper using the CIOMS reporting form.

c. How to Report

The CIOMS-I form (Appendix 1) is a widely accepted standard for expedited adverse event reporting. The CTEC recommends the use of this format for reporting both SAEs and SUSARs. It is important that certain data elements described in Appendix 2, when available, be included in any expedited report (although some items may not be relevant depending on the circumstances).

When completing the CIOMS form, Sponsors should include the protocol number and study name. All reports must be sent to the CTEC and other official parties requiring them (e.g. Institutional Review Boards, Ethics Review Committees). Please refer to Appendix 3 for a summary of the safety reporting requirements for clinical trials to the CTEC.

# APPENDIX 1

## CIOMS-I Format

CIOMS FORM

SUSPECT ADVERSE REACTION REPORT												

### I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day Month Year	2a. AGE Years	3. SEX	4-6 REACTION ONSET Day Month Year	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION  <input type="checkbox"/> PATIENT DIED <input type="checkbox"/> INVOLVED OR PROLONGED INPATIENT HOSPITALISATION <input type="checkbox"/> INVOLVED PERSISTENCE OR SIGNIFICANT DISABILITY OR INCAPACITY <input type="checkbox"/> LIFE THREATENING
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)						

### II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)		20 DID REACTION ABATE AFTER STOPPING DRUG? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> NA
15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION	21. DID REACTION REAPPEAR AFTER REINTRO- DUCTION? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> NA
17. INDICATION(S) FOR USE		
18. THERAPY DATES (from/to)	19. THERAPY DURATION	

### III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

### IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER		
	24b. MFR CONTROL NO.	
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE <input type="checkbox"/> STUDY <input type="checkbox"/> LITERATURE <input type="checkbox"/> HEALTH PROFESSIONAL	
DATE OF THIS REPORT	25a. REPORT TYPE <input type="checkbox"/> INITIAL <input type="checkbox"/> FOLLOWUP	

### Data Elements For Inclusion In Expedited Reports Of Serious Adverse Drug Reactions

The following list of items has its foundation in several established precedents, including those of CIOMS-I, the WHO International Drug Monitoring Centre, and various regulatory authority forms and guidelines. Some items may not be relevant depending on the circumstances. The **minimum information required for expedited reporting** purposes is: an identifiable study participant, the name of a suspect medicinal product, an identifiable reporting source, and an event or outcome that can be identified as serious and unexpected and for which, in clinical investigation cases, there is a reasonable suspected causal relationship. Attempts should be made to obtain follow-up information on as many other listed items pertinent to the case.

#### 1. Study participant Details

Initials  
Other relevant identifier (clinical investigation number, for example)  
Gender  
Age and/or date of birth  
Weight  
Height

#### 2. Suspected Medicinal Product(s)

Brand name as reported  
International Non-Proprietary Name (INN)  
Batch number  
Indication(s) for which suspect medicinal product was prescribed or tested  
Dosage form and strength  
Daily dose and regimen (specify Units - e.g., mg, ml, mg/kg)  
Route of administration  
Starting date and time of day  
Stopping date and time, or duration of treatment

#### 3. Other Treatment(s)

For concomitant medicinal products (including non-prescription/OTC medicinal products) and non-medicinal product therapies, provide the same information as for the suspected product.

#### 4. Details of Suspected Adverse Drug Reaction(s)

Full description of reaction(s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious should be given. In addition to a description of the reported signs and symptoms, whenever possible, attempts should be made to establish a specific diagnosis for the reaction.

Start date (and time) of onset of reaction  
Stop date (and time) or duration of reaction  
Dechallenge and rechallenge information  
Setting (e.g., hospital, out-patient clinic, home, nursing home)

**Outcome:** information on recovery and any sequelae; what specific tests and/or treatment may have been required and their results; for a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction should be provided. Any autopsy or other post-mortem findings (including a coroner's report) should also be provided when available. Other information: anything relevant to facilitate assessment of the case, such as medical history including allergy, drug or alcohol abuse; family history; findings from special investigations.

**5. Details of Reporter of Event (Suspected ADR)**

Name  
Address  
Telephone number  
Profession (specialty)

**6. Administrative and Sponsor/Company Details**

Source of report  
Date event report was first received by sponsor/manufacturer  
Country in which event occurred  
Type of report filed to authorities: initial or follow-up (first, second, etc.)  
Name and address of sponsor/manufacture r/company  
Name, address, telephone number, and Fax number of contact person in reporting company or institution  
CTEC clinical trial application/ reference number

## APPENDIX 3

### Clinical trials safety reporting requirements and timelines to the CTEC

Nature of Report	Report (Y/N)	Timeframe of Report	Form Required	Content of Submission	Responsibility for Reporting to CTEC and relevant ethics review committee
Serious adverse events	YES	As soon as possible	CIOMS-I	Full details as available	The sponsor through the holder of a letter of authorization
Serious, Related and Unexpected Death*/Life Threatening Events	YES	7 calendar days	CIOMS-I	Full details as available	The sponsor through the holder of a letter of authorization
Serious, Related and Unexpected Non-Fatal/Non-Life Threatening Events	YES	15 calendar days	CIOMS-I	Full details as available	The sponsor through the holder of a letter of authorization

\* For reported deaths, the investigator should supply CTEC as well as the relevant ethics review committee and Sponsor with any additional requested information.

Please note that only serious, unexpected adverse drug reactions qualify for expedited reporting as reflected in this guidance. The information provided in this Appendix is only a summary. It is important for investigators to be familiar with all aspects of clinical trials safety reporting.

## **4. DEFINITIONS**

### **(a) Adverse Event (or Adverse Experience)**

Any untoward medical occurrence in a study participant or clinical investigation subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

### **(b) Adverse Drug Reaction (ADR)**

In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: 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 products” 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.

### **(c) Unexpected Adverse Drug Reaction**

An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator’s Brochure for an unapproved investigational medicinal product).

### **(d) CIOMS-I format**

A format for reporting adverse drug reactions according to the Council of International Organizations for Medical Sciences.

### **(e) Clinical Trial**

Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Interventions may include but are not restricted to substances such as drugs, cells and other biological products, vaccines, surgical procedures, radiological procedures, or any other item claimed to have therapeutic benefit. The terms “clinical trial” and “clinical study” are synonymous

### **(f) Contract Research Organization (CRO)**

A scientific organization (commercial, academic or other) to which a sponsor may transfer some of its tasks and obligations. Any such transfer should be defined in writing.

### **(g) Ethics Review Committee**

An independent body (a review board or a committee, institutional, regional or national), constituted of medical professionals and non- medical members, whose responsibility it is to verify that the safety, integrity and human rights of the subjects participating in a particular trial are protected and to consider the general ethics of the trial, thereby providing public reassurance. Ethics review committees should be constituted and operated so that their tasks can be executed free from bias and from any influence of those who are conducting the trial.

**(h) Final Report**

means a comprehensive description of the trial after its completion including a description of experimental methods (including statistical methods) and materials, a presentation and evaluation of the results, statistical analyses and a critical, ethical, statistical and clinical appraisal

**(i) Good Clinical Practices (GCP) Guidelines**

means identified ethical and scientific quality requirements which are internationally recognized and which must be observed for designing, conducting, recording and reporting clinical trials that involve the participation of human subjects. Compliance with GCP provides assurance that the rights, safety, and well-being of the study participants are protected, and the results of the clinical trials are credible;

**(j) Good Manufacturing Practices (GMP)**

means that part of pharmaceutical quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization. In these guidelines, GMP refers to the current GMP Guidelines published by WHO

**(k) Informed Consent**

Voluntary written assent of a study subject's willingness to participate in a particular clinical trial and its documentation. Such consent shall be taken only after information about the clinical trial, including an explanation of its status as research, its objectives, potential benefits, risks and inconveniences, alternative treatment that may be available and the rights and responsibilities of the study subject has been provided to the potential study subject

**(l) Investigational Medicinal Product (IMP)**

Any pharmaceutical product or placebo being tested or used as a reference in a clinical trial.

**(m) Investigational product labeling**

Labeling developed specifically for products involved in a clinical trial

**(n) Investigator**

A doctor or dentist, as the case may be, responsible for the conduct of the clinical trial and for the rights, health and welfare of the participants in the 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;

**(o) Investigator' Brochure**

A collection of data for the investigator consisting of all the relevant information on the investigational medicinal product(s), including chemical and pharmaceutical data and toxicological, pharmacokinetic and pharmacodynamic data obtained from studies in animals as well as in humans, and the results of earlier clinical trials. There should be adequate data to justify the nature, scale and duration of the proposed trial and to evaluate the potential safety and need for special precautions. If new data are generated, the investigator's brochure must be updated.

**(p) Legal representative**

In relation to a person who is to be used as a study subject in a clinical trial, an individual or judicial or other body authorized under the law to grant consent on behalf of that person, to the participation of such person in the clinical trial

**(q) Phase I clinical trials**

The first trials of a new active ingredient or new formulations in man, often carried out in healthy volunteers. Their purpose is to establish a preliminary evaluation of safety, and a first outline of the pharmacokinetic and, where possible, a pharmacodynamic profile of the active ingredient in humans.

**(r) Phase II clinical trials**

The clinical trials performed in a limited number of subjects and are often, at a later stage, of a comparative (e.g. placebo-controlled) design. Their purpose is to demonstrate therapeutic activity and to assess short-term safety of the active ingredient in patients suffering from a disease or condition for which the active ingredient is intended. This phase also aims at the determination of appropriate dose ranges or regimens and (if possible) clarification of dose response relationships in order to provide an optimal background for the design of extensive therapeutic trials.

**(s) Phase III clinical trials**

The clinical trials in larger (and possibly varied) patient groups with the purpose of determining the short and long-term safety/efficacy balance of formulation(s) of the active ingredient, and of assessing its overall and relative therapeutic value. The pattern and profile of any frequent adverse reactions must be investigated and special features of the product must be explored (e.g. clinically-relevant drug interactions, factors leading to differences in effect such as age).

These trials should preferably be of a randomized double-blind design, but other designs may be acceptable, e.g. long-term safety studies. Generally, the conditions under which these trials are carried out should be as close as possible to normal conditions of use.



**(t) Phase IV clinical trials**

Studies performed after marketing of the pharmaceutical product. Trials in phase IV are carried out on the basis of the product characteristics on which the marketing authorization was granted and are normally in the form of post-marketing surveillance, or assessment of therapeutic value or treatment strategies. Although methods may differ, these studies should use the same scientific and ethical standards as applied in premarketing studies. After a product has been placed on the market, clinical trials designed to explore new indications, new methods of administration or new combinations, etc. are normally considered as trials for new pharmaceutical products.

**(u) Principal Investigator (PI)**

A doctor or dentist, as the case may be, having specialized in the area of study and specified in an approval as the person responsible for the conduct and supervision of a clinical trial

**(v) Protocol**

A document that states the background, rationale and objectives of the trial and describes its design, methodology and organization, including statistical considerations, and the conditions under which it is to be performed and managed. The protocol should be dated and signed by the investigator, the institution involved and the sponsor. It can also function as a contract.

**(w) Sponsor**

an individual, a company, an institution or an organization which takes responsibility for the initiation, management and/or financing of a clinical trial. When an investigator initiates and takes full responsibility for a trial, the investigator then also assumes the role of the sponsor.

**(x) Study Participant**

an individual who participates in a clinical trial, either as a recipient of the investigational product under investigation or as a control. The individual may be a healthy person who volunteers to participate in a trial, a person with a condition unrelated to the use of the investigational product, a person (usually a patient) whose condition is relevant to the use of the investigational product.

## **5. RELATED LEGISLATION AND DOCUMENTS**

National Medicine Regulatory Authority Act No. 05 of 2015  
National Medicine (Clinical Trials) Regulations 2145/2, 14th October 2019  
ICH GCP guidelines

## **6. FEEDBACK**

Staff and customers may provide feedback about this document by emailing  
[pathmaperuma.a@nmra.gov.lk](mailto:pathmaperuma.a@nmra.gov.lk)