

**Guidelines for the conduct of clinical trials in  
Sri Lanka**

**Sub-Committee on Clinical Trials  
Cosmetics Devices & Drugs Regulatory Authority  
Ministry of Health**

THESE GUIDELINES ARE ISSUED BY THE  
SUB-COMMITTEE ON CLINICAL TRIALS  
MINISTRY OF HEALTH

[Version 1.0 - October 2014]

## **Introduction**

The importance of research and development in the attainment of national health, social and economic goals is well recognized. Clinical trials of therapeutic interventions following the principles of scientific experimentation that elucidate the efficacy and safety of such therapies form the basis of modern medicine by generating evidence to assess whether these treatments are of genuine benefit to our patients.

The Ministry of Health has always been committed to providing support, guidance and regulatory oversight for the conduct of clinical trials useful to this country. As part of this effort to facilitate and regulate ethical and scientific clinical research, the Sub Committee on Clinical Trial (SCOCT) was established in January 2010 to provide regulatory oversight and issue relevant approvals and certificates required for the conduct of clinical trials in Sri Lanka. In line with this mandate, the SCOCT performs regulatory, coordinating and administrative functions for clinical research under the authority of the CDDRA in the Ministry of Health.

The aim of this guidance document prepared by SCOCT is to provide comprehensive guidelines 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.

These guidelines also 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 relevant international GCP guidelines.

One of the principal objectives of this guidance note 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. This guidance note is also intended to clarify for investigators and sponsors the Regulatory Authority's expectations concerning the investigator's and sponsor's responsibilities to protect the rights, safety, and welfare of research participants whilst conducting clinical research programmes to the highest international standards.

Dr Amal Harsha de Silva  
Chairman  
Sub-Committee on Clinical Trials  
CDDRA, Ministry of Health  
Sri Lanka

October 2014

## Table of Contents

Introduction .....	III
Approvals required to conduct a clinical trial .....	1
Application for approval to conduct a clinical trial.....	2
Issue or refusal to issue approval .....	3
Suspension or revocation of an approval .....	3
Import licenses for import of study material .....	3
Responsibilities of sponsor .....	3
Responsibilities of investigator(s).....	4
Amendments to protocol & other trial-related documents.....	5
Consent required to use a person as a participant in a clinical trial .....	6
Duty to give full explanation and information to the trial participant or person entitled to give proxy consent .....	6
Participants to be treated by designated investigators .....	8
Periodic reports to the SCOCT .....	8
Notification of serious adverse events & SUSARs .....	8
Test material particulars, identification & storage .....	9
Record of clinical trials .....	10
Financial interest in clinical trial .....	10
Clinical Trial Agreement.....	10
Duty to comply with guidelines and instructions of SCOCT .....	11
Glossary .....	12

## Approvals required to conduct a clinical trial

1. A clinical trial may be initiated in Sri Lanka only after:
  - a) Obtaining approval from the Sub-Committee on Clinical Trials (SCOCT), Cosmetics Devices & Drugs Regulatory Authority (CDDRA), Ministry of Health.
  - b) Obtaining clearance from one of the following Ethics Review Committees (ERC), which are accredited by the Sub-Committee on Clinical Trials, CDDRA, Ministry of Health:
    - ERC, Faculty of Medicine, University of Colombo
    - ERC, Faculty of Medical Sciences, University of Sri Jayewardenepura
    - 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, Medical Research Institute, Colombo
    - ERC, Sri Lanka Medical Association, Colombo
  - 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 SCOCT and to the relevant ERC. However, SCOCT approval to conduct a clinical trial will be granted only after clearance from one of the ethics review committees listed under 1(b) above has been obtained for the trial.

2. Approval from the SCOCT 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 SCOCT. Such clinical trials require only ethics approval and registration with the Sri Lanka Clinical Trials Registry.

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

Phases II, III and IV clinical trials are allowed subject to the following condition:

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.

## **Application for approval to conduct a clinical trial**

4. An application for permission to conduct a clinical trial must be made to the Sub-Committee on Clinical Trials (SCOCT), CDDRA, by a suitably qualified Principal Investigator (PI) or in the case of multi-centre studies involving many investigators, the Coordinating Principal Investigator or National Coordinator, who shall be registered with the Sri Lanka Medical Council and employed by/formally attached to the Ministry of Health, a recognized healthcare institution and/or university in Sri Lanka.
5. Where a clinical trial is conducted at multiple sites in Sri Lanka only a single application is required to be submitted to the SCOCT.
6. An application for permission to conduct a clinical trial should be made in triplicate to the Sub-Committee on Clinical Trials (SCOCT) of the CDDRA in the stipulated Application Form accompanied by a covering letter and the following essential documents:
  - 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)
  - Clinical trial protocol
  - 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 SCOCT may require
7. Overseas clinical research organizations and sponsors or their subsidiaries, affiliates, or branch offices in Sri Lanka may engage in commercially-sponsored clinical trial activities at healthcare institutions in Sri Lanka only under legal agreement with recognized Sri Lankan medical research organizations who have ongoing affiliations with a local university or Ministry of Health for the conduct of clinical research or upon entering into legal agreement with local universities or research institutions/units in the Ministry of Health or private healthcare institutions possessing prior approval by SCOCT or medical associations/professional medical bodies registered in Sri Lanka possessing the required knowledge and expertise in the field of such research, and should not engage in directly recruiting patients into clinical trials.

### **Issue or refusal to issue approval**

8. The SCOCT will not issue an approval unless clearance from an Ethics Review Committee accredited by SCOCT (Section 1 of this Guideline) for the conduct of the relevant trial has been obtained and forwarded to the SCOCT along with its recommendation.
9. An approval to conduct a clinical trial issued by the SCOCT may be subject to such terms and conditions as the SCOCT may impose.
10. Every approval granted by the SCOCT may, unless it is cancelled earlier by the SCOCT, or the trial for which the approval had been issued is terminated early by the sponsor, be valid for a period of five years from the date of such approval.
11. If an extension to the period of validity of an approval is required the holder of an approval should make a request for such extension to SCOCT no less than 60 days before the expiry of initial approval.
12. An approval to conduct a clinical trial will be issued in the name of the applicant and the clinical trial should be conducted only at the site(s) specified in the approval.

### **Suspension or revocation of an approval**

13. The SCOCT may suspend or revoke an approval if it is satisfied that the holder of the approval has acted in contravention of the trial protocol, Good Clinical Practice Guidelines (GCP), or any condition subject to which the approval was issued. Where an approval is suspended or revoked the SCOCT will state its reasons for doing so, and the holder of an approval will be required to forthwith discontinue the clinical trial for which such approval was issued. Where a clinical trial is discontinued, the investigator(s) conducting the clinical trial should ensure study subjects are informed of such discontinuation and are referred to the best available standard of care in the country for the condition he has been treated for.
14. Any person aggrieved by such refusal, suspension or revocation may appeal to the CDDRA within 30 days, of receiving such notification.

### **Import licenses for import of study material**

15. Upon receiving approval for the conduct of a clinical trial from SCOCT, the holder of the approval may thereupon apply to the Medical Technology & Supplies (MT&S) Division, CDDRA, Ministry of Health, for an import license and other permits as may be necessary for the import of investigational medicinal products and other drugs and material required for the study.

### **Responsibilities of sponsor**

16. The Sponsor is responsible for implementing and maintaining quality assurance systems to ensure that the clinical trial is conducted and data generated, documented, and reported in compliance with the protocol and Good Clinical Practice (GCP) guidelines of the World Health Organization.

17. The Sponsor is required to register the clinical trial, for which the sponsor is responsible for, in the Sri Lanka Clinical Trials Registry in addition to registration with any other clinical trial registry before initiating patient screening and recruitment.
18. The Sponsor is responsible for selecting investigator(s) to conduct the study. Each investigator should be qualified by training and experience and should have adequate resources to properly conduct the study for which the investigator is selected.
19. The Sponsor is required to submit a status report on the clinical trial to the SCOCT at the prescribed periodicity and a final report of the clinical trial within six months (06) after the completion of the trial or such further period as the SCOCT may allow. In case of premature discontinuation of studies for any reason, a summary report should be submitted within three (03) months of such discontinuation.
20. The sponsor is responsible for the ongoing safety evaluation of the investigational medicinal product(s). The sponsor should promptly notify other investigator(s) participating in the trial, the SCOCT and the relevant Ethics Review Committee of findings that could affect adversely the safety of study participants or impact the conduct of the trial.
21. The sponsor should ensure that the investigational medicinal products, including active comparators and placebo if applicable, is manufactured in accordance with the principles and guidelines of Good Manufacturing Practice (GMP) for medicinal products of the WHO or similar accreditation body.
22. The sponsor should ensure that the product label on outer packaging of investigational medicinal products or, where there is no outer packaging, on the immediate packaging, contains standard, internationally accepted information in English. Unused investigational product(s) should be returned to the sponsor or alternative disposition if authorized by the sponsor and in compliance with the applicable regulatory requirement(s).
23. The sponsor should ensure laboratories used for generating data for clinical trials should be compliant with Good Laboratory Practices.

### **Responsibilities of investigator(s)**

24. Every clinical trial should be conducted under the charge and supervision of a principal investigator. All trial investigator(s), including the principal investigator(s) should possess appropriate qualifications, training, and experience and should have access to such investigational and treatment facilities as are relevant to the trial protocol.
25. The investigator is responsible for the conduct of the trial according to the protocol and GCP Guidelines. The investigator is responsible for giving adequate information to the study participant in respect of the clinical trial in accordance with the GCP Guidelines of the World Health Organization. The investigator should have adequate resources and facilities for the foreseen duration of the trial to conduct the trial to these standards.
26. The investigator should ensure that adequate free medical care is provided to the study subject if there is a trial-related injury until such time as the study subject is completely recovered from the effects of such injury. The investigator should have at the time of applying for a clinical trial approval, entered into an agreement with the sponsor to ensure availability of finances for this purpose.



27. The investigators should be familiar with the appropriate use of the investigational medicinal products, as described in the trial protocol, the investigator's brochure, and in other sources of information provided by the sponsor. The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, investigational product(s), and their trial-related duties and functions.
28. The investigator should submit any information or reports including progress reports to the Sponsor, SCOCT and the relevant Ethics Review Committee at such times as may be required by the Sponsor, SCOCT or the relevant Ethics Review Committee.
29. Where there is a change of principal investigator at a site during a clinical trial, the holder of an approval should forthwith notify the SCOCT of the change and should furnish particulars of the new principal investigator to the SCOCT and to the relevant Ethics Review Committee.

### **Amendments to protocol & other trial-related documents**

30. If amendment(s) to the trial protocol and other trial-related documents (e.g. investigator's brochure, informed consent documents) become necessary before initiation or during the course of a clinical trial, all such amendments should be dealt with as outlined below:

Protocol amendments, which do not require any communication or approval from the SCOCT:

- a) Administrative and logistic changes
- b) Minor protocol amendments and additional safety assessments that have received approval from the relevant Ethics Review Committee

Protocol amendments, which require to be informed to the SCOCT and the relevant Ethics Review Committee as notifications, but need not wait for approval:

- a) Inclusion of additional investigator sites
- b) Amendments that are made to the investigator's brochure and resulting amendments to informed consent documents
- c) Change of principal investigator if he is not the holder of the approval
- d) Recruitment of additional study participants

Protocol amendments, which require prior approval from the SCOCT and relevant Ethics Review Committee before implementation of the amendments:

- a) Change of Principal Investigator if he is the holder of the approval
- b) Substantial amendments to the protocol

Substantial amendments to the conduct of the clinical trial may arise from changes to the protocol or from new information relating to the scientific documents in support of the trial. Amendments to the trial are regarded as "substantial" where they are likely to have a significant impact on: the safety or physical or mental integrity of the subjects, or the scientific value of the trial, or the conduct or management of the trial, or the quality or safety of any investigational medicinal products used in the trial.

### **Consent required to use a person as a participant in a clinical trial**

31. In all clinical trials, a freely given, informed, written consent is required to be obtained from each study participant. The Investigator must provide information about the study verbally as well as using a patient information sheet, in a language that is non-technical and understandable to the study participant.
32. An investigator should not use a person as a participant in a clinical trial unless the following are satisfied:
  - (a) In the case of a person of or above the age of 18 years, with the consent of that person
  - (b) In the case of a person below the age of 18 years, with the consent of that person and;
    - (i) that person's parent or guardian (if there is no parent) and
    - (ii) If different from sub-paragraph (i) above, the legal representative of that person.
33. Where a participant is not able to give informed consent (e.g. an unconscious person or a minor or those suffering from severe mental illness or disability), assent may be obtained from a legally acceptable representative of that person (a legally acceptable representative is a person who is able to give consent for or authorize an intervention in the patient as provided by the law(s) of Sri Lanka). If the participant or his/her legally acceptable representative is unable to read/write, an impartial witness should be present during the entire informed consent process who must attest all documents related to the informed consent process.
34. No person should, by means of any threat or coercion, compel or induce another person to be a participant in a clinical trial.

### **Duty to give full explanation and information to the trial participant or person entitled to give proxy consent**

35. Before a clinical trial is carried out or conducted, the principal investigator should give the participant and any person giving consent on behalf of the participant, a full and reasonable explanation of the following:
  - (a) That the clinical trial involves research
  - (b) The purpose of the clinical trial
  - (c) The treatments to be administered in the clinical trial and the probability for random assignment of each treatment
  - (d) The procedures to be followed in the clinical trial, including all invasive procedures
  - (e) The responsibilities of the participant
  - (f) The aspects of the clinical trial which are experimental
  - (g) The reasonably foreseeable risks or inconveniences to the participant and, where applicable, to any embryo, foetus or nursing infant
  - (h) The reasonably expected benefits, including whether there is any intended clinical benefit to the participant

- (i) Any alternative procedures or treatments available to the participant, and their potential benefits and risks
  - (j) Any compensation and free treatment available to the participant in the event of injury arising from participation in the clinical trial
  - (k) Any anticipated expenses to the participant from participating in the clinical trial
  - (l) Any pro-rated payment to the study participant for participating in the clinical trial
  - (m) That participation in the clinical trial is voluntary and that the participant may refuse to participate in or may withdraw from the clinical trial at any time without penalty or loss of benefit, which the participant would otherwise be entitled
  - (n) The persons who will be granted access to the subject's medical records and the extent of such access, including the possibility that the licensing authority may inspect the records
  - (o) The extent to which records identifying the subject will be kept confidential
  - (p) That the subject or his legally acceptable representative will be informed in a timely manner of any information becoming available which may be relevant to the participant's willingness to continue participating in the clinical trial
  - (q) The persons to contact for further information relating to the clinical trial and the rights of participants and in the event of injury arising from participation in the clinical trial
  - (r) Sponsorship, if any, with name of sponsor, any interests or conflicts of interest declared by the investigators, and name/contact details of the Ethics Review Committee that gave approval to the trial
  - (s) Any foreseeable circumstances under or reasons for which the participant's participation may be terminated
  - (t) The expected duration of the participant's participation in the clinical trial
  - (u) The approximate number of participants involved in the clinical trial
  - (v) Any other information that the SCOCT may require to be given
  - (w) Any other information which the study participant may request to know
36. If any information becomes available which may be relevant to a subject's willingness to continue participating in a clinical trial, the holder of an approval should, at the earliest feasible opportunity, give to the participant or his legally acceptable representative a full and reasonable explanation of that information.
37. If a person referred to in section 32 is used as a participant in a clinical trial and subsequently becomes capable of giving his own consent, the holder of an approval should, at the earliest feasible opportunity, give to that person a full and reasonable explanation of the matters referred to in section 34 and request his/her consent to continue to be used as a participant in the clinical trial.

38. If a participant in a clinical trial refuses to give consent referred to in section 30, the principal investigator should immediately cease to use that person as a participant in the clinical trial.

### **Participants to be treated by designated investigators**

39. During the conduct of a clinical trial, no person, other than a holder of an approval, or a designated principal investigator approved by SCOCT, or any person assisting him in a clinical trial should treat a study participant or administer any test material to such study participant.
40. In an emergency, any doctor or dentist may, in the absence of the holder of an approval, or a designated principal investigator approved by SCOCT or any person assisting him in the clinical trial, treat a study participant if it is in the interest of the study participant.

### **Periodic reports to the SCOCT**

41. The SCOCT 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 SCOCT may require.
42. The holder of an approval should submit to the SCOCT a final report of the clinical trial within six (06) months after the completion of the trial or such longer period as the SCOCT may allow.

In case a clinical trial is prematurely discontinued for any reason a summary report should be submitted within three (03) months. This report 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.

### **Notification of serious adverse events & SUSARs**

43. The investigator(s) should report all serious adverse events (SAEs) immediately to the sponsor except for those SAEs the protocol or investigator's brochure identifies as not requiring immediate reporting. The immediate reports should be followed promptly by detailed, written reports. All SAEs occurring at trial sites in Sri Lanka should be reported as soon as possible to the SCOCT and the relevant Ethics Review Committee by the sponsor.
44. A "serious adverse event" means any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease, whether or not caused by the use of the test material, which;
- (a) results in death,
  - (b) is life-threatening,
  - (c) requires in-patient hospitalization or prolongation of existing hospitalization,
  - (d) results in persistent or significant disability or incapacity, or
  - (e) causes any congenital anomaly or birth defect.
45. All adverse drug reactions that are both serious and unexpected (SUSAR) are subject to expedited reporting. The principal investigator(s) should report all serious and unexpected adverse drug reactions occurring during a clinical trial to the sponsor as soon as possible, but

no later than twenty four hours after he was first aware of the reaction. The sponsor should report any serious unexpected adverse drug reaction (as defined in the Good Clinical Practices (GCP) Guidelines of the World Health Organization) in CIOMS-I format as soon as possible, but no later than fifteen calendar days after the sponsor was first aware of such reaction to the SCOCT, the relevant Ethics Review Committee and the investigator(s) participating in the clinical trial. Any fatal or life-threatening serious unexpected adverse drug reaction should be reported by the sponsor to the SCOCT, the relevant Ethics Review Committee and the investigators participating in the clinical trial as soon as possible, but no later than seven calendar days after the sponsor was first aware of such reaction. All serious and unexpected adverse drug reactions related to the same investigational product reported from all sites involved with the same trial protocol driven clinical trial, should be reported with a causality statement by sponsor to the SCOCT and the relevant Ethics Review Committee that accorded approval to the trial protocol in the form of quarterly line listed reports.

### **Test material particulars, identification and storage**

46. The sponsor must ensure that the investigational product(s), including active comparator(s) and placebo if applicable, is manufactured in accordance with the principles and guidelines of Good Manufacturing Practice (GMP) for medicinal products of the WHO or similar accreditation body.
47. The sponsor must ensure that the product label on outer packaging of investigational medicinal product(s) or, where there is no outer packaging, on the immediate packaging, contains standard, internationally accepted information in English, which should include the following:
  - (a) The reference number or other unique identification mark of each item of such material
  - (b) A trial reference code allowing identification of the trial, site, investigator and sponsor if not given elsewhere
  - (c) The date of manufacture and the expiry date of the test material
  - (d) The storage conditions appropriate for each item of test material as may be indicated by the manufacturer, and
  - (e) The words: "For Clinical Trial Use Only" or similar wording
  - (f) 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
48. No test material should be used in a clinical trial if the container in which the test material is stored is not marked and labeled with the particulars specified in section 47.
49. If any code or cipher is used in the labeling of a test material, the key to the code or cipher should be made available to any doctor or dentist in an emergency and it should be made known to the SCOCT.
50. The Sponsor should ensure all investigational medicinal products are stored in such manner as to be easily identifiable. If the investigational medicinal products cannot be identified, such investigational medicinal products should not be used and should be surrendered to the CDDRA.

51. The sponsor should ensure that written procedures include instructions that the investigator/institution should follow for the handling and storage of investigational product(s). The procedures should address adequate and safe receipt, handling, storage, dispensing, retrieval of unused product from study participant, and return of unused investigational product(s) to the sponsor or alternative disposition if authorized by the sponsor and in compliance with the applicable regulatory requirement(s).

### **Records of clinical trials**

52. The sponsor or holder of an approval should keep adequate clinical records of each study participant for the duration of the clinical trial.
53. The sponsor or holder of an approval should ensure that such records are:
- (a) Available at all times for inspection by the SCOCT or any person or body authorized by the SCOCT in that behalf, and kept up to date at all times,
  - (b) Kept at least for whichever of the following periods that expires later;
    - (i) until there are no pending or contemplated marketing applications of the test material in Sri Lanka,
    - (ii) two (02) years after the last approval of a marketing application for the test material in Sri Lanka,
54. Where the approval for clinical trial is withdrawn or clinical trial is discontinued records shall be maintained for two (02) years after such withdrawal or two (02) years after the SCOCT has been informed of the discontinuation of the clinical trial.
55. Where a clinical trial is completed, records relating to such clinical trial should be maintained for
- (a) Ten (10) years after the completion of the clinical trial, or
  - (b) Such other period as the SCOCT may direct taking into consideration any additional information that is submitted to it.

### **Financial interest in clinical trial**

56. The holder of an approval or any person assisting him in a clinical trial or any participant in a clinical trial must not, directly or indirectly, have any financial interest in the business of the sponsor of the clinical trial.

### **Clinical Trial Agreement**

57. A Clinical Trial Agreement (CTA) is a contract, which describes an agreement between two or more persons/institutions that create an obligation to undertake, or refrain from undertaking, a particular action.
58. All commercially sponsored research carried out in Sri Lanka must have a fully executed contract otherwise known as a Clinical Trial Agreement (CTA) before the study starts. All parties must sign a written agreement that defines the scope of work and formalizes the understanding between the parties. This agreement must define the scope of work, establish

acceptable payment arrangements, and address important issues such as the right to publish research results, protection of confidential information, compensation in case of serious trial-related injury to study participants and circumstances for indemnification.

59. All CTAs for research projects to be conducted at healthcare institutions must be;
- (a) signed by an approved institutional signatory (e.g. Medical Director) or a no-objection certificate should be issued by the Head of such Institution, as the case may be,
  - (b) signed by the relevant principal investigator,
  - (c) signed by the sponsor of the study or designated person by the sponsor (e.g. CRO), and
  - (d) signed by other parties such as local coordinator where relevant.

**Duty to comply with guidelines and instructions of SCOCT**

60. Every sponsor, principal investigator or holder of an approval must comply with all guidelines or instructions relating to the conduct of clinical trials issued by the SCOCT.

## Glossary

- “Adverse Event (AE)” means any untoward medical occurrence in a patient 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 (investigational) product;
- “Adverse Drug Reaction (ADR)” means a response to a pharmaceutical product that is noxious and unintended and which occurs at doses normally used or tested in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function. In clinical trials, injuries caused by overdosing, abuse or dependence and interactions with any other product should be considered adverse reactions.
- “CIOMS-I format” means a format for reporting adverse drug reactions according to the Council of International Organizations for Medical Sciences.
- “Clinical trial” means 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;
- “Contract research organization (CRO)” means 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.
- “Drug” includes a group of drugs.
- “Ethics review committee” means 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.
- “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
- “Good Clinical Practice (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 trial subjects are protected, and the results of the clinical trials are credible;

“Good Manufacturing Practice (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.

“Informed consent” means 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;

“Investigational medicinal product” means any pharmaceutical product or placebo being tested or used as a reference in a clinical trial.

“Investigational product labeling” means labeling developed specifically for products involved in a clinical trial

“Investigator” means 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;

“Investigator’s Brochure” means 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.

"Legal representative", in relation to a person who is to be used as a study subject in a clinical trial, means 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;

“Pharmaceutical product” means any substance or combination of substances which has a therapeutic, prophylactic or diagnostic use, or is intended to modify physiological functions, and is presented in a dosage form suitable for administration to humans.

“Phase I clinical trials” mean 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.

“Phase II clinical trials” mean 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.

“Phase III clinical trials” mean 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.

“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.

"Principal Investigator (PI)" means 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.

“Protocol” means 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.

“Serious Adverse Event (SAE)” or “Serious Adverse Reaction (SAR)” means 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 a congenital anomaly/birth defect.

“Sponsor” means 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.

“Standard operating procedure (SOP)” means standard, detailed, written instructions for the management of clinical trials. They provide a general framework enabling the efficient implementation and performance of all the functions and activities for a particular trial as described in this document.

“Study participant” means 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.

“Unexpected adverse drug reaction” means 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).

“Witness” means person who will not be influenced in any way by those who are involved in the clinical trial, who is present and may provide assistance if required when the participant’s informed consent is obtained, and documents that this consent is given freely by signing and dating the informed consent form.