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PART I : SECTION (I) — GENERAL

Government Notifications

L.D. – B 9/2016 (II)

NATIONAL MEDICINES REGULATORY AUTHORITY ACT, No. 5 OF 2015

REGULATIONS made by the Minister of Health, Nutrition and Indigenous Medicine under section 142 of the National Medicines Regulatory Authority Act, No.5 of 2015 read with section 3(k) of the aforesaid Act.

RAJITHA SENARATNE,

Minister of Health, Nutrition and Indigenous Medicine.

Colombo,
11th October, 2019.

Regulations

1. These regulations may be cited as the National Medicines (Clinical Trials) Regulations, 2019.

PART I

APPLICATION FOR A LETTER OF AUTHORIZATION TO CONDUCT CLINICAL TRIALS

2. (1) No person shall conduct or cause or permit to be conducted a clinical trial for the following categories of medicines, medical devices and borderline products except under the authority of a letter of authorization issued in that behalf by the National Medicines Regulatory Authority established under section 2 of the National Medicines Regulatory Authority Act, No.5 of 2015 (in these regulations referred to as the “Authority”)-

- (a) unregistered medicines, medical devices or borderline products;



- (b) registered medicines, medical devices or borderline products where the proposed clinical trial is outside the conditions of such registration and they may include changes to the –
 - (i) indications and clinical use;
 - (ii) target patient populations;
 - (iii) routes of administration; and
 - (iv) dosage regimens.
 - (2) A clinical trial for any category of medicine, medical devices and borderline products other than the categories specified in subsection (1) may be conducted without a clinical trial authorization issued by the Authority.
 - (3) The Authority shall have the power to delegate in writing to any officer of the Authority to issue letters of authorization in respect of clinical trials.
3.
 - (1) A Principal Investigator with appropriate qualifications or in the case of multi centre studies, the Coordinating Principal Investigator or National Coordinator may make parallel applications to the Authority and Ethics Review Committee for a letter of authorization to conduct a clinical trial and an ethics approval respectively.
 - (2) Every application for the issue of a letter of authorization shall be made in the form as may be determined by the Authority and every application for ethics approval shall be made in the form as may be determined by the Ethics Review Committee.
 - (3) Every application submitted under subsection (2) to the Authority shall contain complete and accurate information of all required particulars and be accompanied by a fee specified in Registration and Licensing of Medicines (fees) Regulations, No. 02 of 2017 as amended, Registration and Licensing of Medical Devices (fees) Regulations, No. 03 of 2017, Registration and Licensing of Borderline Products (fees) Regulations, No. 04 of 2017 published in the *Gazette* Extraordinary No. 2023/30 of June 14, 2017.
 - (4) An application found to contain false, misleading or incorrect information or particulars shall be rejected.
4.
 - (1) Where a clinical trial is conducted at multiple sites in Sri Lanka, a single application shall be required to be submitted to the Authority for a letter of authorization.
 - (2) Every applicant under regulation 3(1) shall submit to the Authority an approval from an Ethics Review Committee for the issue of a letter of authorization.
 - (3) The Clinical Trials Evaluation Committee shall be charged with the task of regulatory review of clinical trials, including assessment of the scientific merit, relevance, risk involved and the expected benefits of each trial protocol.
 - (4) The Authority may, having considered the approval of the Ethics Review Committee and the evaluation of the Clinical Trials Evaluation Committee in relation to the respective clinical trial, issue a letter of authorization for the conduct of the clinical trial or refuse to issue a letter of authorization for reasons assigned therefor.
 - (5) An applicant may withdraw such application at any time prior to the issue of letter of authorization, by notifying the Authority in writing, without prejudice to his right to submit a fresh application. In such circumstances, the application and records relating to such clinical trial shall be maintained by the Authority for a period of two years from the date of withdrawal.

5. (1) A letter of authorization issued under regulation 4, shall-
- (a) be in such form as the Authority may determine;
 - (b) be subject to such terms and conditions as specified in the letter of authorization as the Authority may think appropriate;
 - (c) become operative from such date as shall be specified in the letter of authorization;
 - (d) unless earlier suspended or cancelled or the letter of authorization is terminated by sponsor prior to the expiry of the letter of authorization, be in force for a period specified in the letter of authorization; and
 - (e) specify the site or sites at which the clinical trial is to be conducted.
- (2) The Authority may from time to time, by notice in writing to the holder of a letter of authorization modify or remove any condition on the letter of authorization, or attach any new condition to the letter of authorization with justification.
6. (1) A clinical trial shall be conducted at the site as may be specified in the letter of authorization.
- (2) A multi-centre clinical trial may be conducted at more than one site as may be specified in the letter of authorization.
- (3) Any individual member of the clinical trial may be designated as sub-investigator and supervised by the principal investigator at the clinical trial site to perform clinical trial related procedures.
7. (1) Any Overseas clinical research organization and any sponsors or their subsidiaries, affiliates or branch offices in Sri Lanka shall prior to being engaged in any clinical trial activity -
- (a) enter into an agreement with any recognized Sri Lankan medical research organization, which has ongoing affiliation with a University established or deemed to be established under the Universities Act, No. 16 of 1978 or Ministry of Health for the conduct of clinical research; or
 - (b) enter into an agreement with a University established or deemed to be established under the Universities Act, No. 16 of 1978 or research institution or unit functioning under the Ministry of Health or private healthcare institutions or medical associations or professional medical bodies registered in Sri Lanka with the prior written approval of the Authority to conduct clinical trials possessing the required knowledge, experience and expertise in the field of such research.
- (2) The overseas clinical research organization shall not engage any clinical trial activity or recruit patients into clinical trials prior to such agreement.
8. (1) An applicant shall have at the time of applying for a letter of authorization for a clinical trial, entered into an agreement with the sponsor to ensure availability of finances to provide medical care to the study participant in case of a clinical trial related injury until such time as the study participant is completely recovered from the effects of such injury.
- (2) In the case of clinical trial-related injury to the study participant, the medical treatment and, the method and manner of compensation to the study participant shall be in compliance with guidelines issued by the Authority.
9. All clinical trial participants shall be satisfactorily insured against possible injuries that might arise during the conduct of the clinical trial and a valid insurance certificate for the duration of the study shall be provided prior to study initiation.

- 10.** The Authority may consider expedited review of a clinical trial application as a non-routine procedure for a therapy with the potential to address an unmet medical need, especially during a global pandemic, a national epidemic or other similar emergency situation.
- 11.** (1) The period of validity specified in the letter of authorization may be extended upon a request made for that purpose to the Authority, not less than sixty days prior to the date of expiration of the letter of authorization previously issued. Every such request shall include the reasons for the extension.
- (2) The holder of a letter of authorization shall, prior to such request get extended the period of validity specified in the approval of the Ethics Review Committee.
- (3) The Authority may extend the time period of validity under subsection (1), where-
- (a) the holder of a letter of authorization has not violated or done anything in contravention of the terms and conditions of the letter of authorization issued;
 - (b) the holder of a letter of authorization has not contravened any provisions of the National Medicines Regulatory Authority Act, No.5 of 2015 or any regulations made thereunder or the clinical trial protocol or the Good Clinical Practice Guidelines or ethical principles or, guidelines issued under these regulations; or
 - (c) the continuation of the clinical trial concerned will not have any adverse impact on the study participant; and
 - (d) it is necessary to enable the investigator to complete such clinical trial for reasons to be recorded by the Authority.
- (4) The Authority may verify the legitimacy of the request and if the Authority is satisfied with the legitimacy of such request, within thirty days of receipt of such request, grant such extension for a further period as may be determined by Authority to enable the investigator to complete such clinical trial or for reasons to be recorded by the Authority, refuse to extend the period of such letter of authorization.
- 12.** (1) A letter of authorization issued under regulation 4 may be suspended by the Authority, where-
- (a) it becomes necessary in order to implement any management measures adopted in consequence of a determination made by the Authority;
 - (b) the holder of a letter of authorization has been charged for the commission of an offence under the provisions of the National Medicines Regulatory Authority Act, No.5 of 2015 or any regulations made thereunder; or
 - (c) the holder of a letter of authorization has contravened any provisions of the National Medicines Regulatory Authority Act, No.5 of 2015 or any regulations made thereunder or the clinical trial protocol or the Good Clinical Practice Guidelines or ethical principles or, guidelines issued under these regulations, and the severity of such contravention does not warrant a cancellation of the letter of authorization.
- (2) Where a letter of authorization is suspended under paragraph (a) of subsection (1), the holder of a letter of authorization shall be entitled to a pro rata refund of the fee paid by him for the issue of the letter of authorization.
- 13.** (1) A letter of authorization issued under regulation 4 shall be cancelled by the Authority, where -
- (a) it is found that the letter of authorization had been obtained by providing false, misleading or inaccurate information;

- (b) the holder of a letter of authorization has been convicted of an offence under the provisions of the National Medicines Regulatory Authority Act, No.5 of 2015 or any regulations made thereunder or the clinical trial protocol or the Good Clinical Practice Guidelines or ethical principles or, guidelines issued under these regulations;
 - (c) the holder of a letter of authorization has acted in contravention or in violation of any terms or conditions subject to which such letter of authorization was issued; or
 - (d) the continuation of the clinical trial concerned will have adverse impact on the study participant.
- (2) Where a letter of authorization issued is suspended or cancelled as the case may be under regulation 12 or this regulation, it shall be the duty of the Authority to forthwith inform the holder of a letter of authorization of such suspension or cancellation, by a written communication together with reasons therefor.
- (3) Upon the suspension or cancellation under sub-regulation (2), the holder of a letter of authorization shall discontinue the clinical trial for which the letter of authorization was issued.
- 14.** Upon the suspension or cancellation of a letter of authorization, or discontinuation, the investigator shall ensure study participants or legally acceptable representatives are informed of such suspension, cancellation or discontinuation, and reasons therefor and adequate medical care is provided to the study participants.
- 15.** (1) In the event of a premature discontinuation of a clinical trial, the Authority shall forthwith take steps to cancel such letter of authorization.
- (2) A summary report should be submitted within three months to the Authority and the relevant Ethics Review Committee. This report shall 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 reasons for discontinuation.
- (3) Where it is later proposed to carry on the same clinical trial, a fresh letter of authorization shall be obtained therefor.
- 16.** (1) Any person aggrieved by a decision refusing the issue or renewal, as the case may be, of a letter of authorization or the suspension or cancellation of a letter of authorization issued, may, within thirty days of the date of receipt of the written communication informing such person, of the refusal or the suspension or cancellation, as the case may be, appeal against such decision to the Appeals Committee appointed under section 123 of the National Medicines Regulatory Authority Act.
- (2) The decision on any appeal submitted under subsection (1) shall be made within sixty days of the receipt of such appeal and the person making such appeal shall be informed of the decision made on it, forthwith.
- (3) Where the Appeals Committee considers it appropriate, it may hold such inquiry as deem necessary in the circumstances of the case, prior to arriving at any decision on any appeal made to it under subsection (1).
- (4) The decision of the Appeals Committee on any appeal made under this section, shall be final.

PART II

CONDUCT OF CLINICAL TRIALS

17. The applicant to whom a letter of authorization issued or renewed under these regulations (hereinafter referred to as the “holder of a letter of authorization”), sponsor and investigator shall comply with the guidelines issued by the Authority in respect of any clinical trial.
18. The holder of a letter of authorization and the other principal investigators designated in such letter of authorization shall commence the clinical trial in Sri Lanka upon-
 - (a) the approval issued by an Ethics Review Committee recognized by the Authority;
 - (b) issue of letter of authorization to conduct for a clinical trial from the Authority;
 - (c) the registration of the clinical trial on Sri Lanka Clinical Trial Registry; and
 - (d) the approval or no-objection certificate from the head of the institution in charge of the clinical trial site or sites, as the case may be, specified in the letter of authorization.
19. The holder of a letter of authorization or his designated nominee in Sri Lanka shall thereupon apply to the Authority for an import license and such other permits as may be necessary for the import of investigational medicinal products and other drugs and devices and material required for the study.
20. (1) Every clinical trial shall be conducted under the charge and supervision of a principal investigator. All investigators, including the principal investigator shall possess appropriate qualifications, training, and experience and shall have access to such investigational and treatment facilities as are relevant to the clinical trial protocol.
(2) All investigators in a clinical trial shall have formal training in Good Clinical Practice (GCP) and a valid GCP certificate.
21. All clinical trials, including bioavailability and bioequivalence studies shall be designed, conducted and reported in accordance with the clinical trial protocol, the principles of ICH Good Clinical Practice (GCP) Guidelines, and other applicable requirements.
22. (1) Every holder of a letter of authorization shall, where there is a change of principal investigator at a clinical trial site during any clinical trial, forthwith inform such fact to the Authority, and furnish particulars of the new principal investigator to the Authority and the relevant Ethics Review Committee.
(2) Any site involved in a clinical trial may be subjected to the Good Clinical Practice inspection by the Authority.
23. The holder of a letter of authorization shall where at such times and such manner as the Authority may require such holder of a letter of authorization to provide any information or report in respect of the clinical trial for which the letter of authorization has been issued, comply with such requirement.
24. The holder of a letter of authorization shall submit to the Authority a final report of the clinical trial within a period of six months after completion of such clinical trial or within such a longer period as the Authority may determine.
25. Where any clinical trial is completed, the records relating to such clinical trial shall be maintained for a period of ten years after the completion of such clinical trial or such other period as the Authority may determine taking into consideration the additional information submitted to it.

- 26.** The holder of a letter of authorization or the sponsor, as the case may be, keep adequate clinical records of each study participant for the duration of the clinical trial and ensure that –
- (a) such records are available at all times for inspection by the Authority or any person authorized by the Authority in that behalf; and
 - (b) such records are kept at least until there are no pending or contemplated marketing applications of the investigational medicinal product in Sri Lanka or for two years after the last approval of a marketing application for the investigational medicinal product in Sri Lanka, which ever expires later.
- 27.** Where the site for a clinical trial is a government healthcare institution or a private hospital and the study participants are in-patients of such institution or hospital, relevant records shall be maintained in the source notes of such patient in respect of the clinical trial.
- 28.** (1) The clinical trial protocol may be amended if any amendments become necessary before initiation or during the conduct of a clinical trial.
- (2) (a) Any amendment to a clinical trial protocol which relates only to administrative and logistic changes or minor amendments and additional safety assessments to which an Ethics Review Committee has already granted approval shall not require an approval of the Authority.
 - (b) Any amendment to a clinical trial protocol under paragraph (a) shall be recorded and be available upon request for inspection at the clinical trial site.
- (3) Any amendment to the clinical trial which relates to changes to the following shall be communicated as a notification to Authority and relevant Ethics Review Committee -
- (a) inclusion of additional investigator sites;
 - (b) amendments which are made to the investigator's brochure;
 - (c) amendments to the informed consent form to be given to a study participant of a specific clinical trial;
 - (d) change of principal investigator if he is not the holder of a letter of authorization; or
 - (e) recruitment of additional study participants.
- (4) (a) Any amendments, which require prior approval from the Authority and relevant Ethics Review Committee before implementation of the amendments-
- (i) change of principal investigator if he is the holder of a letter of authorization for clinical trial; and
 - (ii) substantial amendments to the protocol.
- (b) Any 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 clinical trial.
- (c) Any amendments to the clinical trial are regarded as “substantial” where they are likely to have a significant impact on the safety or physical or mental integrity of the participants, or the scientific value of the clinical trial, or the conduct or management of the clinical trial, or the quality or safety of any investigational medicinal product used in the clinical trial
- (5) Any amendments made to the clinical trial protocol under this regulation shall be agreed upon and signed by the persons who are the signatories to such clinical trial protocol.

PART III

CONSENT OF STUDY PARTICIPANTS OF A CLINICAL TRIAL

- 29.** No person shall, by means of any threat or coercion, compel or induce another person to be a study participant in a clinical trial.
- 30.** (1) In all clinical trials, a freely given, informed and written consent shall be obtained from each study participant.
- (2) The principal investigator shall provide to the study participant, information about the study verbally and using a patient information document in the form as may be determined by the Authority. Such form shall be in a language that is non-technical and understandable by the study participant, to which the consent of the study participant shall be obtained in writing.
- 31.** (1) An investigator shall not use a person as a study subject in a clinical trial unless the following requirements 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 assent of that person and consent of -
- (i) the parent or guardian (if there is no parent) of that person; and
- (ii) if different from sub-paragraph (i), the legal representative of that person.
- (2) Where a study participant is not able to give informed consent in the manner as specified in these regulation (e.g. an unconscious person or a minor or those suffering from severe mental illness or disability), the assent of such person may be obtained from a manager, guardian, curator or next of kin appointed by Court in terms of the Civil Procedure Code (Chapter 101).
- (3) If the study participant or manager, guardian, curator or next of kin as the case may be is unable to read or write, an impartial witness shall be present during the entire informed consent process and such witness shall be required to attest all the documents relating to the informed consent process.
- (4) For the purpose of this regulation, “an impartial witness” means a person who is independent of the clinical trial and not influenced by the persons who are involved in the clinical trial and shall attend the entire informed consent process where the study participant or manager, guardian, curator or next of kin as the case may be is unable to read or write. Such witness shall read the informed consent form and any other relevant information supplied to the study participant and sign and personally date the consent form.
- 32.** Prior to the commencement of a clinical trial, the principal investigator or his nominee shall give the study participant and any person giving consent on behalf of a study 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 to the study participant 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 study participant;
- (f) the aspects of the clinical trial which are experimental;
- (g) the reasonably foreseeable risks or inconveniences to the study subject and, where applicable, to any embryo, fetus or nursing infant;
- (h) the reasonably expected benefits, including whether there is any intended clinical benefit to the study participant;
- (i) any alternative procedures or treatments available to the study participant, and their potential benefits and risks;
- (j) any compensation and free treatment to the study participant in the event of injury arising from participation in the clinical trial and compensation in the case of disability or death resulting from such injury;
- (k) any pro-rated payment to the study participant for participating in the clinical trial;
- (l) any anticipated expenses to the study participant from participating in the clinical trial;
- (m) that the participation of the study participant in the clinical trial is voluntary and that he may refuse to participate in or may withdraw from the clinical trial at any time without penalty or loss of benefit which the study participant would otherwise be entitled to;
- (n) the persons who will be granted access to the medical records of the study participant 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 study participant will be kept confidential;
- (p) that the study participant or his legal representative will be informed in a timely manner of any information becoming available which may be relevant to the study 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 study participants and in the event of injury arising from participation in the clinical trial;
- (r) any foreseeable circumstances under or reasons for which the participation of the study participant may be terminated;
- (s) the expected duration of participation of the study participant in the clinical trial;
- (t) the approximate number of study participants involved in the clinical trial;
- (u) sponsorship, if any, with name of sponsor, any interests or conflict of interests declared by the investigator and contact details of the Authority and the Ethics Review Committee;
- (v) any other information which the licensing authority may require to be given; and
- (w) any other information which the study participant may request to know.

33. If any information becomes available which may be relevant to a study participant's willingness to continue participating in a clinical trial, the investigator shall, at the earliest feasible opportunity, give to the study participant or his legal representative a full and reasonable explanation of that information.
34. If a person specified in regulation 31(2) is used as a study participant in a clinical trial and subsequently becomes capable of giving his own consent, the principal investigator shall, at the earliest feasible opportunity, give to that person a full and reasonable explanation of the matters referred to in regulation 32 and request the consent of the study participant to continue to be used as a study participant in the clinical trial.
35. If a study participant in a clinical trial refuses to give or withdraws consent as required by this regulation, the investigator shall immediately cease to use that person as a study participant in the clinical trial.
36. During the continuance of a clinical trial, no person, other than the holder of a letter of authorization or a designated principal investigator or any person assisting him in a clinical trial shall treat a study participant or administer any test material to such study participant.
37. In an emergency, any doctor or dentist may, in the absence of the holder of a letter of authorization or a designated principal investigator or any person assisting him in the clinical trial, treat a study participant if it is in the interest of the study participant.
38. The Authority, or any other person including the investigator, sponsor or any member of the Ethics Review Committee involved in a clinical trial in whatsoever capacity shall subject to the provisions of the Right to Information Act, No. 12 of 2016 maintain the confidentiality of the information provided or relating to any study participant which may come to his knowledge in the discharge of his functions under these regulations.
39. All the study participants in a clinical trial shall be assigned with a unique identification number in order to protect the identity of such study subject which shall be used in lieu of the name of such study participant for all matters relating to the clinical trial.

PART IV

RESPONSIBILITIES OF AN INVESTIGATOR OF A CLINICAL TRIAL

40. The investigator shall be responsible for the conduct of the clinical trial in compliance with the provisions of these regulations, according to the clinical trial protocol and ICH Good Clinical Practice Guidelines, the guidelines issued by the Authority, from time to time and shall have adequate resources and facilities to conduct the clinical trial adhering to the standards as specified in the clinical trial protocol and the ICH GCP Guidelines.
41. The investigator shall be familiar with the appropriate use of the investigational medicinal products, as described in the clinical trial protocol, in the investigator's brochure, and in other sources of information provided by the sponsor and shall ensure that all persons assisting him with the clinical trial are adequately informed about the clinical trial protocol, investigational medicinal products and the duties and functions relating to such clinical trial.
42. The investigator shall report immediately to the sponsor, all serious adverse events except for those serious adverse events the protocol or investigator's brochure identifies as not requiring immediate reporting. Such reports shall be followed promptly by detailed, written reports.
43. The investigator shall be responsible for giving adequate information to the study participant in respect of the clinical trial in accordance with the ICH GCP Guidelines.

44. The investigator shall submit any information or reports including progress reports to the Authority, the sponsor or the relevant Ethics Review Committee at such times as may be required by the Authority, the sponsor or the relevant Ethics Review Committee, as the case may be.
45. (1) The investigator shall ensure that adequate free medical care is provided to the study participants, if there is any clinical trial related injury until such time as the study participant is completely recovered from the effects of such injury.
- (2) The investigator shall at the time of applying for a letter of authorization for clinical trial under these regulations, enter into an agreement with the sponsor to ensure the availability of finances and appropriate insurance cover for this purpose.
46. The principal investigator shall ensure that the clinical trial has received all approvals required under these regulations and is registered in the Sri Lanka Clinical Trials Registry in addition to registration with any other clinical trial registry before initiating patient screening and recruitment.

PART V

RESPONSIBILITIES OF A SPONSOR

47. (1) A clinical trial shall be undertaken only if the foreseeable risks and inconvenience have been weighed against the anticipated benefit for the individual study participant and to society.
- (2) The sponsor should ensure provision has been made for insurance or indemnity to cover the liability of the investigator and the institution in which the clinical trial is carried out against claims arising from the clinical trial, except for claims that arise from malpractice or negligence.
48. The sponsor is responsible for selecting investigator to conduct the study. Each investigator should be qualified by training and experience and should have adequate resources to conduct the study.
49. The sponsor of a clinical trial shall be 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 requirements of the clinical trial Protocol and ICH GCP guidelines. Any transfer of ownership of the data shall be reported to the Authority.
50. The sponsor of a clinical trial is required to ensure that the clinical trial, for which the sponsor is responsible for, has received all approvals required under these regulations, and is registered in the Sri Lanka Clinical Trials Registry in addition to registration with any other clinical trial registry before initiating patient screening and recruitment.
51. Every sponsor shall be required to submit a status report on the clinical trial to the Authority through the holder of a letter of authorization at such intervals as shall be determined by the Authority, and a final report of the clinical trial within six months after the completion of the clinical trial or such further period as the Authority may allow. In the case of premature discontinuation of a clinical trial for which a letter of authorization has been issued, a summary report shall be submitted to the Authority within three months of such discontinuation.
52. The sponsor shall be responsible for the ongoing safety evaluation of the investigational medicinal products and shall notify other investigators participating in the clinical trial, the Authority and the relevant Ethics Review Committee of the findings that could affect adversely the safety of study participants or impact the conduct of the clinical trial.

- 53.** The sponsor shall report as soon as possible to the Authority and the relevant Ethics Review Committee about all serious adverse events occurring at any clinical trial site in Sri Lanka.
- 54.** (1) The sponsor shall communicate to the Authority, the relevant Ethics Review Committee and the investigators participating in the clinical trial about any serious unexpected adverse drug reaction as soon as possible but no later than fifteen calendar days after the sponsor was first aware of such reaction.
- (2) Any serious unexpected adverse drug reaction that is fatal or life-threatening shall be reported to the Authority, relevant Ethics Review Committee and the investigators participating in the clinical trial as soon as possible but not later than seven calendar days after the sponsor was first aware of such reaction.
- 55.** The sponsor shall 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 Practices for medicinal products of the WHO or similar accreditation body.
- 56.** The sponsor shall 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, which shall include the following:-
- (a) the reference number or other unique identification mark of each item of such investigational medicinal products;
- (b) a clinical trial reference code allowing identification of the clinical trial, site, investigator and sponsor if not given elsewhere;
- (c) the date of manufacture and the expiry date of the investigational medicinal products in month and year format and in a manner that avoids any ambiguity;
- (d) the storage conditions appropriate for each item of investigational medicinal products as may be indicated by the manufacturer; and
- (e) the words: "For Clinical Trial Use Only" or similar wording to indicate that the investigational medicinal products will be used only for clinical trials.
- 57.** The sponsor shall not permit the investigator to use any investigational medicinal product in a clinical trial if the container in which the investigational medicinal product is stored is not marked and labeled with the particulars specified in regulation 56.
- 58.** (1) If any code or cipher is used in the labeling of an investigational medicinal product, the key to the code or cipher shall be made available to any doctor or dentist in an emergency and it shall be made known to the Authority.
- (2) The code or cipher should permit rapid identification of the product in case of a medical emergency, but shall not permit undetectable breaks of the blinding.
- 59.** The sponsor shall cause all investigational medicinal products be stored in such manner as to be easily identifiable. Where the investigational medicinal products cannot be identified, such investigational medicinal products shall not be used and shall be surrendered to the Authority.
- 60.** (1) The sponsor shall ensure that written procedures include instructions that the investigator or institution shall follow for the handling and storage of any investigational product for the clinical trial and documentation thereof.

- (2) The procedures shall address adequate and safe receipt, handling, storage, dispensing, retrieval of unused product from study participant, and return of any unused investigational product to the sponsor or alternative disposal if authorized by the sponsor and in compliance with the applicable regulatory requirements for disposal of such products.
61. The sponsor or the holder of a letter of authorization shall keep adequate clinical records of each study participant for the duration of such clinical trial. Such sponsor or the holder of a letter of authorization shall ensure that such records are-
- (a) available at all times for inspection by the Authority or any person authorized by the Authority in that behalf, and kept up to date at all times;
 - (b) kept at least for whichever of the following periods expires later-
 - (i) until there are no pending or contemplated marketing applications of the investigational medicinal product in Sri Lanka; and
 - (ii) two years after the last approval of a marketing application for the investigational medicinal product in Sri Lanka.
62. Where the letter of authorization for clinical trial is withdrawn or clinical trial is discontinued records shall be maintained for a period of two years after such withdrawal or two years after the Authority has been informed of the discontinuation of the clinical trial.
63. Where a clinical trial is completed, records relating to such clinical trial shall be maintained –
- (a) for ten years after the completion of the clinical trial; or
 - (b) such other period as the Authority may direct taking into consideration any additional information that is submitted to it.
64. The sponsor or the holder of a letter of authorization shall maintain a record containing the names and such other particulars of every person assisting or participating in a clinical trial.
65. The sponsor shall ensure that the laboratories used for generating data in respect of clinical trials are complied with Good Laboratory Practices.
66. The sponsor shall ensure that the investigator's Brochure for any clinical trial provides information in a concise and objective form which enables an investigator to understand the contents thereof and make unbiased risk-benefit assessment of the appropriateness of the clinical trial. Such contents shall be kept up-to-date.

PART VI

CLINICAL TRIAL AGREEMENT

67. There shall be a written agreement between two or more parties involved in a clinical trial which describes all the matters relating to a clinical trial conducted under these regulations.
68. (1) All commercially sponsored research carried out at healthcare institutions in Sri Lanka shall have a fully executed contract otherwise known as a Clinical Trial Agreement before the commencement of the clinical trial.
- (2) All relevant parties to such contract shall sign the agreement which shall define the scope of work and formalizes the understanding between the parties.

- (3) The agreement shall 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 clinicaltrial-related injury to study participants and circumstances for indemnification.

69. All Clinical Trial Agreements for conduct of clinical trials at healthcare institutions shall be signed by –

- (a) an approved institutional signatory (e.g. Medical Director) or a no objection certificate shall be issued by the Head of such institution;
- (b) the relevant principal investigator;
- (c) the sponsor of the study or person designated by the sponsor (e.g. CRO) where relevant; and
- (d) other parties such as the local coordinator, where relevant.

70. Where the site for a clinical trial is a private hospital, the necessary approvals shall be obtained from the relevant person or persons, as the case may be, in accordance with the requirements of each such institution, in addition to obtaining the letter of authorization from the Authority and the approval from the relevant Ethics Review Committee.

71. The holder of a letter of authorization or the principal investigator or any person assisting him in a clinical trial or any study participant in a clinical trial shall not, directly or indirectly, have any financial interest in the business of the sponsor of the clinical trial.

PART VII

GENERAL

72. The International Conference on Harmonization Good Clinical Practice (ICH GCP) Guidelines relating to the conduct of clinical trials including ICH E2A, E3, E7, E8, E9, E11, and E6 (R2)) shall be applicable in addition to these regulations.

73. The Declaration of Helsinki as a statement of ethical principles for medical research shall be applicable in relation to the guidance to physicians engaged in clinical research and the responsibilities of researchers.

74. (1) Every person who intends to conduct a clinical trial shall ensure the following-

- (a) before any clinical trial is initiated, foreseeable risks and inconveniences of such clinical trial shall be weighed against the anticipated benefit for the study participant of such clinical trial and the society and, be continued only if such anticipated benefits justify the foreseeable risk;
- (b) the rights, safety and wellbeing of the study participants of a clinical trial shall be the most important considerations and shall prevail over the interests of science;
- (c) any available clinical and non-clinical information of any investigational medicinal product shall be adequate to support any proposed clinical trial;
- (d) any clinical trial shall be scientifically sound and described in a clear, detailed and complete clinicaltrial protocol;
- (e) a clinical trial shall be conducted in compliance with a clinical trial protocol approved by an Ethics Review Committee recognized by the Authority for the review of clinical trials;
- (f) the medical care given to and any medical decision made on behalf of any study participant shall be the responsibility of a qualified medical practitioner with the reasonable training and experience;

- (g) every person involved in conducting a clinical trial shall be qualified in education, training and experience to perform such person's task;
- (h) freely given and informed consent shall be obtained from every study participant prior to the initiation of any clinical trial;
- (i) all information relating to any clinical trial shall be recorded, handled and deposited in such manner as it allows its accurate reporting, interpretation and verification;
- (j) any record by which the study participant can be identified shall be protected respecting the privacy and confidentiality of rules in terms of applicable written law;
- (k) systems of procedures which assure the quality of each aspect of the clinical trial shall be implemented; and
- (l) possession of valid GCP certification.

(2) The Authority may require any person who conducts a clinical trial to furnish any information or to produce for inspection any document or record within the possession of such person.

75. The Authority shall recognize Ethics Review Committees for the purpose of approval of clinical trials for any category of medicine medical devices and borderline products specified in subsection (1) of regulation 2 and the list of such recognized Ethics Review Committees shall be published in the website of the Authority.

76. The Authority may use relevant clinical trial decisions, reports or information of a regulatory authority of another country as may be recognized by the Authority.

77. (1) The Authority may make guidelines in relation to the following matters: -

- (a) the format and supporting documents for the application for a letter of authorization to conduct a clinical trial;
- (b) the Manual of ICH Good Clinical Practice Guidelines;
- (c) the format of the import license;
- (d) the report of serious adverse events;
- (e) the compensation in the event of a serious clinical trial-related injury;
- (f) phases of clinical trials that can be conducted in Sri Lanka.

(2) The Authority may issue instructions from time to time in relation to the conduct of clinical trials.

78. Every sponsor, principal investigator or holder of a letter of authorization shall comply with provisions of the National Medicines Regulatory Authority Act, No. 5 of 2015, regulations made thereunder, guidelines issued under these regulations and instructions relating to the conduct of clinical trials issued by the National Medicines Regulatory Authority.

79. The Authority may at any time require any person –

- (a) to furnish any information with the person's knowledge; or
- (b) to produce for inspection any document or record within the person's possession,

that the Authority believes on reasonable grounds to be connected with any suspected contravention of these regulations or to be otherwise relevant to the administration or enforcement of these regulations.

80. Any person who contravenes the provisions of these regulations commits an offence and shall on conviction liable to the punishment as provided in section 131 of the National Medicines Regulatory Authority Act, No. 5 of 2015.

81. In these regulations, unless the context otherwise requires –

“adverse drug reaction” means a response to a pharmaceutical product that is noxious and unintended and which occurs at doses normally used or tested in humans 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.

“adverse event” means any untoward medical occurrence in a patient or study participant administered an investigational 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 an investigational medicinal product, whether or not considered related to the investigational medicinal product;

“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;

“clinical research organization” means a scientific organization to which a sponsor may transfer in writing some of its duties and functions;

“clinical trial protocol” means a document explaining the background, rationale and the objectives of the clinical trial and describes its design, methodology and the organization which is involved in such clinical trial and shall include the statistical considerations, the conditions under which the clinical trial is to be carried out and managed. The clinical trial protocol shall be dated and signed by the investigator, the institution involved in such clinical trial and the sponsor;

“drug” includes a group of drugs;

“Ethics Review Committee” means an independent body recognized by the National Medicines Regulatory Authority consisting of medical professionals and non-medical persons whose responsibility is to verify whether the safety, integrity and human rights of the clinical trial participants in a given clinical trial are protected and to consider the general ethics of such clinical trial;

“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 the study participants are protected, and the results of the clinical trials are credible;

“informed consent” means voluntary written assent of a study participant’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;

“investigator” means a doctor or dentist, as the case may be, involved or engaged in a clinical trial under the supervision of a principal investigator specified in a letter of authorization as the person responsible for the conduct and supervision of a clinical trial;

“investigator’s brochure” means A collection of data for the investigator consisting of all the relevant information on the Investigational medicinal product, 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 clinical trial and to evaluate the potential safety and need for special precautions. If new data are generated, the investigator’s brochure must be updated;

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

“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;

“principal investigator or in the case of multi centre studies, the coordinating principal investigator or national coordinator” means a doctor or dentist who shall be registered with the Sri Lanka Medical Council and attached to the Ministry of Health or recognized health care institution or any university established or deemed to be established under Universities Act, No. 16 of 1978 and, specified in a letter of authorization as the person responsible for the conduct and supervision of a clinical trial;

“serious adverse event” or “serious adverse reaction” 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 any individual, a company, an institution or an organization responsible for the initiation, management or financing of a clinical trial. Where an investigator initiates and is fully responsible for a clinical trial, such investigator also acts as the sponsor of such clinical trial;

“study participant” means an individual participating in a clinical trial either as a recipient of the investigational product which is under investigation or as a control. Such individual may be a healthy person who volunteers to participate in the clinical trial or a person whose condition is unrelated to the use of such investigational product or a person (usually a patient) whose condition is relevant to the use of such investigational product;

“unexpected adverse drug reaction” means an adverse reaction, the nature or severity of which is not consistent with the applicable investigational product information.