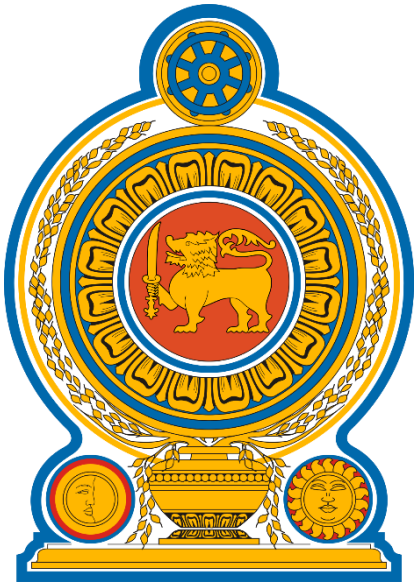

GUIDELINES ON SAFETY REPORTING REQUIREMENTS FOR CLINICAL TRIALS

AUGUST 04, 2021

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

GUIDELINES ON SAFETY REPORTING REQUIREMENTS FOR CLINICAL TRIALS

CONTENTS

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1. PURPOSE

The purpose of this document is to provide guidance to the research community on the submission of safety information that occur in all phases of clinical trials to the Clinical Trials Regulatory Division of the NMRA.

There is limited safety information on the use of a new medicinal product being developed so monitoring patient safety is an integral and critical part of the clinical trial process. The objective of collecting safety data from clinical trials is early detection of important safety signals, protecting patients from unnecessary risks, and developing the safety profile of the drug contributing to its benefit-risk assessment.

Therefore safety data from ongoing clinical trials has a direct impact on the safety and clinical care of patients enrolled in these trials. The ultimate goal of clinical trial safety monitoring is to evolve medically relevant safety label information for the product under development.

Therefore it is of great importance to acquire safety information starting from early stages of clinical development of the product being developed so that a broader picture of its clinical safety would be available prior to its approval for marketing authorization. It is also important for the assurance of safety and protection to the participating volunteers, to detect previously unidentified problems related to the product.

The guidelines would assist investigators, sponsors, ethics review committees, and members of the Clinical Trials Evaluation Committee (CTEC) in interpreting requirements for submitting reports of adverse events, especially those which are unanticipated. Particularly for multicentre trials involving investigational new molecules, it is the sponsor who is ultimately responsible for ongoing safety evaluation of the product.

2. SCOPE

These guidelines stipulates the types of documents to be submitted to CTEC which functions under the Clinical Trials Regulatory Division (CTRD) of National Medicines Regulatory Authority (NMRA), the timelines for submission, and the requirements for reporting of safety information relevant to all clinical trials authorized to be conducted in Sri Lanka by NMRA.

3. SAFETY REPORTING

Precautions to ensure patient safety require that clinical investigators must report to the sponsors all serious adverse events - SAE on an expedited basis, regardless of whether they are considered drug-related or not, relieving them of the burden of making a judgment on the causal association with the drug. We recognize that the sponsor has the broadest view of the drug's history and characteristics, and is therefore in the best position to attribute causality.

The holder of letter of authorization for a particular trial has an obligation to furnish reports concerning safety of the investigational medicinal product (IMP) including SAEs to NMRA and the relevant Ethics Review Committee (ERC) that granted ethics approval for the trial.
For multicenter trials, the coordinating principal investigator may rely on the sponsor’s assessment and provide the ERC and NMRA a report of the safety issue prepared by the sponsor.

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During the course of the study, the following safety reports should be submitted to NMRA, the ERC, and where applicable, to the sponsor.

1. Serious adverse events (SAEs) experienced by study participants relevant to trial centres in Sri Lanka should be immediately reported to the sponsor, relevant ERC and CTEC, except for those SAEs that the protocol or other document (e.g. Investigator's Brochure) identifies as not needing immediate reporting.
2. The principal investigator should report all serious and unexpected adverse drug reactions (SUSARs) which occur in a study participant at a trial site at which he is responsible to the sponsor as soon as possible, but not later than 24 hours after he was first aware of the event or the reaction.
3. The immediate reports should be promptly followed by detailed written reports.
4. Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluation should be reported to the sponsor according to the reporting requirements and within the time periods specified in the protocol.
5. For reported deaths, the investigator should furnish CTEC, ERC and sponsor with any additional requested information (e.g. autopsy reports, terminal medical reports)
6. All SUSARs including those experienced by study participants relevant to trial centres outside Sri Lanka should be submitted to CTEC and ERC. In addition, the sponsor is obliged to notify serious and unanticipated adverse reactions reported from one centre to all the participating investigators.
7. The sponsor should submit to the CTEC and ERC all safety updates and periodic reports such as quarterly line-listings of SUSARs and DSURs.

Multicentre trials are usually studies involving investigational new drugs seeking to prove safety and efficacy prior to product licensing and the sponsor is in a better position to analyze adverse event information for the entire study, and to assess whether an adverse event occurrence is unanticipated and a drawback to the trial.

An independent expert group, i.e Data Monitoring Committee (DMC) or Data Safety Monitoring Board (DSMB) is established by the sponsor whose responsibilities include assessing of safety data generated by individual trial centers. The protocol of the trial should include the mechanism for adverse event monitoring and composition of the DMC/DSMB. Recommendations of the DMC/DSMB should be notified to CTEC, ERC and all participating investigators.

4. REPORTING ADVERSE EVENTS EXPERIENCED BY STUDY PARTICIPANTS

Information about adverse events must be communicated among investigators, sponsors, ERCs and to the CTEC through CTRD, NMRA as follows:

- Investigators are required to report promptly to the sponsor any adverse event that may reasonably be regarded as caused by, or probably caused by the IMP.
- Sponsors are specifically required to expedite the reporting to all participating investigators, the relevant ERC, and CTEC of any adverse reaction associated with the use of the IMP that is both serious and unexpected and any finding from tests in laboratory animals that suggests a significant risk for human subjects.

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- More generally, sponsors are required to keep each participating investigator informed of new observations discovered by or reported to the sponsor on the IMP, particularly with respect to adverse events and reactions, and safe use.
- Investigators are required to report promptly to the relevant ERC and CTEC all unanticipated AEs involving risks to human study participants.
- Expedited reports should comply with ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.

4.1 Serious Adverse Event or Adverse Drug Reaction

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

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

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

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

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

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

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

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

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In general, serious adverse events or reactions occurring in Sri Lanka should be considered an unanticipated problem involving risk to human participants and reported to the relevant ethics review committee and the CTEC by the sponsor, as per required timelines.

4.2 Expectedness of an Adverse Drug Reaction

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

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

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

a. The Investigator's Brochure will serve as the source document for a medicinal product that is not yet approved for marketing;
b. The summary of product characteristics (SmPC) for a medicinal product that has been approved for marketing;
c. Reports which add significant information on specificity or severity of a known, already documented serious ADR constitute unexpected events. For example, an event more specific or more severe than described in the Investigator's Brochure would be considered "unexpected".
d. The sponsor of a study should amend the Investigator's Brochure as needed, so as to keep the description of safety information updated.

4.3 Standards for Expedited Reporting

1. What Should Be Reported

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

These include reports of the following:

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

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

Expedited reporting of reactions, which are serious but expected, will ordinarily be *inappropriate*. Expedited reporting is also *inappropriate* for serious events from clinical investigations that are considered not related to study product, whether the event is expected or not. Similarly, non-serious

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adverse reactions, whether expected or not, will ordinarily *not* be subjected to expedited reporting. Figure 1 is a flow chart of the safety reporting decision process for drugs used in clinical trials.

2. Other safety issues requiring expedited reporting

Other safety issues also qualify for expedited reporting where there might materially alter the current benefit-risk assessment of an IMP or that would be sufficient to consider changes in the IMP administration or in the overall conduct of the study, such as:

i. A significant hazard to the subject population such as lack of efficacy of the IMP used for the treatment of a life-threatening disease.

ii. A major safety finding from a newly completed animal study (such as carcinogenicity)

3. Reporting Time Frames

i. Fatal or life-threatening unexpected ADRs

Certain ADRs may be sufficiently alarming so as to require very rapid notification to regulators in countries where the medicinal product or indication, formulation, or population for the medicinal product are still not approved for marketing, because such reports may lead to consideration of suspension of, or other limitations to, a clinical investigation programme.

The sponsor shall ensure that all relevant information about a **SUSAR** which occurs during the course of a clinical trial in Sri Lanka and is **fatal or life-threatening** is reported as soon as possible to the CTEC, the relevant ethics committee(s), and the investigator(s) participating in the study. This needs to be done **not later than seven (07) calendar days** after the sponsor was first aware of the reaction.

This report may include an assessment of the importance and implication of the findings, including relevant previous experience with the same or similar medicinal products. This report shall be communicated to the relevant authorities in Sri Lanka through the holder of a letter of authorization.

ii. All other serious unexpected ADRs

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

iii. Minimum criteria for reporting

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

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

- An identifiable study participant;

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

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

iv. Investigator responsibilities

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

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

v. Sponsor responsibilities

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

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

A sponsor shall ensure that a suspected unexpected serious adverse reaction (SUSAR) which is not fatal or life-threatening is reported as soon as possible, and in any event not later than **15 calendar days** after the sponsor is first aware of the reaction, to the CTEC, the relevant ethics committee(s), and the investigator(s) participating in the study. The holder of the letter of authorization will notify the SUSAR report to the relevant ERC and CTEC. These reports or information may be provided on paper using the CIOMS reporting form.

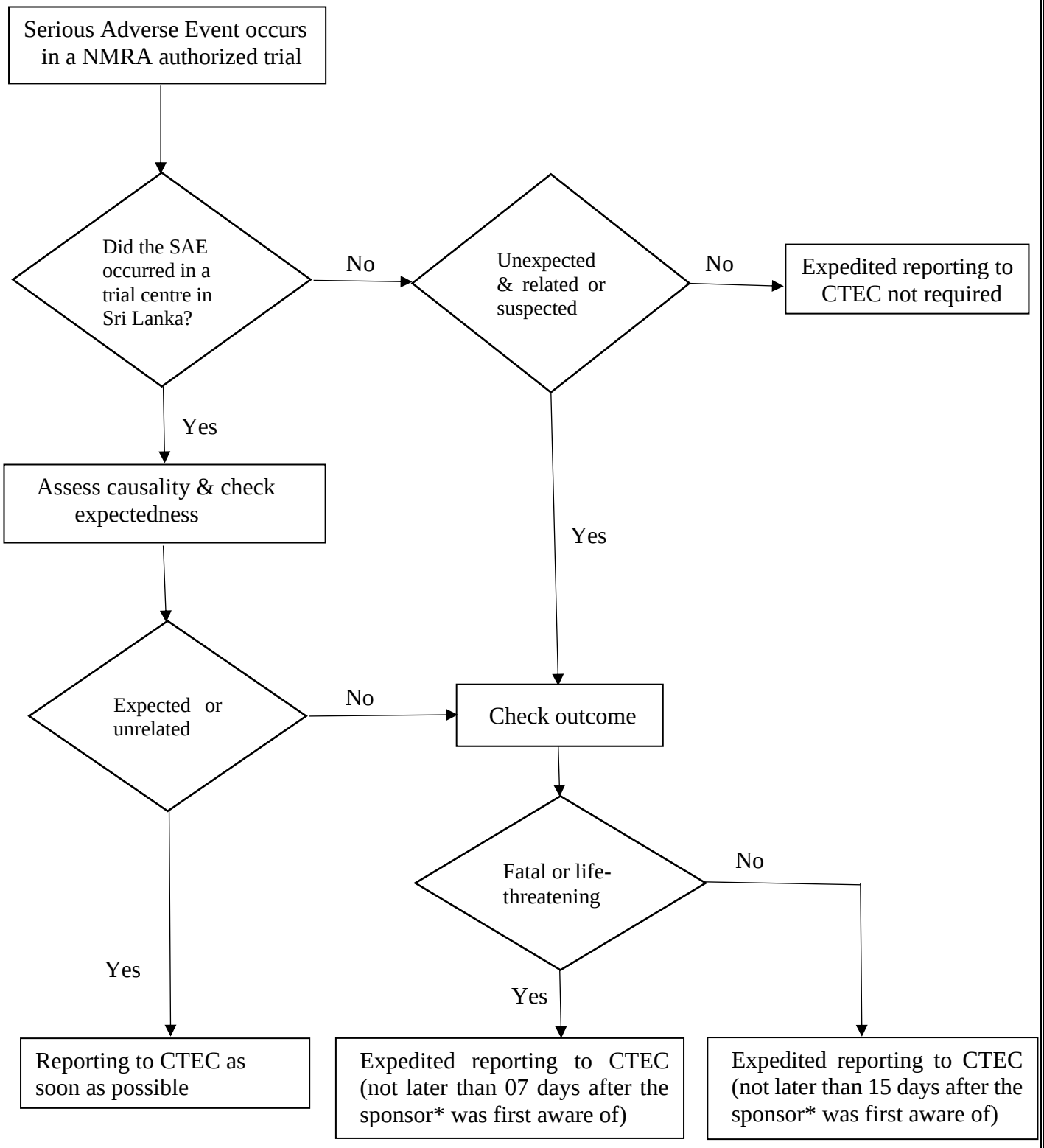
4. How to Report

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

When completing the CIOMS form, Sponsors should include the protocol number and study name. All reports must be sent to the CTEC and other official parties requiring them (e.g. Institutional

Review Boards, Ethics Review Committees). Please refer to Appendix 3 for a summary of the safety reporting requirements for clinical trials to the CTEC.

Figure 1: flow chart of the safety reporting decision process for drugs used in clinical trials.



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*The sponsor submits reports in CIOMS, through the holder of letter of authorization. For clinical trials funded by non-commercial sponsors (e.g. academic trials), holder of letter of authorization is responsible for directly reporting SAEs and SUSARs to the CTEC.

5. MANAGING SUSARs ASSOCIATED WITH ACTIVE COMPARARORR OR PLACEBO

All SUSARs associated with a comparator product in the concerned clinical trial even if this product has marketing authorization should be reported to CTEC and the relevant ERC. It is recommended that sponsor report them to the marketing authorization holder of the comparator. But, in all cases of reporting SUSARs from a clinical trial to CTEC should only take place through the holder of letter of authorization.

Events associated with placebo will usually not satisfy the criteria for serious adverse drug reactions and therefore expedite reporting. However, where SUSARs are associated with placebo (e.g. reaction due to an excipient), sponsor should report such cases to the NMRA through the holder of letter of authorization.

6. ABBREVIATIONS

AE – Adverse Event
ADR – Adverse Drug Reaction
CIOMS – Council for International Organization of Medical Science
CPI – Coordinating Principal Investigator
CTEC – Clinical Trials Evaluation Committee
CTRD – Clinical Trials Regulatory Division
DMC – Data Monitoring Committee
DSMB – Data Safety Monitoring Board
DSUR – Development Safety Update report
ERC – Ethics Review Committee
ICH – International Conference on Harmonization
IMP – Investigational Medicinal Product
NMRA – National Medicines Regulatory Authority
PI – Principal Investigator
SAE – Serious Adverse Event
SmPC – Summary of Product Characteristics
SUSAR – Suspected Unexpected Serious Adverse Reaction

7. DEFINITIONS

Adverse Event (or Adverse Experience)

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

Adverse Drug Reaction (ADR)

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In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase "responses to a medicinal products" means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.

CIOMS-I format

A format for reporting adverse drug reactions according to the Council of International Organizations for Medical Sciences. https://cioms.ch/cioms-i-form/

Clinical Trial

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

Coordinating Principal Investigator (CPI)

An investigator assigned the responsibility for the coordination of investigators at different centre participating in a multicentre trial. CPI would become the holder of letter of authorization once the trial gets approved by NMRA.

Ethics Review Committee (ERC)

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.

Investigational Medicinal Product (IMP)

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

Investigator's Brochure

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

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Principal Investigator (PI)

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

Protocol

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

Sponsor

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

Study Participant

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

Unexpected Adverse Drug Reaction

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

8. RELATED LEGISLATION AND DOCUMENTS

- National Medicine Regulatory Authority Act No. 05 of 2015
- National Medicine (Clinical Trials) Regulations 2145/2, 14th October 2019
- Guideline for the conduct of Clinical Trials in Sri Lanka

9. REFERENCES

- ICH harmonized tripartite guideline; Clinical safety data management: Definitions and standards for expedited reporting, ICH, October 1994
- Guidance for clinical investigators, sponsors, and IRBs; Adverse event reporting to IRBs – Improving human subject protection, USFDA, January 2009

- Details guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use, ENTR/CT3, Revision 1, April 2004
- Clinical trial guidance; expedited safety reporting requirements for therapeutic products and medicinal products used in clinical trials, HSA, Singapore, 2 May 2017

10. FEEDBACK

Staff and customers may provide feedback about this document by emailing pathmaperuma.a@nmra.gov.lk

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APPENDIX 1
CIOMS-I Format

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CIOMS FORM

SUSPECT ADVERSE REACTION REPORT	

I. REACTION INFORMATION

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

II. SUSPECT DRUG(S) INFORMATION

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

III. CONCOMITANT DRUG(S) AND HISTORY

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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER		
	24b. MFR CONTROL NO.	
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE ☐ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL	
DATE OF THIS REPORT	25a. REPORT TYPE ☐ INITIAL ☐ FOLLOWUP	

APPENDIX 2

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Elements for Inclusion in Expedited Reports of Serious Adverse Drug Reactions

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

1. Study participant Details

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

2. Suspected Medicinal Product(s)

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

3. Other Treatment(s)

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

4. Details of Suspected Adverse Drug Reaction(s)

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

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

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

5. Details of Reporter of Event (Suspected ADR)

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Name
Address
Telephone number
Profession (specialty)

6. Administrative and Sponsor/Company Details

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

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APPENDIX 3

Clinical trial safety reporting requirements and timelines to the CTEC

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

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

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

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