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TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

GUIDELINES FOR REPORTING SAFETY DATA IN CLINICAL TRIALS

SECOND EDITION

November, 2020

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Acknowledgments

This second edition of the guidelines for Reporting Safety Data in Clinical Trial have been developed to embrace the new knowledge gained during implementation of the previous edition and incorporates administrative changes.

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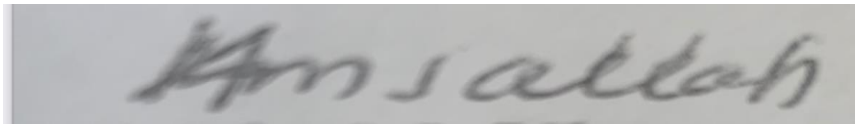

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Abbreviations

ADRs	**-**	Adverse Drug Reactions
AEs	**-**	Adverse Events
CRF	**-**	Case Report Form
GCP	**-**	Good Clinical Practice
ICH	**-**	International Conference on Harmonization
IP	**-**	Investigational Product
NHMRC	-	National Health and Medical Research Council, Australia
SAE	**-**	Serious Adverse Event
SUSARs	**-**	Suspected Unexpected Serious Adverse Reactions
SOPS	**-**	Standard Operating Procedures
TMDA	**-**	Tanzania Medicines and Medical Devices Authority
USFDA	-	U.S. Food and Drug Administration

Foreword

These revised Guidelines for Reporting of Safety data in Clinical Trials in Tanzania have been prepared by Tanzania Medicines and Medical Devices Authority (TMDA). The guidelines have been made under Section 63(1) of Tanzania Medicines and Medical Devices Authority Act, Cap 219.

The authority has a legal responsibility of receiving and assessing all safety data occurring in clinical trials conducted in Tanzania. It is therefore anticipated that safety data for clinical trials conducted in Tanzania will be managed and reported accordingly.

These guidelines provide stipulated information on the minimum requirements for a complete adverse event report. It has clarified the types of adverse events needed to be reported and the corresponding time frame. The reported adverse events should have been assessed and in this guide it has been stated clearly that the Sponsors of clinical trials are obliged to assess and report adverse events.

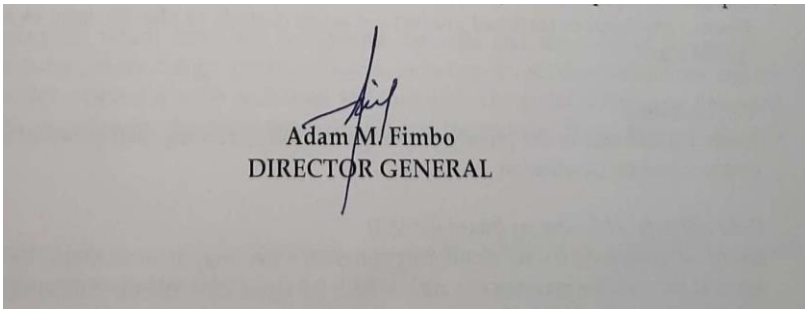
The current edition has made no changes with regards to the requirements for reporting of safety data in clinical trials. The edition is a result of amendments of legislation done through the Finance Act of 2019 which transformed the then TFDA to TMDA and to be in consistence with the requirements of the quality management system being implemented by the Authority.

The guidelines can be used as a guiding tool on reporting of adverse events by Sponsors of clinical trials, Principal Investigators, Researchers, Contract Research Organizations (CROs), National Ethics Committee and whoever participates in clinical trials.

The credibility of safety data will depend on completeness and good handling of the particular data and therefore these guidelines will guide scientists involved in clinical trials at each level to ensure that the report content is always reliable.

It is the expectation of TMDA that the guidelines will enable consistent and uniform documentation of safety data on clinical trials and make it easier for the Authority to evaluate and make proper conclusions, recommendations or any mandatory regulatory decisions.

The edition will be modified whenever necessary depending on the scientific innovative development in management of clinical trials safety data and any other requirements at specific time.



Definition of terms

In the context of these guidelines, the following terms and phrases are defined as follows:

Adverse Drug Reactions (ADRs)

Means all noxious and unintended responses to a clinical trial medicinal product related to any dose or all unintended noxious responses to a registered medicinal product which occurs at doses normally used in humans for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function.

Adverse Event (AE)

Means any untoward medical occurrence in a participant or clinical investigation study participant administered a pharmaceutical product and which does not necessarily have a causal relationship with the treatment. An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of an investigational product (IP), whether or not related to the IP.

Blinding

Means a procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the study participant(s) being unaware and double-blinding usually refers to the study participant(s), investigator(s), monitor, and in some cases, data analyst(s) being unaware of the treatment assignment(s).

Case Report Form (CRF)

Means a document that is used to record data on each trial participant during the course of the trial, as defined by the protocol. The data should be collected by procedures which guarantee preservation, retention and retrieval of information and allow easy access for verification, audit and inspection.

Clinical Trial/Study Report

Means a written description of a trial/study of any therapeutic or prophylactic agent conducted in human study participants in which the clinical and statistical description, presentations and analyses are fully integrated into a single report.

Comparator (Product)

Means a medicinal or marketed product (i.e. active control), or placebo, used as a reference in a clinical trial.

Confidentiality

Means maintenance of the privacy of trial participants including their personal identity and all personal medical information.

Data and Safety Monitoring Board (DSMB)

Means an independent data monitoring committee that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety data and the critical efficacy endpoints and to recommend to the sponsor whether to continue, modify, or stop a trial.

Good Clinical Practice (GCP)
Means a standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials that provide assurance that the data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial study participants are protected.

Interim Clinical Trial/Study Report
Means a report of intermediate results and their evaluation based on analyses performed during the course of a trial.

Investigator
Means a physician, dentist or other qualified person who conducts a clinical trial at a trial site. See also Sub-investigator.

Investigator's Brochure (IB)
Means a compilation of the clinical and non-clinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human study participants.

Investigational Product (IP)
Means a pharmaceutical form of an active ingredient or placebo, nutritional supplements, in vitro diagnostics, medical device, herbal drugs being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

Multi-center Trial
Means a clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.

Principal Investigator (PI)
Means a person responsible for the conduct of the clinical trial at a trial site who is a physician, dentist or other qualified person, citizen of Tanzania and a member of good standing of a professional association. If a trial is conducted by a team of individuals at a trial site, the principle investigator is the responsible leader of the team.

Protocol
Means a document which 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
Means an individual, company, institution or organization which takes responsibility for the initiation, management and/or financing of a clinical trial.

Trial participant
Means an individual who participates in a clinical trial either as a recipient of the investigational product(s) or as a control

Study participant Identification Code
Means a unique identifier assigned by the investigator to each trial study participant to protect the study participant's identity and used in lieu of the study participant's name when the investigator reports adverse events and/or other trial related data.

Trial Site
Means the location(s) where trial-related activities are actually conducted.

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 product or package insert/summary of product characteristics for an approved product).

Suspected Unexpected Serious Adverse Reaction (SUSAR)
Means a serious adverse reaction where the nature and severity of the event is not consistent with the medical product. Any serious adverse event occurring in one or more participants in research protocols, the nature and severity or frequency of which is not consistent with either:

i. The known or foreseeable risk of adverse event associated with the procedures involved in the research that are described in (a) the protocol-related document, such as the approved research protocol, any applicable investigator brochure, and the current approved informed consent document and (b) other relevant sources of information, such as product labelling and package insert or

ii. The expected natural progression of any underlying diseases, disorder, or condition of the participant(s) experiencing the adverse event and the participant's predisposing risk factor profile for the adverse event.

1. INTRODUCTION

The safety of human participants in clinical research is of paramount importance. There is a need for systematic clinical evaluation of safety reports to ensure that reported cases are correctly interpreted given the symptoms and or diagnosis of the conditions presented by participants. Conversely, comprehensive assessment of safety data is crucial to allow continuation of the trial and understanding of the product potential benefits and risks before marketing.

The safety evaluation during clinical drug development is expected to characterize and quantify the safety profile of a drug over a reasonable duration of time consistent with the intended long-term use of the drug.

The Tanzania, Medicines and Medical Devices Act, Cap 219, provides for regulation of clinical trials in Tanzania. Section 70 (2) requires any person conducting clinical trials to immediately report any serious or adverse effects or reactions observed during the trial.

The purpose of expedited reporting is to make regulators, investigators, and other relevant parties aware of new and important information on serious reactions. While there are benefits associated with participation in clinical trials e.g. gaining access to new treatments that are not yet available to the public, clinical trials may also have risks for participants.

These guidelines therefore outlines the reporting requirements among Investigators, CROs and Sponsors. In this respect it defines proper management of safety report from collection at the clinical trial site to communications with TMDA. The guide describes how such data should be handled, collected and submitted to TMDA.
It further focuses on reporting timelines where SUSARs and SAE are required to be expeditiously reported in order to bring awareness to regulators, investigators studying the product and sponsors on new important reaction and possibly to facilitate other actions.

This document also lays down information to be included in the safety report, the format and content of the safety report in clinical research carried out in the country.

2. SCOPE AND RESPONSIBILITY

These guidelines apply to Clinical trials of medicinal products, medical devices, herbal medicines and biologicals (e.g. vaccines, blood products etc). They also cover Bioavailability and Bioequivalence studies.

Site Investigators have obligation to document and report safety information to the Sponsor. The Sponsor must retain detailed records of safety information reported by the investigator (s) and ensure that all reports required by TMDA are submitted on time.

Such reporting is not merely a legal requirement, but a necessity for safeguarding study participants.

3. REPORTING OF ADVERSE EVENTS

When an adverse event occurs, Investigator has to fill the CRF and complete the Adverse Event Reporting form approved in the protocol or CIOMS form (Appendix 1) and send to the sponsor.
The protocol for approved event reporting form shall contain as a minimum key data element stipulated in section 3.0 of these guidelines.

Adverse events occurring during clinical trials that shall be reported to TMDA includes; Serious Adverse Events, Suspected Unexpected Serious Adverse Reaction and Other protocol – defined reporting. Also SAEs and SUSARs occurring from sites outside the country for multicenter trials shall be reported to TMDA.

The report should include laboratory abnormalities, abnormal vital signs and abnormal physical observations that were considered serious adverse events.

The sponsor shall also ensure that the interim safety data analyses from Data Safety Committee or Data Safety Monitoring Board are submitted to TMDA.

The report will be submitted to TMDA by the sponsor or sponsor's designee by courier, mail, e-mail (as an attachment) to **info@tmda.go.tz** or fax.

All reports submitted will be kept CONFIDENTIAL.

Some of the reports should be reported expeditedly while other will need to be reported under routine basis as provided below.

3.1 Expedited reporting

3.1.1 Fatal or Life-Threatening SAEs and SUSARs

These should be reported to TMDA within 24 hours by telephone, facsimile transmission, or e-mail followed by a complete report within 7 additional calendar days. The report must include an assessment of the importance and implication of the findings, including relevant previous experience with the same or similar medicinal products.

All deaths during the study, including the post treatment follow-up period, and deaths that

resulted from a process that began during the study, should be reported.

3.1.2 Other SAEs and SUSARs

All other SAEs and SUSARs that are not fatal or life-threatening must be filled as soon as possible but no later than 14 calendar days after first knowledge by the sponsor.

3.2 Any other protocol- defined event(s)

They should be reported as defined in the protocol.

3.3 Other Unanticipated problems

Other situations that should be communicated to TMDA within 14 calendar days are those that;

a) Might materially influence the benefit-risk assessment of Investigational Product or would be sufficient to consider changes in product administration or in the overall conduct of a clinical investigation.

b) Marked haematological and other laboratory abnormalities (other than those meeting the definition of serious) and any events that led to an intervention, including withdrawal of test drug/investigational product treatment, dose reduction, or significant additional concomitant therapy, other than those reported as serious adverse events.

c) Appropriate medical and scientific judgment should be applied for each situation e.g.

   i. For an "expected," serious ADR, an increase in the rate of occurrence which is judged to be clinically important.

   ii. A significant hazard to the patient population, such as lack of efficacy/perfomance with Investigational product used in treating life- threatening disease.

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

NB:

- Regulatory clock starts when the sponsor receives a safety or problem report.
- SAEs, SUSARs and unanticipated problems occurring from sites outside the country for multicenter trials shall be reported expeditedly.

3.4 Reports from blinded trials

In blinded trials e.g double blind studies, when a serious adverse event is judged reportable on an expedited basis, the blind may only be broken for that specific patient by the sponsor even if the investigator has not broken the blind. It is recommended that, when possible and appropriate, the blind be maintained for those persons, such as biometrics personnel, responsible for analysis and interpretation of results at the study's conclusion.

When a fatal or other "serious" outcome is the primary efficacy endpoint in a clinical investigation,

the integrity of the clinical investigation may be compromised if the blind is broken. Under these and similar circumstances, it may be appropriate to reach agreement with TMDA in advance concerning serious events that would be treated as disease-related and not participant to routine expedited reporting.

Blinded trials are complex to set up. Maintenance of the blind is important for the integrity of a trial. Systems for SUSAR and SAR reporting should, as far as possible, maintain blinding of individual clinicians and of staff involved in the day-to-day running of the trial. Unblinding clinicians may be unavoidable if the information is necessary for the medical management of particular subjects. The safety of subjects in the trial always takes priority. It is important that the details of the unblinding process are included in the trial protocol/SOPs. For blinded trials involving a placebo and an active drug, seriousness, causality and expectedness should be evaluated as though the subject was on active drug. Cases that are considered serious, unexpected and possibly, probably or definitely related (i.e. possible SUSARs) would have to be unblinded before they are reported to the TMDA. It may be that individuals who are not directly involved in the management of the trial could perform unblinding (for example, in a trials unit, staff working on a separate trial might undertake the unblinding). For blinded trials involving two active drugs, the evaluation is more complex. However, the person responsible for the evaluation for causality and expectedness might be able to state that if the subject was on drug A, the event would be causal and/or unexpected, but if on drug B it would be expected. If the event were unexpected for either of the active drugs, the case should be unblinded by the individual charged with unblinding, who would then classify the event accordingly. An independent Data Monitoring Committee (DMC) has access to semi-blinded or unblinded data and can oversee the assessment of emerging risks.

3.5 Post-study Events

Any Post study serious adverse events collected by sponsor after the patient has completed a clinical trial (including any protocol required post-treatment follow- up) should be reported to TMDA.

Such cases shall be regarded for expedited reporting purposes as though they were study reports. Therefore, a causality assessment and determination of expectedness are needed for a decision on whether or not expedited reporting is required.

When additional medically relevant information is received for a previously reported case, the reporting time is considered to begin again for submission of the follow-up report. In addition, a case initially classified as a non-expedited report, would qualify for expedited reporting upon receipt of follow-up information that indicates the case should be re-classified (e.g., from non-serious to serious).

3.6 Routine reporting

All interim safety data analysis reports and a compilation of safety data after completion of the study should be reported as soon as the analysis is completed.

If reactions associated with active comparator drug or placebo occur, the sponsor shall report such reactions to TMDA on routine basis.

4 ASSESSMENT OF ADVERSE EVENTS

Analysis of safety-related data can be considered at three levels. First, the extent of exposure (dose, duration, number of patients) should be examined to determine the degree to which safety can be assessed from the study.

Second, the more common adverse events, laboratory test changes etc. should be identified, classified in some reasonable way, compared for treatment groups, and analysed, as appropriate, for factors that may affect the frequency of adverse reactions/events, such as time dependence, relation to demographic characteristics, relation to dose or drug concentration etc. Finally, serious adverse events and other significant adverse events should be identified, usually by close examination of patients who left the study prematurely because of an adverse event, whether or not identified as drug related, or who died.

Sponsors should ensure that all adverse events reports are assessed before being submitted to TMDA. The assessment should consider the following;

4.1 Seriousness

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

a. Results in death,
b. Is life-threatening, NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the patient 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.
c. Requires inpatient hospitalization or prolongation of
d. existing hospitalization,
e. Results in persistent or significant disability/incapacity, or
f. Is a congenital anomaly/birth defect.
g. Any other event which may jeopardize the patient or may require intervention to prevent one of the above outcomes.

4.2 Relationship to the Investigational Product

The site investigator shall assess the relationship between the AE and the Investigational Product(s) to determine whether there is a reasonable possibility that the Investigational Product(s) caused or contributed to the SAE. The assessment shall be based on clinical judgment which often relies on the following:

a. A temporal relationship between the event and administration of the Investigational Product(s)
b. A plausible biological mechanism for the agent to cause the AE
c. Another possible etiology for the AE
d. Previous reports of similar AEs associated with the Investigational Product or other agents in the same class
e. Recurrence of the AE after re-challenge or resolution after de-challenge, if applicable

The outcome of assessment will be categorized into:

a. Related when there is a reasonable possibility that the AE may be related to the Investigational Product(s) and
b. Not related when there is not a reasonable possibility that the AE is related to the Investigational Product (s)

When a SAE is assessed as "not related" to Investigational Product(s), an alternative etiology, diagnosis, or explanation for the SAE should be provided. If new information becomes available, the relationship assessment of any AE should be reviewed again and updated, as required.

When the Investigational Product is fixed dose combination agent, an assessment of attribution will be made for each component and the combination agent.

4.3 Expectedness

When there is reasonable possibility that the adverse event may be related to Investigational Product, the investigator should further classify them into either expected or unexpected.

Assessment of the expectedness of an AE with the IP is performed only for the SUSAR reporting category.

4.4 Expected AEs

These are AEs that have been previously observed with use of the Investigational Product (s) and are listed in the package insert or Investigator's brochure. Expectedness is not based on what might be anticipated from the pharmacological properties of the Investigational Product.

4.5 Unexpected AEs

These are AEs for which the nature or severity (intensity) is not consistent with the applicable agent information (Investigator's Brochure, package insert, or summary of agent characteristics).

4.6 Severity

The term „"severity' describes the intensity of a specific event.

All events reported to TMDA in an expedited fashion must be graded for severity.

The severity of the parameters ranges from grade 1 (mild) to grade 4 (potentially life threatening). Death is defined as grade 5 severity.

Unless stated otherwise in the protocol, Investigators shall use the following Adverse Event grading scale to determine the severity of the AE;

a. Mild,
b. Moderate,
c. Severe (3),
d. Potentially Life-Threatening,
e. Death,

The severity of an AE does not determine whether an event meets the definition of seriousness, which is based on participant/event outcome or action criteria associated with events that pose a threat to a participant's life or functioning.

4.7 Individual Clinically Significant Laboratory Abnormalities

Clinically significant changes should be discussed. A narrative of each patient whose laboratory abnormality was considered a serious adverse event and, in certain cases, considered another significant adverse event, should be provided.

When toxicity grading scales are used, changes graded as severe should be discussed regardless of seriousness. An analysis of the clinically significant changes, together with a recapitulation of discontinuations due to laboratory measurements, should be provided for each parameter.

The significance of the changes and likely relation to the treatment should be assessed, e.g., by analysis of such features as relationship to dose, relationship to drug concentration, disappearance on continued therapy, positive dechallenge, positive rechallenge, and the nature of concomitant therapy.

4.8 Safety conclusions

The overall safety evaluation of the test drug(s)/investigational product(s) should be reviewed, with particular attention to events resulting in changes of dose or need for concomitant medication, serious adverse events, events resulting in withdrawal, and deaths. Any patients or patient groups at increased risk should be identified and particular attention paid to potentially vulnerable patients who may be present in small numbers, e.g., children, pregnant women, frail elderly, people with marked abnormalities of drug metabolism or excretion etc. The implication of the safety evaluation for the possible uses of the drug should be described.

The discussion and conclusions should clearly identify any new or unexpected findings, comment on their significance and discuss any potential problems such as inconsistencies between related measures. The clinical relevance and importance of the results should also be discussed in the light of other existing data. Any specific benefits or special precautions required for individual subjects or at-risk groups and any implications for the conduct of future studies should be identified.

5 KEY DATA ELEMENTS FOR AE REPORTING

The AE reporting form should contain key data elements about the participant, the suspected IP, the adverse reaction, the action taken and the outcome as follows;

5.1 Participant Details

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

5.2 Suspected Investigational Product

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

5.3 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.

5.4 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-participant clinic, home, nursing home)

5.5 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 specialinvestigations.

5.6 Details on Reporter of Event

Name, Address, Telephone number, Profession (specialty)

5.7 Administrative and Sponsor/Company Details

Source of report: Site name

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, TMDA reference number, Sponsor/manufacturer's identification number for the case (this number must be the, same for the initial and follow-up reports on the same case).

5.8 Follow-up report for an Adverse Event

Any follow-up information for event that has already been reported shall be sent on another AE form to TMDA indicating that it is a follow up information. The date of the original report and the report case number must be retrieved from the participant's file so that the follow up information can be matched with the original report. It is very important that follow-up reports

are identified and linked to the original report.

5.9 Case Narratives

This summarize all relevant clinical and related information, including patient characteristics, therapy details, medical history, clinical course of the event(s), diagnosis, and SAE/SUSAR including the outcome, laboratory evidence (including normal ranges), and any other information that supports or refutes an Event.

The narrative should serve as a comprehensive, stand-alone "medical story". The information should be presented in a logical time sequence; this should be presented in the chronology of the patient's experience, rather than in the chronology in which the information was received. In follow-up reports, new information should be clearly identified.

Abbreviations and acronyms should be avoided, with the possible exception of laboratory parameters and units. Key information from supplementary records should be included in the report, and their availability should be mentioned in the narrative and supplied on request. Any relevant autopsy or post-mortem findings should also be summarized in the narrative and related documents should be provided according to local regulation and if allowed by local data privacy laws.

Terms (e.g., AEs/ADRs, indication, and medical conditions) in the narrative should be accurately reflected in appropriate data fields.

Investigator's opinion on causality and sponsor's opinion on causality shall also be included.

5.10 Feedback on Reports

Once TMDA receives the safety reports, it will assess them and give feedback to the sponsor or take appropriate regulatory action.

Appendix 1: CIOMS Reporting Form

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
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)										☐ PATIENT DIED ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION ☐ INVOLVED PERSISTENCE OR SIGNIFICANT DISABILITY OR INCAPACITY ☐ LIFE THREATENING

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 REINTRODUCTION? ☐ 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	

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