DRAFT
GUIDANCE FOR INDUSTRY

ON

REPORTING SERIOUS ADVERSE EVENTS

OCCURING IN CLINICAL TRIALS

Suggestion/comments on the guidance documents if any may please be forwarded to CDSCO within fifteen days

Drugs Controller General (India)
Directorate General of Health Services
Central Drugs Standard Control Organization
New Delhi

1 ABBREVIATIONS AND DEFINITIONS

1.1 ABBREVIATIONS

AE	Adverse Event
BE	Bioequivalence
CDSCO	Central Drugs Standard Control Organization
CRO	Contract Research Organization
CT	Clinical Trial
DCGI	Drugs Controller General (India)
DGHS	Directorate General of Health Services
IND	Investigational New Drug
NCE	New Chemical Entity
SAE	Serious Adverse Event

1.2 DEFINITIONS

1.2.1 Adverse Event (AE)

Any untoward medical occurrence (including a symptom / disease or an abnormal laboratory finding) during treatment with a pharmaceutical product in a patient or a human volunteer that does not necessarily have a relationship with the treatment being given.

1.2.2 Serious Adverse Event (SAE)

An AE that is associated with death, inpatient hospitalisation (in case the study was being conducted on out-patients), prolongation of hospitalisation (in case the study was being conducted on in-patients), persistent or significant disability or incapacity, a congenital anomaly or birth defect, or is otherwise life threatening.

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GUIDANCE FOR INDUSTRY

REPORTING SERIOUS ADVERSE EVENTS OCCURING IN CLINICAL TRIALS

3 BACKGROUND

At present various pharmaceutical companies and contract research organizations (CROs) are using multiple / different formats and procedures for reporting serious adverse events (SAEs) to CDSCO. Though most reports adhere to Appendix XI of Schedule Y, multiple formats and missing information, including improper referencing for submission of follow-up reports have lead to difficulties in segregation and further processing of these reports by this office.

Hence, this guidance document has been developed to achieve uniformity and completeness of data received by this office with respect to SAE reporting in clinical trials.

4 SCOPE & RESPONSIBILITIES

All SAEs occurring in clinical trials should be reported as per the details provided in Appendix XI of Schedule Y (Annexure I) within the applicable timeline (14 calendar days), to,

The Drugs Controller General (India)
Directorate General of Health Services
Central Drugs Standard Control Organization
FDA Bhawan, Kotla Road, New Delhi – 110 002

Pharmaceutical company / the sponsor / CRO (Investigator in investigator-initiated studies) is responsible for reporting SAEs within the applicable timelines.

5 SAE REPORTING IN CLINICAL TRIALS

A. As per the regulations (Schedule Y of Drugs & Cosmetics Rules), all Unexpected SAEs have to be reported to CDSCO within 14 calendar days.
B. Every report (both initial as well as follow-up reports) should be submitted along with a covering letter. A template of covering letter is available in Annexure II.
C. Covering letter should be prepared using the template as guide, and printed on the company's/ CRO's letter head.
D. Instructions are provided in the template as highlighted text in *"Italics"*. Please delete all instructions from your final letter.

E. All the sections of the covering letter should be completed. When some information is not available at the time of report e.g. causality assessment by medical monitor of Sponsor / CRO, compensation provided for study related injury or death, the same has to be provided as a follow-up report

F. Covering letter of every report arising from the clinical trials (CT) has to capture, (at stipulated box provided in the template) as per the format (Annexure II)

   a. DCGI CT file number

   b. Complete address of Sponsor and CRO (if any) including phone & e-mail address

   c. Phase of clinical trial

   d. Category of clinical trial as per below codes, (Please mark the appropriate Code from the list provided in the covering letter using below details)

Code	SAEs occurring in clinical trial
CT-1-IND	New Drug - Investigational New Drug (IND) study (where IND is filed in India and is an NCE)
CT-2-Reg	New Drug – Local Clinical Trial– For product approval in India
CT-3-GCT	New Drug – Global CTs
CT-4-rDNA	Biological – Recombinant products (Global CTs, India IND and study for product approval)
CT-5-Vac	Biological – Vaccines (Global CTs, India IND and study for product approval)
CT-6-Oth	Biological – Others (e.g. stem cell studies)
CT-7-Dev	Device study (Global CTs, India IND and study for product approval)
CT-8-Oth	Others

   e. Protocol or Study No. / Code / ID and the study title

   f. Adverse event term / diagnosis (Whenever possible provide a ‘preferred term’)

   g. A brief narrative of the event, not exceeding 10 lines. A detailed narrative may be enclosed, if available.

h. Unexpected SAEs have to be submitted to this office as per Schedule Y of Drugs and Cosmetics Rules, 1945

i. Causality assessment by investigator and the medical monitor of Sponsor /CRO. **The assessment report should clearly mention whether the SAE occurred is related or not related (Situations like unlikely, possibly, suspected, doubtful etc should not be used).**

j. Whether the outcome is fatal

k. **Details of compensations provided for injury or death. In case no compensation has been paid, reason for the same should be submitted. It is pertinent to mention that in case of study related injury or death, complete medical care as well as compensation for the injury or death should be provided.**

G. Capture whether it is "initial" or "follow-up" report. For follow-ups, clearly mention the follow-up report number e.g Follow-up #01, Follow-up #02, etc. In case of follow-up reports, please mention the date of submission of initial (first) report somewhere in narrative.

H. Filled CIOMS-I, MedWatch or Any other forms (company specific, self designed) can be submitted. However, one needs to ensure that the forms capture basic (mandatory) information as per the Appendix XI of Schedule Y.

I. Forms should be completed in legible English.

J. Illegible forms, incomplete with respect to critical information and improperly scanned / fax copies would be rejected.

K. Relevant supportive documents may be enclosed.

NOTE:

Submission of same SAE in different forms/ format, in different occasions to be avoided (e.g. submitting CIOMS forms and then later submitting the same event details as per Appendix XI, separately)

6 ANNEXURES

ANNEXURE I: Data elements for reporting SAE occurring in clinical trials

DATA ELEMENTS FOR REPORTING SAE OCCURRING IN A CLINICAL TRIAL

1. **Subject details**
   i. Subject initials & other relevant identifier*
   ii. Gender
   iii. Age and/or date of birth
   iv. Weight
   v. Height
2. **Suspected Drug(s)**
   i. Generic name of the drug*
   ii. Indication(s) for which suspect drug was prescribed or tested
   iii. Dosage form and strength
   iv. Daily dose and regimen (specify units - e.g., mg, ml, mg/kg)
   v. Route of administration
   vi. Starting date and time of day
   vii. Stopping date and time, or duration of treatment
3. **Other Treatment(s)**

Provide the same information for concomitant drugs (including non prescription/OTC drugs) and non-drug therapies, as for the suspected drug(s).

4. **Details of Serious Adverse Event (s)**

Full description of reaction (s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious has to be provided. In addition to a description of the reported signs and symptoms, whenever possible, describe a specific diagnosis for the reaction.* Causality assessment by the investigator.

   i. Start date (and time) of onset of event
   ii. Stop date (and time) or duration of event
   iii. Dechallenge and rechallenge information
   iv. Setting (e.g., hospital, out-patient clinic, home, nursing home)
   v. Results of specific tests and/or treatment that may have been conducted

5. **Outcome**

Information on recovery and any sequelae; for a fatal outcome, cause of death and a comment on its relationship to the suspected reaction; any post-mortem findings

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 etc.

Details of compensations provided for injury or death. In case no compensation has been paid, reason for the same should be submitted. It is pertinent to mention that in case of study related injury or death, complete medical care as well as compensation for the injury or death should be provided.

6. **Details about the Investigator***
   i. Name, Address & Telephone number
   ii. Profession (specialty)

iii. Date of reporting the event to Licensing Authority
iv. Date of reporting the event to Ethics Committee overseeing the site:
v. Signature of the Investigator
vi. Note: Information marked * must be provided.

ANNEXURE II: Covering letter template for SAE reporting in CTs

<Please print on company / CRO letter head>

*Ref No.: <Insert Company's letter ref /tracking No**., if any***>* Date: <*DDMMMYYYY*>

To
The Drugs Controller General (India)
CDSCO, FDA Bhawan, CHEB Campus
Kotla Road, New Delhi - 110002

Subject: Reporting Serious Adverse Event (SAE)

CT File No. (CDSCO File No.): _____	**Sponsor Address:**	**CRO Address (if any):**	
Trial ID/Protocol No./Study Code: **Phase of Study:**	**Phone:** **E-mail:**	**Phone:** **E-mail:**	
Investigational Drug(s): **Initial Report** ☐ **/ Follow-up # _ _**	**Study Title:**		
CT Category <*(Please select appropriate category from the list)*>	☐ **CT-1-IND** ☐ **CT-2-Reg** ☐ **CT-3-GCT** ☐ **CT-4-rDNA** ☐ **CT-5-Vac** ☐ **CT-6-Oth** ☐ **CT-7-Dev** ☐ **CT-8-Oth**		
Adverse Event term / Diagnosis:	**Whether the event is an Unexpected**	**Causality Assessment** (Related/Not related)	
		Investigator	Medical Monitor
	SAE: ☐ **Yes**	**SAE:** ☐ **Yes**	
	Fatal: ☐ **Yes**	☐ **No**	
Details of compensation provided for injury or death . In case no compensation has been paid , reason for the same :			

Dear Sir,

This is to bring to your kind notice that <*Dr.*_____>, investigator at <_____ _____>, has informed us that a subject with initials <"____"> has suffered with a SAE on <*DDMMMYYYY*>. Brief details are as below:

<Insert a brief narrative - not exceeding 10 lines> <Incase, this is a follow-up report, please capture the date of submission of initial report in the narrative>

Following documents are enclosed for your perusal, < *(please edit the list as appropriate)*

1. *Duly filled SAE form as per Appendix XI of Schedule Y or CIOMS-I / MedWatch form*
2. *Laboratory investigations report /Discharge summary (if available and applicable i.e. only the reports that are critical for causality assessment should be provided)*
3. *Postmortem report (if applicable)/ Any additional documents>*

Yours faithfully,

(Authorised Signatory)