GUIDANCE DOCUMENT FOR INDUSTRY

ON REPORTING SERIOUS ADVERSE EVENTS

(SAEs)

OCCURING IN CLINICAL TRIALS

(As per the New Drugs and Clinical Trials Rules 2019)

Drugs Controller General (India),

Directorate General of Health Services,

Central Drugs Standard Control Organization (CDSCO),

New Delhi

TABLE OF CONTENTS

GUIDANCE FOR INDUSTRY REPORTING SERIOUS ADVERSE EVENTS (SAEs) OCCURING IN CLINICAL TRIALS

1. Purpose

This guidance document provides a uniform procedure for reporting Serious Adverse Events (SAEs) by **Principal Investigator (PI), Sponsor and Ethics Committee (EC)** occurring during clinical trials conducted in India in accordance with the provisions of the **New Drugs and Clinical Trials Rules (NDCT), 2019**. It aims to ensure timely reporting, proper causality assessment, participant safety, and regulatory compliance.

2. Scope

All SAEs occurring in clinical trials should be reported as per the Check List provided on SUGAM Portal based on Chapter VI of New Drugs and Clinical Trials Rules (NDCT), 2019 by the Pharmaceutical Companies / Sponsors / CROs/ Investigators /Ethics Committee's / Clinical Trial Sites conducting Clinical Trials /CT of New Drugs/ Bio Availability & Bio Equivalence Studies (included in Human Beings) /Investigational New Drugs **within the applicable timelines.**

3. Definitions

3.1 Adverse Event (AE)

Any untoward medical occurrence (including a symptom or disease or an abnormal laboratory finding) during treatment with an investigational drug or a pharmaceutical product in a patient or a trial subject that does not necessarily have a relationship with the treatment being given

3.2 Serious Adverse Event (SAE)

An untoward medical occurrence during clinical trial resulting in death or permanent disability, or hospitalisation of the trial subject where the trial subject is an outdoor patient or a healthy person, prolongation of hospitalisation where the trial subject is an indoor-patient, persistent or significant disability or incapacity, congenital anomaly, birth defect or life threatening even.

4. Responsibilities

4.1 Investigator

(i) The investigator shall be responsible for the conduct of the trial according to the protocol approved by CLA and Good Clinical Practices(GCP) Guidelines and also for compliance as per the undertaking given in Table 4, Third Schedule, Chapter V of New Drugs and Clinical Trials Rules , 2019. Standard operating procedures are required to be documented by the investigators for the tasks performed by them.

(ii) During and following a subject's participation in trial, the investigator should ensure that adequate medical care is provided to the participant for any adverse events.

(iii) Investigator shall report all serious adverse events to the Central Licencing Authority, the sponsor or his representative, whosoever had obtained permission from the Central Licencing Authority for conduct of the clinical trial, and the ethics committee that accorded approval to the study protocol, within twenty-four hours of their occurrence.

(iv) In case, the investigator fails to report any serious adverse event within the stipulated period, he shall have to furnish the reason for the delay to the satisfaction of the Central Licencing Authority along with the report of the serious adverse event. The report of the serious adverse event, after due analysis, shall be forwarded by the investigator to the Central Licencing Authority, the Chairperson of the ethics committee and the Head of the institution where the trial has been conducted within fourteen days of the occurrence of the serious adverse event.

(v) The investigator shall provide information to the trial subject through informed consent process as provided in Table 3, Third Schedule, Chapter V of New Drugs and Clinical Trials Rules,2019 about the essential elements of the clinical trial and the subject's right to claim compensation in case of trial related injury or death. He shall also inform the subject his or her nominee of their rights to contact the sponsor or his representative whosoever had obtained permission from the Central Licencing Authority for conduct of the clinical trial for the purpose of making claims in the case of trial related injury or death.

4.2 Sponsor

(i) The clinical trial sponsor is responsible for implementing and maintaining quality assurance systems to ensure that the clinical trial is conducted and data generated, documented and reported in compliance with the protocol and Good Clinical Practices Guidelines as well as with all applicable statutory provisions. Standard operating procedures should be documented to ensure compliance with Good Clinical Practices Guidelines and applicable regulations.

(ii) Sponsors are required to submit a status report on the clinical trial to the Central Licencing Authority at the prescribed periodicity.

(iii) In case of studies prematurely discontinued for any reason including lack of commercial interest in pursuing the new drug application, a summary report should be submitted within 3 months. The summary report should provide a brief description of the study, the number of patients exposed to the drug, dose and duration of exposure,

details of adverse drug reactions, if any, and the reason for discontinuation of the study or non-pursuit of the new drug application;

(iv) Any report of the serious adverse event, after due analysis shall be forwarded by the sponsor to the Central Licencing Authority, the Chairperson of the ethics committee and the head of the institution where the trial has been conducted, within fourteen days of knowledge of occurrence of the serious adverse event as specified in Table 5, Third Schedule, Chapter V of New Drugs and Clinical Trials Rules, 2019.

(v) In case of injury or death occurring to the trial subject, the sponsor (whether a pharmaceutical company or an institution) or his representative or the investigator or the institution or centre where the study was conducted, as the case may be, shall make payment for medical management of the subject and also provide financial compensation for the clinical trial related injury or death in accordance with the procedure as prescribed in Chapter VI of New Drugs and Clinical Trials Rules, 2019.

(vi) The sponsor (whether a pharmaceutical company or an Institution) or his representative, whosoever had obtained permission from the Central Licencing Authority for conduct of the clinical trial, shall submit details of compensation provided or paid for clinical trial related injury or death, to the Central Licencing Authority thirty days of the receipt of the order of the Central Licencing Authority.

(vii) The sponsor shall provide post-trial access of the investigational drug by giving the drug free of cost to the trial subject as per directions of the Central Licencing Authority in special circumstances on the recommendations of the investigator and the ethics committee and written consent of the patient in accordance with Rule 27 of New Drugs and Clinical Trials Rules, 2019.

4.3 Ethics Committee

(i) It is the responsibility of the ethics committee that reviews and accords its approval to a trial protocol to safeguard the rights, safety and well-being of all trial subjects.

(ii) The ethics committee should exercise particular care to protect the rights, safety and well-being of all vulnerable subjects participating in the study, e.g., members of a group with hierarchical structure (e.g. prisoners armed forces personnel, staff and students of medical, nursing and pharmacy academic institutions), patients with incurable diseases, unemployed or impoverished persons, patients in emergency situation, ethnic minority groups, homeless persons, nomads, refugees, minors or other incapable of personally giving consent.

(iii) Ethics committee should get documented standard operating procedures and should maintain a record of its proceedings.

(iv) Ethics committee should make, at appropriate intervals, an ongoing review of the trials for which they have reviewed the protocol. Such a review may be based on the periodic study progress reports furnished by the investigators or monitoring and internal audit reports furnished by the sponsor or visiting the study sites.

(v) In case an ethics committee revokes its approval accorded to a trial protocol, it must record the reasons for doing so and at once communicate such a decision to the Investigator as well as to the Central Licensing Authority.

(vi) In case of serious adverse event occurring to the trial subject, the ethics committee shall forward its report or order on the event, after due analysis, along with its opinion on the financial compensation, if any, to be paid by the sponsor or his representative or institution or centre, as the case may be, in accordance with Chapter VI of New Drugs and Clinical Trials Rules, 2019.

5. Timelines for SAE Reporting

Activity	Timeline
Initial reporting of SAE by Investigator to Sponsor, Ethics Committee and CLA	Within **24 hours** of occurrence of SAE
Detailed SAE analysis report by Investigator	Within **14 calendar days**
Analysis report by Sponsor	Within **14 calendar days**
Opinion of Ethics Committee	Within **30 calendar days**

6 SAE REPORTING IN CLINICAL TRIALS / BIOAVAILABILITY AND BIOEQUIVALENCE STUDY

6.1 Information to be submitted by the Principal Investigator (24 Hours & 14 Days), Sponsor (14 Days) and Ethics Committee (30 Days) as per the individual Check list available on SUGAM Portal for Reporting SAEs

PI (24 Hours) Checklist :-

1.1 1.1.1 Country (Name of the country should be specified)

1.1.2 SAE report of death or other than death
1.1.3 Protocol Title
1.1.4 Protocol Study No./ ID /Code
1.1.5 Copy of Clinical Trial permission/ BE-NOC obtained from CDSCO
1.1.6 CTRI Registration No. (Mandatory for Clinical Trial Permitted after 15/06/09)
1.1.7 Sponsor/CT NOC holder (Address with contact no and Email)
1.1.8 CRO (Address with contact no and Email)
1.1.9 Clinical Trial Site address and site number.
1.1.10 Initial / Follow-up (FU)
1.1.11 In case of follow-up: Date & Diary no of initial or recently submitted report information

1.2. Patient/Subject Details

1.2.1 Initials & other relevant identifier (hospital/OPD record number etc.)
1.2.2 Gender
1.2.3 Age and/or date of birth, Weight, Height

1.3. Details about the Investigator

1.3.1 Name
1.3.2 Address
1.3.3 Telephone/Mobile Number & Email
1.3.4 Profession (speciality)
1.3.5 Date of reporting the event to Licensing Authority:
1.3.6 Date of reporting the event to Ethics Committee overseeing the site:
1.3.7 Date of reporting the event to Sponsor/CRO

PI (14 Days) Checklist :-

2.1 Suspected Drug(s)/Investigational Drug(s)/Study Drug(s)/Medical Device

2.1.1 Generic name of the Drug/Device.
2.1.2 Indication(s) for which suspect/study drug was prescribed or tested.
2.1.3 Dosage form and strength, Dosage regimen
2.1.4 Route of administration.
2.1.5 Starting date and time of day.
2.1.6 Stopping date and time, or duration of treatment.

2.2 Other Treatment(s)

2.2.1 Generic name of the Drug/Device.
2.2.2 Indication(s) for which suspect/study drug was prescribed or tested.
2.2.3 Dosage form and strength, Dosage regimen
2.2.4 Route of administration.
2.2.5 Starting date and time of day.
2.2.6 Stopping date and time, or duration of treatment

2.3 Details of the events

2.3.1 Full description of event (s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious. In addition to a description of the reported signs and symptoms, whenever possible, describe a specific diagnosis for the reaction.
2.3.2 Start date (and time) of onset of reaction.
2.3.3 Stop date (and time) or duration of reaction.
2.3.4 Dechallenge and rechallenge information.
2.3.5 Setting (e.g., hospital, out-patient clinic, home, nursing home).
2.3.6 Expectedness of SAE (Expected / Unexpected) as per IB.

2.4 Outcome

2.4.1 Information on recovery and any sequelae; results of specific tests and/or treatment that may have been conducted.
2.4.2 For a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction; any post-mortem findings.
2.4.3 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.

2.5 Adverse Event Term / Details of SAE

2.6 Causality Assessment by Investigator with justification for Relatedness/Un-relatedness and supporting documents

2.7 Duly filled SAE Form as per Table-5 of New Drugs and Clinical trial Rules, 2019

2.8 Laboratory investigations report /Discharge summary (if available and applicable)

2.9 Autopsy Report

2.10 Copy of Signed Informed Consent Form of the Subject/Patient.

2.11 Socioeconomic background of subject/patient viz. Qualification, Occupation, Monthly income

2.12 Baseline Investigations Report

2.13 Copy of Discharge Summary

2.14 Copy of Death Certificate

Sponsor (14 Days) Checklist :-

3.0 Causality Assessment by Sponsor/CRO with justification for Relatedness/Unrelatedness and supporting documents

3.1 Details of compensation provided for injury or death. In case no compensation has been paid, reason for the same:

3.2 Filled copy of CRF/Patient admission records

3.3 Copy of Protocol version on which the subject was at the time of occurrence of SAE-death/injury

3.4 Copy of Investigator Brochure

ETHICS COMMITTEE (30 Days) Checklist :-

4. Details about the Ethics Committee

4.1.1 Name & Address

4.1.2 Name of Chairman & Address

4.1.3 Telephone/Mobile Number

4.1.4 Email

4.2 EC Registration Certificate copy obtained from CDSCO

4.3 Ethics Committee Opinion on the Relatedness/ Unrelatedness with Justification

NOTE TO PRINCIPAL INVESTIGATOR, SPONSOR AND ETHICS COMMITTEE

- It is to inform that as per the Directorate's Order File No. CT/SAE-Misc-10/2020-Part.B dated 25.02.2021 (Notice issued by DCG(I) regarding implementation of SUGAM Online system for reporting of SAEs (1) (2).pdf), this division shall receive files only through a dedicated SUGAM Portal w.e.f. 14.03.2021.Accordingly, you are hereby requested to furnish the relevant documents i.e. Principal Investigator's Report (24 Hours) , Principal Investigator's Report(14 Days) , Sponsor's Report (14 Days) and Ethics Committee Report (30 Days) on Causality Assessment of SAE through the Online SUGAM Portal for further processing of the application. In case of any technical issue while submission of application, may kindly contact CDAC for resolution of the same.

- The Details of the PI, Sponsor and Ethics Committee including information pertaining to the Name & Contact Number, Address, Email ID etc. shall be provided. (Such Details & changes, if any, shall promptly be informed to this Directorate).

- The PI, Sponsor and Ethics Committee should strictly follow the prescribed time lines while reporting SAEs. Non-compliance of the same shall result in issuance of Show cause Notice(s) to the PI/Sponsor/EC for violation of rules under the provision of New Drugs & Clinical Trial Rules, 2019. Further, in case of failure of submission of valid clarification/justification, it shall be construed that there is nothing to say in the matter and the action deemed fit shall be initiated as per New Drugs & Clinical Trial Rules, 2019 under the provision of Drugs and Cosmetics Act, 1940 without further communication.

- Note- It is further apprised that a feature- E-Vartalap is available on SUGAM portal for easy communication amongst the officials and the firms through which the documents pertaining to the SAE(s) can also be uploaded. So, the applicants are encouraged to make use of the feature for any updates/ clarification in the application(s).

For any Technical Issue in uploading the Online SUGAM portal for reporting SAE Reported Please Contact CDAC SUGAM portal (CDSCO)

Phone Number: +91-11-23502918 (IT Helpdesk)

General IT / Sugam Portal Helpdesk Email: ***helpdesk.sugam@cdsco.nic.in***

SAE Division Email: ***sae@cdsco.nic.in.***

7. ABBREVIATIONS

AE	Adverse Event
BE	Bioequivalence
CLA	Central Licensing Authority
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