Standard Operating Procedures of Institutional Ethics Committee

ICMR – NIRRCH Ethics Committee for Human Studies

Title: Review of Adverse Events (AE) and Serious Adverse Events (SAE) Reports

SOP Code: 18/V1.5 Dated:8th November 2024 Page Nos: 211 to 227

18.1. Purpose

The purpose of this SOP is to provide instructions on the review and follow-up reports of adverse events (AE) and serious adverse events (SAE) for any active study approved by the ICMR-NIRRCH Ethics Committee for Human Studies. The SAE must be reported by the investigators to the IEC within 24 hours after the incident. The unexpected events should be included in the continuing review report submitted to IEC.

Unanticipated risks are sometimes discovered during the course of studies. Information that may impact the risk/benefit ratio should be promptly reported to and reviewed by the IEC to ensure adequate protection of the welfare of the study participants.

The unanticipated risks may as well include any event that in the investigator's opinion, may adversely affect the rights, welfare or safety of the participants in the study.

18.2. Scope

This SOP applies to the review of SAE reports submitted by Investigators to IEC members or other concerned parties.

18.3. Responsibility

The researcher is responsible to report SAEs for all trials and if applicable timelines as specified by regulators have to be followed (within 24 hours after knowledge of occurrence of SAE to the sponsor, EC and regulator, if applicable, followed by a due analysis report in 14 days). Reporting of SAE may be done through the Sugam portal for regulatory clinical trials, and for others by email or fax communication (including on non-working days). A report on how the SAE was related to the research must also be submitted within 14 days.

The IEC Secretariat is responsible for initial screening of the reports and assessing / seeing whether they need a review of full Board, Chairperson, other qualified IEC members or experts.

The EC is responsible for reviewing the relatedness of the SAE to the research as reported by the researcher and determining the quantum of compensation to be provided to the participants.

A SAE subcommittee or expedited review committee could be formed for the specific study under consideration. These should be part of the main committee and comprise Chairperson/ Member Secretary and one to two appropriate designated members of the main EC as defined in the SOPs. These subcommittees can report to the concerned main EC.

a. For clinical trials under the purview of CDSCO, the timeline and procedures as notified from time to time may be followed.

b. All research participants who suffer harm, whether related or not, should be offered appropriate medical care as required, psycho-social support, referrals, clinical facilities, etc.
c. Medical management should be free if the harm is related to the research
d. Compensation should be given to any participant when the injury is related to the research. This is applicable to participants in any of the arms of research, such as intervention and standard of care/placebo.
e. While deliberating on the quantum of compensation to be awarded to participants who have suffered research-related injury, the IEC should consider aspects including the type of research (interventional, observational, etc.), extent of injury (temporary/permanent, short/long term), loss of wages, etc.
f. For other sponsored research, it is the responsibility of the sponsor (whether a pharmaceutical company, government or non-governmental organization (NGO), national or international/bilateral/multilateral donor agency/institution) to include insurance coverage or provision for possible compensation for research related injury or harm within the budget.
g. In investigator-initiated research/student research, the investigator/institution where the research is conducted becomes the sponsor. If any extramural project has no provision for such funds, the Director must extend support from core institutional budget until relatedness is proven. Hence in the applications for research grants to funding agencies – national or international, government or non-government agencies – the researcher should keep a budgetary provision for insurance coverage and/or compensation depending upon the type of research, anticipated risks and proposed number of participants.
h. For participants who are availing routine medical care at hospitals where they were recruited, the concerned clinical collaborator and hospital will take responsibility if it is not directly related to participation in research. This point must be clearly mentioned in the MoU

All AEs should be recorded and reported to the EC according to a pre-planned timetable, depending on the level of risk and as recommended by the IEC.

The primary responsibility of the IEC is to review and address SAE and unexpected events involving risks to participants.

IEC should also make sure that researchers are made aware of the policies and procedures concerning reporting and continuing review requirements of SAE and unexpected events.

a. The Principal Investigator should submit within 24 hours on site SAE report or the unexpected adverse event report to the IEC or by email.
b. The report of SAE of death after due analysis shall be forwarded by the Investigator to the regulator, chairperson of the IEC with a copy of the report to the Head of the institution where the trial is being conducted within 14 calendar days of knowledge of occurrence of SAE of death.

c. The sponsor should submit the report of due analysis to the DCGI (CLA) and Head of the institution within 14 days of knowledge of occurrence of the SAE event.
d. The report of the SAE other than death after due analysis shall be forwarded by the Investigator to Chairman of the IEC and the Head of the institution where the trial is being conducted within 14 calendar days of occurrence of SAE.
e. The report should be accompanied by detailed narrative of the SAE in Table 5 format of the NDCT Rules, 2019.
f. After due consideration and opinion on compensation, Chairperson of EC should submit the report to DCGI (CLA) within 30 days of the SAE event.

The sponsor or his representative shall pay the compensation in case of clinical trial related injury or death within 30 days of the receipt of such an order from Central Licensing Authority.

18.4. Flow chart

Sr. No.	Activity	Responsibility
1	SAE related activities before an IEC meeting	IEC Secretariat, SAE or sub-committee members
2	Review and determine the review channel	IEC Secretariat, members
3	Decide the criteria for the review	IEC Secretariat, members
4	Review and discuss during the IEC meeting	IEC members and Chairperson
5	Decide what action should be taken	IEC members and Chairperson
6	Inform investigator**,** regulatory authorities and head of institution within 30 days of receipt of the SAE	Secretariat and Chairperson

18.5. Detailed instructions

18.5.1 Before each IEC meeting

18.5.1.1 Review and determine the review channel

IEC Secretariat or members review the reporter's assessment to determine whether the report requires review by the full Board or by the Chairperson or other qualified IEC member(s).

18.5.1.2 Criteria for the review

The **review criteria** are as follows:

a. Assessment of adverse event is unknown or unlikely

b. Report is forwarded to the Chairperson for review and determination if report should be reviewed at the convened meeting by full committee.
c. Assessment of relatedness of the SAE as per the NDCT Rules, 2019 .
d. Assessment of SAE management for biomedical or academic research studies as per ICMR's ethical guidelines, 2017
e. The report is added to the agenda for review at a convened meeting by full committee.
f. The Chairperson may request to invite an appropriate external expert in addition to the SAE committee to review the AE/SAE if needed
g. An adverse event/Investigational New Drug Safety Report has been previously seen by full committee but being submitted by another investigator participating in the multi-study site (as part of a multi-center/site study).
    i This notification does not require holding and emergency/unscheduled full committee meeting.
    ii Report reviewed by the Chairperson or other qualified IEC members and Member Secretary

17.5.2 During the IEC meeting

17.5.2.1 Review and discuss

After reading and reviewing the report, the Chairperson or designee discusses on the study and similar adverse events or advisories.

If appropriate to the discussions, the Chairperson or another EC member may call for a consensus on whether to:

i Request an amendment to the protocol or the consent form.
ii Request further information on the AE/SAE and its management in case of academic studies
iii Suspend or terminate the study.

17.5.2.2 Decide what action should be taken

i If any of the above *actions are taken*, the IEC Secretariat or designee notifies the investigator of the action taken.
ii If the IEC *takes no action*, a notation is made in the minutes and the study is allowed to continue.

17.5.2.3 Inform investigator or clinical trial office

i The IEC secretariat member drafts a formal letter to the investigators or the clinical trial office to notify them of the action they should take according to the IEC decision.
ii Get the Chairperson to approve, sign and date the letter.
iii Send the letter and record the delivery date.

17.6 ANNEX

ANNEX 1	AF/01/18/V1.5	AE Summary Report
ANNEX 2	AF/02/18/V1.5	SAE reporting format (Biomedical Health Research)
ANNEX 3	AF/03/18/V1.5	SAE reporting format (Clinical Trials)
ANNEX 4	AF/04/18/V1.5	Checklist for Submission of Serious Adverse Event Report (SAE) Occurring in Clinical Trial/ Bio-Equivalence Study
ANNEX 5	AF/05/18/V1.5	Document History

ANNEX 1 **AF/01/18/V1.5**

Adverse Event (AE) Summary Report

Principal Investigator:…….

Study Title:……..

Name of the studied medicine/device……..

Sponsor:……..

#	Description of Adverse Events (AE)	Date of Event (D/M/Y)	Date start and end of Tx (D/M/Y)	F or M	Initial	Age (Y)	Serious Yes/ No	Related to Study Yes/ No	Concomitant medic ation	Inter-vention

Comment:

Reviewed by**:……**

Date:

ANNEX 2 **AF/02/18/V1.5**

Serious Adverse Event Reporting Format (Biomedical and Health Research)

icmr NIRRCH INDIAN COUNCIL OF MEDICAL RESEARCH | NATIONAL INSTITUTE FOR RESEARCH IN REPRODUCTIVE AND CHILD HEALTH	**Serious Adverse Event Reporting Format (Biomedical Health Research)** ICMR-NIRRCH Ethics Committee for Human Studies

Project no……. Duration of the project :……
Title of study:
……
……
Principal Investigator (Name, Designation and Affiliation): ……
Co-PIs/Collaborators (Name, Designation and Affiliation): ……
……

1. Participant details :

Initials and ID Age at the time of event Gender Male / Female

…… …….. Weight:……..(Kgs)

…… …….. Height:……..(cms)

2. Suspected SAE diagnosis: ……

3. Date of onset of SAE : …… Date of reporting SAE: ……

Describe the event (*Duration, setting, site, signs, symptoms, severity, criteria for regarding the event serious.)* : ……

……

4. Details of suspected intervention causing SAE (*Refers to research intervention including basic, applied and operational research or clinical research, except for investigational new drugs. If it is an academic clinical trial, mention name, indications, dosage, form and strength of the drug(s).*

……

……

5. Report type: Initial/ Follow-up/ Final

If Follow-up report, state date of Initial report: ……..

6. Have any similar SAE occurred previously in this study? Yes/ No

   If yes, please provide details……..

   ……

   ……

7. In case of a multi-centric study, have any of the other study sites reported similar SAEs?

   (Please list number of cases with details if available)

   ……

   ……

8. Tick whichever is applicable for the SAE: (Kindly note that this refers to the Intervention being evaluated and NOT disease process)
   a. Expected event/ Unexpected event
   b. Hospitalization
   c. Increased Hospital Stay
   d. Persistent or significant disability/incapacity
   e. Event requiring intervention (surgical or medical) to prevent SAE
   f. Death
   g. Congenital anomaly/ birth defect
   h. Event which poses a threat to life
   i. Others ……

   In case of death, state probable cause of death……

   C. No permanent/significant functional/cosmetic impairment

   Permanent/significant functional/cosmetic impairment

   Not Applicable

9. Describe the medical management provided for adverse reaction (if any) to the research participant. (Include information on who paid, how much was paid and to whom).

   ……

   ……

10. Provide details of compensation provided / to be provided to participants. (Include information on who pays, how much, and to whom) ……
……

11. Outcome of SAE Resolved/ Ongoing/ Death
Others (specify) ……..
……

12. Provide any other relevant information that can facilitate assessment of the case such as medical history……
……..
……
……

13. Provide details about PI's final assessment of SAE relatedness to trial.
……..
……..
……..

Signature of PI with date : ……
Reviewed by:……..
Comment:……
Date:……
Action:……

ANNEX 3 **AF/03/18/V1.5**

Serious Adverse Event Reporting Format (Clinical Trials)

	Serious Adverse Event Reporting Format (Clinical trials) **ICMR-NIRRCH Ethics Committee for Human Studies**

Project No. …… Duration of the study: …….
Title of study:
……
……
……
Principal Investigator (Name, Designation and Affiliation): ……
Co-PIs/Collaborators (Name, Designation and Affiliation): ……
……

1. Participant details :
   a. Initials and Case No. ID
   b. Age at the time of event
   c. Gender: Male/ Female
   d. Weight: ……..(Kgs)
   e. Height: ……..(cms)
2. Report type: Initial/ Follow-up/ Final
   If Follow-up report, state date of Initial report: ……
   What was the assessment of relatedness to the trial in the Initial report?
   a. By PI – Related/ Unrelated
   b. By Sponsor – Related/ Unrelated
   c. By EC – Related/ Unrelated
3. Describe the event and specify suspected SAE diagnosis:……
   ……
   ……
4. Date of onset of SAE : …… Date of reporting:……
5. Onset lag time after administration of intervention: ……
6. Location of SAE(Clinic/Ward/Home/Other)……..
7. Details of suspected drug/device/investigational procedure causing SAE:

a. Suspect drug (include generic name) device/intervention: ……

……

b. Indication(s) for which suspect drug was prescribed or tested:……

……

c. Route(s) of administration, daily dose and regimen, dosage form and strength:……

……

d. Therapy start date:…… Stop Date: ……

8. Was study intervention discontinued due to event? Yes/ No

9. Did the reaction decline after stopping the drug/procedure? Yes/ No
If yes, provide details about the reduced dose:……

10. Did the reaction reappear after reintroducing the drug/procedure? Yes/ No/NA
If yes, provide details about the dose:……

11. Concomitant drugs history and lab investigations:

a. Concomitant drug(s) and date of administration: .....

.....

.....

b. Relevant test/laboratory data with dates:.....

.....

.....

c. Patient relevant history including pre-existing medical conditions (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/renal dysfunction etc).....

.....

.....

12. Have any similar SAE occurred previously in this study? If yes, please provide details. Yes/□No□

.....

.....

13. Seriousness of the SAE:

a. Death

b. Congenital anomaly
c. Life threatening
d. Required intervention to prevent
e. Hospitalization-initial or prolonged
f. Permanent impairment/damage
g. Disability
h. Others (specify): .....

14. Describe the medical management provided for adverse reaction (if any) to the research participant. (Include information on who paid, how much was paid and to whom)
.....
.....

15. Outcome of SAE:
a. Fatal
b. Recovered
c. Continuing
d. Unknown
e. Recovering
f. Other (Specify)……..

16. Was the research participant continued on the trial? Yes/No/NA

17. Provide details about PI's final assessment of SAE relatedness to trial.
.....
.....

18. Has this information been communicated to sponsor/CRO/regulatory agencies? Yes/No
Provide details if communicated (including date)

19. Does this report require any alternation in trial protocol? Yes/No

20. Provide details of compensation provided/to be provided the participants (Include information on who pays, how much and to whom).....
.....

Signature of PI with date:.....

ANNEX 4 **AF/EC/04/18/V1.5**

CHECKLIST FOR SUBMISSION OF SERIOUS ADVERSE EVENT REPORT (SAE) OCCURRING IN CLINICAL TRIAL/BIO-EQUIVALENCE STUDY

Sr. No.	**Details**		
1.	**Country (Name of the country should be specified)**		
2.	**SAE report of death or other than death, Please tick (✓)**	Death ☐	Other Than ☐ Death
		Yes/No	**Page No.**
3.	**In case of Serious Adverse Event(SAE), please specify if there is any injury to the participant (Please specify Yes/No) in the box**		
4.	Protocol Title		
5.	Protocol Study No./ ID /Code		
6.	Copy of Clinical Trial permission/ BE-NOC obtained from CDSCO		
7.	CTRI Registration No. (Mandatory for Clinical Trial Permitted after 15/06/09)		
8.	Sponsor (Address with contact no and Email)		
9.	CRO (Address with contact no and Email)		
10.	Clinical Trial Site address and site number.		
11.	Initial / Follow-up (FU)		
12.	In case of follow-up: Date & Diary no of initial or recently submitted report information		
13.	**Patient/Participants Details**		
a.	Initials & other relevant identifier (Hospital/OPD record number etc.)		
b.	Gender		
c.	Age, Date of birth, Weight & Height		
14.	**Suspected Drug(s)/Medical Device**		
a.	Generic name of the Drug(s)/Device.		
b.	Indication(s) for which suspect/study drug was prescribed or tested.		
c.	Dosage form and strength / Dosage regimen		
d.	Route of administration.		
e.	Starting date and time of day.		
f.	Stopping date and time & duration of treatment		
g.	Baseline values of investigations prior to administration of Suspected Drug(s)/ Medical Device.		
15.	**Other Treatment(s) / Concomitant Drug History**		
	Provide the same information for concomitant drugs (including non- Prescription /OTC Drugs) and non-drug therapies, as for the suspected drug(s)		

a.	Generic name of the Drug(s)/Device.		
b.	Indication(s) for which suspect/study drug was prescribed or tested.		
c.	Dosage form and strength / Dosage regimen		
d.	Route of administration.		
e.	Starting date and time of day.		
f.	Stopping date and time & duration of treatment		
16.	**Details of the events**		
a.	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.		
b.	Start date (and time) of onset of reaction.		
c.	Stop date (and time) or duration of reaction.		
d.	Dechallenge and rechallenge information.		
e.	Setting (e.g., hospital, out-patient clinic, home, nursing home).		
f.	Expectedness of SAE (Expected / Unexpected) as per IB		
17.	Outcome		
a.	Information on recovery and any sequelae; results of specific tests and/or treatment that may have been conducted.		
b.	For a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction; any post-mortem findings.		
c.	Other information: anything relevant to facilitate assessment of the case, such as medical history with date including allergy, drug or alcohol abuse; family history; findings from special investigations etc.		
18.	Details about the Investigator		
a.	Name		
b.	Address		
c.	Telephone/Mobile Number & Email		
d.	Profession (specialty)		
e.	Date of reporting the event to Licensing Authority:		
f.	Date of reporting the event to Ethics Committee overseeing the site:		
g.	Date of reporting the event to Sponsor/CRO		
h.	Signature of the Investigator		
19.	Details about the Ethics Committee		
a.	Name & Address		
b.	Name of Chairman & Address		
c.	Telephone/Mobile Number		
d.	Email		
20.	Adverse Event Term / Details of SAE		

21.	Causality Assessment by Investigator with reasoning for Relatedness/Un- relatedness along with supporting investigational documents. For SAE-Death the name(s) of the suspected drug(s) must be provided after Unblinding.		
22.	Causality Assessment by Sponsor/ CRO with reasoning for Relatedness /Un-relatedness. For SAE-Death the name(s) of the suspected drug(s) must be provided after Unblinding.		
23.	Causality Assessment by Ethics Committee with reasoning for Relatedness /Un-relatedness. For SAE-Death the name(s) of the suspected drug(s) must be provided after Unblinding.		
24.	Details of compensation provided for injury or death. In case no compensation has been paid, reason for the same.		
25.	Duly filled SAE Form as per Appendix XI of Schedule Y		
26.	Laboratory investigations report /Discharge summary during the time of SAE.		
27.	Post-mortem report & Medical death certificate (if applicable)		
27.	Copy of Signed Informed Consent Form of the participant /patient along with English version.		
28.	Filled copy of CRF		
29.	Socioeconomic background of participant/ patient viz. Qualification, Occupation, Monthly income.		
30.	Copy of latest amended version of Protocol approved by CDSCO.		
31.	Copy of Investigator's Brochure (In case of SAE-death)		

ANNEX 5 **AF/05/18/V1.5**

Document History

Author	Version	Date	Description of the Change
Dr. Ragini Kulkarni	Version 1.0	20th March 2013	First approved copy
Dr. Ragini Kulkarni	Version 1.1	24th September 2014	Timelines for reporting SAEs included on page no.3
Dr. Ragini Kulkarni	Version 1.2	1st September 2016	Pg.4, added under flow chart point 6- regulatory authorities and head of institution within 30 days of receipt of the SAE
Dr. Ragini Kulkarni	Version 1.3	7th November 2017	Pg.10 Annexure 4 for Checklist for submission of SAE added
Dr. Beena Joshi	Version 1.4	1st May 2019	SOP no. changed from 15 to 18 ICMR common ethical review forms for SAE reporting format (Biomedical Health Research) and SAE reporting format (Clinical Trials)added
Dr. Vikrant Bhor	Version 1.5	8th November 2024	All bullets are numbered. • 18.3 Responsibilities modified