Category : Study conduct
Title : Adverse Event (AE) Monitoring, Recording and Reporting
SOP No. : D 14/07
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SOP No.: 14/07 **Total pages:** 10

Date first effective: 01 Jan 2025 **Next Review date:** 31 Dec 2025

Version: 07

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1. Purpose

This standard operating procedure (SOP) describes the responsibilities of the study team for monitoring, recording and reporting adverse events from the time an adverse event is identified until all follow-up activities associated with its resolution have been completed.

2. Scope

This SOP applies to all clinical studies involving human participants.

3. Responsibilities

Principal investigator, Co-investigator, Study Coordinator or any other appropriately qualified staff in the team, as delegated by the Principal Investigator, will be responsible for monitoring, recording and reporting adverse events.

4. Applicable rules, regulations and guidelines

- ICMR's Ethical Guidelines for Biomedical and Health research involving Human Participants, ICMR(2017)
  http://www.icmr.nic.in/guidelines/ICMR_Ethical_Guidelines_2017.pdf
- International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) ICH E6 (R3)
  https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf (Adopted on 06 January 2025)
- Indian GCP guidelines 2001
  https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=MzM5NQ (Last accessed 20 Dec 2024)
- New Drugs and Clinical Trials 2019
  https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf documents/NewDrugs_CTRules_2019.pdf (Last accessed 20 Dec 2024)

5. Reference to other applicable SOPs

SOP No 03/07: Responsibilities of the Study Team
SOP No 17/07: Continued communication with IEC

6. Detailed Instructions:

1. Ensure that all the staff members in contact with participants are aware of their responsibility to monitor, record and report to appropriate study personnel all adverse events (See Appendix 1 for definition of adverse event) reported by the participant or directly observed by the physician (Refer SOP No 03/07: Responsibilities of the Study Team).
2. Assess the patient for AEs at every visit, unscheduled visit, and during ward/ ICU rounds in case the participant is admitted.
3. Ensure that the following are appropriately investigated:
   - Spontaneous reports of adverse events by participants
   - Observations by study team members
   - Reports to study team members by family members of the participant
   - Possible AEs documented in medical records, progress notes, laboratory reports [if applicable]
4. Medically manage the adverse event(s) to ensure that all appropriate measures are directed toward participant safety and well-being.
5. Follow up appropriately when a research participant experiences any adverse change from baseline or pretreatment condition until resolution.
6. Document the nature of the AE (in Appendix IV), which includes onset, duration, progress, causality assessment (as per Appendix II), severity (Appendix III), management and outcome in the participant's source document/s.
7. Medically manage all AEs appropriately.

8. Follow up the patient till complete resolution.
9. If a chronic disorder is diagnosed, ensure that patient/ participant is referred to the appropriate department for further medical care.
10. Various steps may be taken with respect to further use of the investigational product, comparator or placebo (in the interest of participant safety). This decision may only be made by the PI and will be as prescribed in the protocol, for example,
    - Discontinue the investigational product, comparator, or placebo (De-challenge)
    - Reduce dose
    - If necessary for the immediate medical care of the participant, break the drug blind after consultation with the sponsor
11. Complete documentation should be done in the source documents and case record forms (CRFs).
12. Submit to the IEC, the list of AEs occurring for a given project at the time of submission of the biannual Continuing Review Report and the Annual Study Progress Report (six monthly ADR reporting to the IEC

(Refer SOP No 17/07: Continued communication with IEC).

7. Appendices:

Appendix I

Definition of an Adverse Event (AE)

An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease

temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product).
[ICH E6 (R2) www.ich.org, accessed on 30th April 2021 International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) ICH E6 (R3) https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf, Adopted on 06 January 2025]

Appendix II

WHO UMC causality assessment scale

Causality term	Assessment criteria*
Certain	• Event or laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon) • Re challenge satisfactory, if necessary
Probable / Likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable

	• Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) • Disease or other drugs provide plausible explanations
Conditional / Unclassified	• Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Unassessable / Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient or contradictory • Data cannot be supplemented or verified

* All points should be reasonably complied with

Appendix III

Assessment of ADR severity Modified Hartwig and Siegel scale (Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm. 1992; 49(9):2229-32.)

Mild

Level 1: The ADR requires no change in treatment with the suspected drug

Level 2: The ADR requires that the suspected drug be withheld, discontinued, or

otherwise changed.

No antidote, No treatment, no increase in length of stay

Moderate

Level 3: Drug withheld, changed, and/or antidote given, no increase in length of stay

OR

Level 4a: Any level 3 ADR that increases length of stay by at least 1 day

OR

Level 4b: ADR is the reason for admission

Severe

Level 5: Any level 4 ADR that requires intensive medical IEC-2

OR

Level 6: The ADR causes permanent harm to the patient

OR

Level 7: The ADR directly or indirectly leads to the death of the patient

Appendix IV: Adverse Event Reporting Form

A. PATIENT INFORMATION			Reg. No. /IPD No. /OPD No. /CR No. :
1. Patient Initials	2. Age at the time of Event or Date of Birth _____	3. M ☐ F ☐ Other ☐	AMC Report No. :
		4. Weight_____Kgs	Worldwide Unique No. :
B. SUSPECTED ADVERSE REACTION			12. Relevant tests/ laboratory data with dates
5. Event/Reaction start date (dd/mm/yyyy)			
6. Event/Reaction stop date (dd/mm/yyyy)			
6 (A). Onset Lag Time			
7. Describe Event/Reaction with treatment details, if any			13. Relevant medical/medication history (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/renal dysfunction, past surgery etc.)
			14. Seriousness of the reaction: No ☐ if Yes ☐(please tick anyone) ☐ Death (dd/mm/yyyy) ☐ Congenital-anomaly ☐ Life threatening ☐ Disability ☐Hospitalization/Prolonged ☐ Other Medically important
			15. Outcomes ☐ Recovered ☐ Recovering ☐ Not recovered ☐ Fatal ☐ Recovered with sequelae ☐ Unknown

C. SUSPECTED MEDICATION(S)

S.No	8. Name (Brand/Generic)	Manufacturer (if known)	Batch No. / Lot No.	Exp. Date (if known)	Dose used	Route used	Frequency (OD, BD etc.)	Therapy dates		Indication	Causality Assessment
								Date started	Date stopped		
i											
ii											
iii											
iv*											

S.No as per C	9. Action Taken (please tick)						10. Reaction reappeared after reintroduction (please tick)			
	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown	Yes	No	Effect unknown	Dose (if reintroduced)
i										
ii										
iii										
iv										

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S.No	Name (Brand/Generic)	Dose used	Route used	Frequency (OD, BD, etc.)	Therapy dates		Indication
					Date started	Date stopped	
i							
ii							
iii*							

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Additional Information:	D. REPORTER DETAILS
	16. Name and Professional Address:_____ _____ Pin:_____E-mail_____ Tel. No. (with STD code)_____ Occupation:_____Signature:_____
	17. Date of this report (dd/mm/yyyy):
	Sig. and Name of Receiver-

Confidentiality: The patient's identity is held in strict confidence and protected to the fullest extent. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction. Submission of an ADR report does not have any legal implication on the reporter.

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