



YENEPOYA

[DEEMED TO BE UNIVERSITY]

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YENEPOYA ETHICS COMMITTEE 2

DCGI Registration No.: ECR/1337/Inst/KA/2020

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Serious Adverse Event

YEC2/SOP012/v2

Effective Date: 25.02.2023



Title: Serious Adverse Event

SOP Code: YEC2/SOP12/v2

Prepared by:

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Reviewed by:

Dr. Vijaya Hegde Member, YEC2 SOP committee	Signature with Date <i>Vijaya</i>
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Approved by:

Dr. Animesh Jain Chairperson, YEC2	Signature with Date <i>Animesh</i> 25/04/23
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Notified by:

Registrar, Yenepoya (Deemed to be university) Notification No: Ref: No/YU/REG/ACA/YEC-2/SOP/2023 Date: 25.02.2023	Signature with Date <i>Keerthi</i> 29/04/23 Registrar Yenepoya (Deemed to be University) University Road, Devalakatte Mangalore - 575 018
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Details of superseded SOP 12/v1

Subcommittee Convenor name	Version no	Effective date (dd/mm/yy)	Describe the main changes
Dr.H.Hari Kishore Bhat	v1	14.06.2018	Major revision in the SOP

Details of Current SOP 12/v2

SOP subcommittee convenor name	Version no	Effective date (dd-mm-yyyy)	Describe the main changes
Dr. Vijaya Hegde	V2	25.02.2023	Major revision in the SOP



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1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe the procedures to be followed for the review and assessment of initial and follow-up reports of onsite and offsite adverse events (AE) including serious adverse events (SAE) and adverse drug reports (ADR) reported to the YEC2 for any study approved by the Yenepoya Ethics Committee (YEC2). The purpose of this SOP is also to describe the functioning of the SAE subcommittee.

2. Scope:

This SOP applies to all YEC2 activities related to the review of onsite/offsite AE/SAE/ADR reports submitted to the YEC2 and to the functioning of the SAE subcommittee

3. Definitions:

Adverse Event: “An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavourable 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.”

Adverse Drug Report: “In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase “response to a medicinal product” means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out. Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function.”

Serious Adverse Event or Serious Adverse Drug Reaction: “An AE or ADR that is associated with death, inpatient hospitalization (in case the study was being conducted on out-patients), prolongation of hospitalization (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.”

SAE Subcommittee: “Institutions could have subcommittees such as the SAE subcommittee or expedited review committee. 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.”

4. Responsibilities:

YEC2 Chairperson will:

Nominate members for the SAE subcommittee

Oversee the functioning of the SAE subcommittee

YEC2 Member-Secretary will:

Communicate the nomination of the SAE subcommittee members to the Registrar, Yenepoya deemed to be University

Communicate the notification of the SAE subcommittee to the Chairperson and the concerned members

Provide logistic and administrative support to the SAE subcommittee to facilitate its smooth functioning

Table the minutes and reports of the SAE subcommittee in the YEC2 meetings

Prepare the communication letters related to the adverse event reports.

Communicate with the YEC2 members, regulatory authorities and investigators in a timely manner.

Registrar, Yenepoya deemed to be University will:

Notify the constitution of the SAE subcommittee

YEC2 SAE subcommittee Chairperson will:

Ensure that all AEs/ADRs/SAEs are reviewed and necessary action taken in a timely manner.

Ensure that the quorum for the meeting is met.

Be responsible for conducting meetings, and lead all discussions and deliberations pertinent to the review of adverse event reports including:

Review of AE/SAE/ADR reports submitted to the SAE subcommittee

Determining the relatedness of SAE to the research

Determining quantum and type of assistance/compensation required for research participants as per the licensing authorities

4.4.4.4. Reviewing measures taken for SAEs

4.4.4.5 Nominate another SAE subcommittee member as acting Chairperson, if he/she anticipates being absent on the meeting day. The acting Chairperson will have all the powers of the Chairperson of the SAE subcommittee for that meeting.

4.4.4.6. Approve the minutes of the SAE subcommittee meeting

YEC2 SAE subcommittee Executive-Secretary will:

Assign subcommittee members for review of AE/SAE reports

Prepare and circulate the agenda for the SAE subcommittee meeting

Schedule, organize and conduct the SAE subcommittee meetings.

Prepare and circulate the minutes of the meetings after due approval

Communicate the decisions of the SAE subcommittee in the YEC2 meeting

Ensure adherence of the SAE subcommittee functioning to the SOPs

YEC2 SAE subcommittee member(s) will:

Attend the meetings regularly and inform absence in writing

Review and assess the AEs/SAEs assigned to him/her

YEC2 layperson will

In addition to what is described in 4.6, check the compensation provided to the participants in case of SAEs

YEC2 Secretariat will:

Receive communications from the PI regarding onsite/offsite AEs/SAEs/Dear Investigator Letter (DIL) and inform the SAE subcommittee Chairperson

Provide support to the Chairperson/Executive-Secretary of the SAE subcommittee in the conduct of its meetings, preparation of agenda and minutes

Communicate with the concerned authorities and maintain files of subcommittee.

Detailed instructions:

Formation of SAE subcommittee:

The members of the SAE subcommittee will be suggested by the YEC2 members and approved by the Chairperson of YEC2

The Registrar, Yenepoya (deemed to be University) will notify the subcommittee.

Composition of SAE subcommittee:

The SAE subcommittee will be composed of at least 4 and a maximum of 10 members from within the YEC2

The Subcommittee will be multidisciplinary and multi-sectoral in composition.

The committee will consist of members who collectively have the qualifications and experience to review and evaluate the scientific, medical and ethical aspects of adverse event reports involving human participants.

Members of the SAE subcommittee: the SAE subcommittee will consist of

Chairperson

Executive-Secretary

At least one member with postgraduate qualification (preferably in the discipline of Medicine or Pharmacology or any other relevant clinical specialty).

The Member-Secretary shall be an ex-officio member of the SAE subcommittee.

The SAE subcommittee may invite legal experts of YEC2 to provide opinion on the legal implication of adverse events.

The subcommittee may invite IC to provide opinion on the scientific or bureaucratic aspects of the event.

Quorum for the SAE subcommittee meetings:

A quorum will consist of at least 3 members as follows:

Chairperson/Acting Chairperson of the SAE subcommittee

Executive-Secretary and

One member (preferably pharmacologist)

Tenure and terms of reference of the SAE subcommittee member

The tenure of the SAE subcommittee will be for a continuous period from the date of appointment until the end of the tenure of the existing YEC2 committee/SAE subcommittee members.

The SAE subcommittee may be reconstituted each time the YEC2 is reconstituted, or if the existing subcommittee members have changed.

A YEC2 member will be eligible to be appointed for the new tenure of the SAE subcommittee consecutively for two terms.

A member is expected to attend the regular and extraordinary meetings and contribute responsibly to the review and decision making on SAE related reports.

When an SAE subcommittee member is unable to attend the meeting, he/she will inform the Executive Secretary in writing or by email.

An SAE subcommittee member may resign from membership by submitting a letter of resignation to the Executive Secretary of the SAE subcommittee. The member may or may not assign reasons for resignation.

A member may be liable to be disqualified from the subcommittee if the member fails to attend 3 consecutive SAE meetings without prior intimation in writing.

Chairperson of the subcommittee will inform Chairperson YEC2, in writing, if a member has not attended 3 consecutive meetings of the SAE subcommittee.

The Chairperson, YEC2 will take up the issue of disqualification for discussion at the YEC2 meeting and allow the concerned SAE subcommittee member to state his reasons for unauthorized absence.

Schedule of the SAE subcommittee meetings

Ordinary meetings of the subcommittee will be conducted at least once a month.

In the event of a report of SAE, the subcommittee will convene an extraordinary meeting within two calendar days of receiving the report at the YEC2 office and may conduct such meetings as many times as necessary

Timeliness for submission of online SAE reports:

Initial SAE report will be submitted by the Principal Investigator (PI) within 24 hours of occurrence as per the format specified in Ann01/SOP12/v2.

Due analysis (follow up report) will be submitted by the PI/sponsor within 14 calendar days in the format specified in Ann02/SOP12/v2.

The opinion of YEC2 with regard to causality and compensation will be communicated to the Drugs Controller General of India, Central Drugs Standard Control Organization, Ministry of Health and Family Welfare, Government of India within 30 calendar days of the occurrence of the SAE.

The follow up reports of all onsite SAEs till the events are resolved will be submitted by the PI as and when required.

Onsite SAE reporting:

Receipt of onsite SAE related reports by the YEC2:

The YEC2 Secretariat will receive, sign and date the report

The Secretariat will inform the reports to the YEC2 SAE subcommittee Executive-Secretary on the same day of receiving the report

The YEC2 SAE subcommittee Executive-Secretary will verify the completeness of the report and adherence to timelines

If the report is received beyond the specified time, it will be considered as a protocol violation and action will be taken as described in SOP11/v2. Review of onsite SAE Reports:

The Executive-Secretary will review the SAE-related reports. Alternatively, the Executive-Secretary will assign a reviewer from within the subcommittee to review the report and present in the meeting.

Executive-Secretary, in collaboration with Member-Secretary, YEC2, will review the seriousness and urgency of the SAE and decide to call an extraordinary meeting of the SAE subcommittee within 2 calendar days or consider the matter for the subsequent SAE subcommittee meeting.

Reviewers will take into consideration the possibility of research-related causality, quantum of harm caused, quantum of compensation, immediate and ancillary care provided to the participant, and the need for change in protocol/informed consent documents to safeguard the participants.

Even before the SAE subcommittee meets to discuss and deliberate on the SAE report, the Executive-Secretary can write to the PI seeking further clarification. The report and the clarification(s) can be tabled together for discussion in the SAE subcommittee meeting.

SAE subcommittee meeting (for onsite SAE reporting):

Chairperson will confirm the quorum

The Executive-Secretary/reviewing member will present the findings to the SAE subcommittee in the meeting

Members will discuss the findings of the SAE reports and clarifications (if any), with a special focus on relatedness to the clinical trial, medical management and financial compensation to the research participants.

The subcommittee will discuss compensation issues based on the current applicable formulae and guidelines from the regulatory authority 4 , including formula for calculating the amount of compensation in case of study-related death 5,6 and study-related injury other than death .

The subcommittee may refer the report to YEC2 for review if necessary.

The subcommittee may recommend calling an emergency YEC2 meeting to decide on the financial compensation issues, if deemed necessary, within 2 calendar days of the decision.

If necessary, the subcommittee may seek the opinion of an IC to establish relatedness and medical management as per SOP04/v2.

The Executive-Secretary will prepare the minutes within 2 calendar days of the meeting.

YEC2 emergency meeting (for onsite SAE reporting):

If the Executive-Secretary concurs, an emergency YEC2 meeting may be scheduled within 2 calendar days from the subcommittee meeting

The Executive-Secretary will present the findings of the SAE subcommittee, for YEC2 members to deliberate and decide on the relatedness, medical management and financial compensation

YEC2 Scheduled Meeting (for onsite SAE reporting):

The Executive-Secretary will present the findings in the YEC2 meeting to inform the members on the relatedness, medical management and financial compensation

Minutes of the SAE subcommittee/emergency YEC2 meeting will be read, discussed and approved in the YEC2 meeting.

Minutes will be circulated to the YEC2 members as per SOP08/v2..

YEC2 SAE Subcommittee decision-making (for onsite SAE reporting):

The following should be considered during the decision making

The outcome of the SAE

The possible relatedness to the intervention

The number of participants and bystanders affected

The immediate and ancillary medical care provided

Compensation 5.8.5.1.6. Need for change in the protocol/informed consent process/participant information sheet

Need for change in the research team/training

Need for withholding the investigational drug

Need for suspending/terminating the study

5.8.5.1.10. Need for site monitoring

5.8.5.1.11. Adherence to timelines of SAE reporting and protocol deviations/violations, if any

5.8.5.1.12. Need for more clarification

Type of Actions Taken by YEC2 SAE subcommittee on Review of SAE Report:

Following detailed review of the SAE reports and related documents, the SAE subcommittee can suggest one of the following actions:

No further action required: Note the information about the SAE in records for future reference

Request further follow-up information and/or additional details

Recommend further action

Ask for periodic follow-up till SAE is resolved

Provide recommendations regarding/raise queries related to compensation for study-related injury/death.

Type of possible actions taken by YEC2 following full review:

YEC2 may take one or more of the following actions on review of the onsite SAE report:

Suggest changes, amendments in protocol, participant information sheet/informed consent document/ investigator brochure/any other study-related documents.

Suspend the study until additional information is available.

Suspend the study till review is completed (safety monitoring of ongoing patients to be continued).

Suspend study until YEC2 requested amendments are carried out.

Suspend enrolment of new participants.

Suspend certain activities under the protocol.

Direct the PI to inform participants enrolled in the study about AEs and if required obtain re-consent for continuation in the trial.

Direct the PI to inform participants enrolled in the study about the AE and request them to undertake additional visits, procedures, investigations, etc as prescribed in the amendment.

Inform the Yenepoya deemed to be University authorities if the PI is not cooperating with YEC2

Any other appropriate action

The decision shall be recorded in the minutes of the YEC2 meeting.

YEC2 decisions requiring immediate action, from the PI, will be conveyed to the PI through email within 24 hours. Such a communication will be documented by the YEC2 Member-Secretary in the study file.

A letter to the PI informing about the YEC2 recommendations will be sent within 5 calendar days of the YEC2 meeting having taken place.

YEC2 communications and archiving (for onsite SAE reporting):

The YEC2 Member-Secretary will draft a letter to the concerned PI and inform him/ her about the YEC2 decision. This letter will be signed and dated by the Member-Secretary/Chairperson and will be sent to PI within 7 calendar days from the date of SAE subcommittee meeting.

If there is a need for more clarification, Member-Secretary will request the PI to reply to the query letter on SAE report within 7 calendar days.

The opinion regarding relatedness, medical management and compensation for research-related injury will be communicated to the central licensing authority (DCGI) within 30 calendar days of the occurrence of the SAE in case of regulatory CT.

The YEC2 will confirm the nature of action taken by the PI/Sponsor regarding the management of the AEs as per the existing guidelines, including ancillary care, emergency care and compensation paid.
5.8.8.5. YEC2 Secretariat will file a copy of the letters in the study file

5.9. Reporting of the offsite AE/ADR/SAE (DIL):

Receipt of offsite AE/ADR/SAE & related reports to YEC2 :

The investigator will submit the offsite AE/ADR/SAE reports (also known as Dear Investigator Letter - DIL) occurring at other sites in the form of soft /hard copies along with a covering letter mentioning the total number of reports and its details as per the format: (Ann01/SOP12/v2) with details of each SAE separately and its relatedness to the IP.

The PI must submit the offsite AE/ADR/SAE reports within 2 days after receipt of the same from the Sponsor.

Review of the offsite AE/ADR/SAE (DIL):

The offsite AE/ADR/SAE (DIL) will be reviewed by the YEC2SAE subcommittee Executive-Secretary/Member and tabled for the subsequent SAE subcommittee meeting.

Reviewers will take into consideration the need for change in protocol/ IC documents to safeguard the participants in view of the AE/ADR/SAE.

SAE subcommittee meeting (for offsite AE/ADR/SAE):

offsite AE/ADR/SAE (DIL) will be discussed with regard to the outcome and relatedness to the investigational product and the possible impact on the participants

Minutes will be tabled for discussion in the subsequent YEC2 meeting.

YEC2 Meeting (for offsite AE/ADR/SAE - DIL): Minutes of the subcommittee will be read out and discussed

Decision making (for offsite AE/ADR/SAE - DIL): The agenda and minutes of the meeting will include decisions based on the information on SAEs at other sites.

Communication and Filing (for offsite AE/ADR/SAE):

The Secretariat will sign one copy of the covering letter that is submitted by the PI to acknowledge the receipt of the DIL report.

After discussion and deliberation in the meeting, the Secretariat will file a copy of the reports and communications in the study file.

6. References:

New Drugs and Clinical Trials Rules, 2019 of Drugs and Cosmetics Act, 1940

ICMR's National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017

Indian GCP guidelines, 2001

SOP04/v4 - Independent Consultant

SOP 7A/v4 - Initial Full Review of Research Study Protocols

SOP 08/v4 - Agenda, Meeting Procedures and Recording of Minutes

SOP 10/v4 - Continuing Review of Study Protocols

Annexures

Ann01/SOP12/v4: Checklist for Adverse Events/Serious Adverse Event (SAE) submission (For Onsite SAE)

Annexure 1: Ann01/SOP12/v4

Checklist for Adverse Events/Serious Adverse Event (SAE) submission (For Onsite SAE)

SI No.	Reporting 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
		Yes/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	Yes/No



4.	Protocol Title	
5.	Protocol Study No./ ID /Code	
6.	Copy of trial permission obtained from CDSCO	
7.	CTRI Registration No.	
8.	Sponsor (Address with contact no and Email)	
9.	CRO (Address with contact no and Email)	
10.	Initial/Follow-up (FU)	
11.	In case of follow-up: Date & Diary no of initial or recently submitted report information	
12.	Participant Details: Initials & other relevant identifiers Gender Age and/or date of birth Weight Height	
13	Nature of the intervention: a. 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 b. Any other intervention (specify) Provide the same information for concomitant drugs (including non prescription/ OTC drugs) and non-drug therapies, as for the suspected	



	drug(s).	
14	<p>Details of clinical findings:</p> <ul style="list-style-type: none">a. Full description of reaction(s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious.b. In addition to a description of the reported signs and symptoms, whenever possible, assign a specific diagnosis for the reaction.c. Start date (and time) of onset of reaction.d. Stop date (and time) or duration of reaction.e. Dechallenge/rechallenge information (if any)f. Setting (e.g. hospital, out-patient clinic, home, nursing home).	
15	<p>Outcome:</p> <ul style="list-style-type: none">a. Required hospitalization: Yes/Nob. Number of admission days:c. Please provide results of specific tests and other laboratory reports (if any) that were carried out in relation to the adverse event:d. Details of the treatment provided (including procedures or surgeries or other interventions done in relation to the adverse event):	



	<p>e. Details on the recovery or other sequelae:</p> <p>f. If discharge summary is available please provide a copy:</p> <p>g. Any permanent disability or functional loss?</p> <p>h. Is the adverse event associated with a congenital anomaly?</p> <p>i. For a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction (include post mortem findings - if any):</p>	
16.	<p>Other Information:</p> <p><i>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</i></p>	
17.	<p>Details about the Investigator</p> <p>CT Site number, if any</p> <p>Name</p> <p>Address</p> <p>Telephone/Mobile Number & Email</p> <p>Profession (speciality)</p> <p>Date of reporting the event to Licensing Authority</p> <p>Date of reporting the event to Yenepoya Ethics Committee 2</p>	
18	<p>Details about Yenepoya Ethics Committee 2</p> <p>Name and address</p> <p>Name of Chairman & Address</p> <p>Telephone/Mobile Number</p> <p>Email</p> <p>Whether EC is recognized by DCGI</p>	Yes/No
20	<p>Causality assessment by investigator.</p>	Related/Unrelated



21	Causality Assessment by sponsor/CRO	Related/Unrelated
22	Details of compensation provided for injury or death. <i>If no compensation paid, reason for the same</i>	
23	Other related documents: a. Filled SAE Form as per current regulations b. Post-mortem report (if applicable) c. Any additional documents	
24	Details of payment for medical management of SAE? (please give information who paid, how much, to whom and evidence of the same)	
25	What is the investigator's assessment for the amount of compensation to be paid?	
26	What is the sponsor's assessment for the amount of compensation to be paid?	
27	Has the participant made a claim?	Yes/No Comment
28	If yes for 27, then, for how much amount?	
29	If no, please ensure that the participant/nominee have been made aware of his/her rights regarding compensation. Please submit documentation regarding the same.	



30	Signature of Principal Investigator with date	
Review of the SAE subcommittee		
31	Brief summary:	
32	Possibility of relatedness Need for compensation Quantum of compensation	
33	Decision: <ol style="list-style-type: none">1. No further action required:2. Request information:3. Recommend further action	

Note: Information not relevant to a particular SAE should be marked with NA



7. Flow chart:

