Constituting SAE Subcommittee

For Institutional Ethics Committee

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1. Purpose

The purpose of this Standard operating procedure (SOP) describes the Terms of References (TOR), which provide the framework for constitution, responsibilities and activities of the SAE subcommittee.

2. Scope

The SOP applies to all activities performed by the SAE Subcommittee.

3. Responsibility

It is the responsibility of the Institutional Ethics Committee members and the Secretariat to read, understand, follow and respect the SOP set by the Institutional Ethics Committee.

4. Flow chart

No.	Activity	Responsibility
1	Composition of the SAE Subcommittee	Head of the Institute, Chairperson, IEC Members and Secretariat.
2	Membership requirements	Head of the Institute, Chairperson.
3	Tenure of Membership	Chairperson, IEC Members and Secretariat.
4	Initiation of the process of appointment	Secretariat.
5.	Appointment of new members	Head of the Institute.
6.	Resignation and disqualification of members	IEC Members and Secretariat.
7.	Conditions of appointment	IEC Members and Secretariat.
8.	Selection and appointment of Head of the SAE subcommittee	Head of the Institute.
9.	Quorum requirements	IEC Members and Secretariat.

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5. Detailed Instructions

5.1 Ethical basis:

• The SAE Subcommittee will review all serious adverse events (SAE) and unexpected adverse events (UAE) and adverse events (AEs) at this site / other sites in all types of research studies involving human participants approved by IEC.
• 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.
• In evaluating all the adverse event reports, the SAE Subcommittee is aware of the diversity of laws, culture and practices governing research and medical practices in various countries around the world and especially in India.
• The SAE subcommittee attempts to keep itself informed of the requirements and conditions of the various localities where proposed research is being considered.
• The SAE Subcommittee is guided in its reflection, advice and decision by the ethical principles expressed in Declaration of Helsinki (Adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964, and amended by the 29th World Medical Assembly, Tokyo, Japan, October 1975; 35th World Medical Assembly, Venice, Italy, October 1983; 41st World Medical Assembly, Hong Kong, September 1989; 48th World Medical Assembly, Somerset West, Republic of South Africa, October 1996; and the 52nd World Medical Assembly, Edinburgh, Scotland, October 2000; Note of Clarification on Paragraph 29 added by the World Medical Assembly, Washington 2002; Note of Clarification on Paragraph 30 added by the World Medical Assembly, Tokyo 2004), 59th WMA General Assembly, Seoul, October 2008, 64th WMA General Assembly, Fortaleza, Brazil October 2013.
• It makes further reference to the International Ethical Guidelines for e.g.: The Nuremberg Code (1945), Belmont Report (1979), The Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving

Human Subjects (Geneva 2002), and the European Convention on Human rights and Biomedicine (1997), draft CIOMS guidelines 2015.

• The SAE Subcommittee will work according to its established Standard Operating Procedures based on the Operational Guidelines for Ethics Committees that review Biomedical Research (WHO, 2000), International Conference on Harmonization- Good Clinical Practices (ICH-GCP) Guidelines (1996), Schedule Y (Drugs and Cosmetic Act 1940; amendment 20th January 2005, 30th January 2013 and 8th February 2013) and Ethical Guidelines for Biomedical Research on Human Participants by ICMR (2006), draft ICMR guidelines 2016. The mandate will be

a. To ensure the protection of the rights, safety and wellbeing of human participants involved in a research project.

b. Provide public assurance of that protection.

c. To ensure appropriate compensation as per amended Schedule Y, G.S.R 53 (E) dated 30th January 2013 amendment, G.S.R 889(E) dated 12th December 2014 is provided to the research participants.

• The SAE Subcommittee is established and functions in accordance with the relevant national law and regulations in force from time to time.

5.2 Composition of the SAE Subcommittee:

• The SAE Subcommittee will be appointed by the Chairperson of Ethics Committee.
• The SAE Subcommittee will be multidisciplinary and multi-sectoral in composition.
• The SAE Subcommittee will be composed of at least 5 and a maximum of 10 members.
• The members preferably should be from medical and scientific backgrounds.
• The Composition shall be as follows:
  - Head of the SAE Subcommittee (who is a member of the IEC).
  - One Executive Secretary (who is a member of the IEC).
  - Any IEC member with post graduate qualifications in the discipline of Medicine.
  - Atleast one member possessing post graduate degree in the subject of Pharmacology (who is the member of the IEC).

- At least one member possessing post graduate degree in the subject of General Medicine (who is the member of the IEC).
- IEC Secretary will be Ex-Officio member of the SAE Subcommittee.
- The requirement, appointment and terms of membership will be the same as described below in sections 5.3 to 5.8.
- The SAE Subcommittee may invite legal expert member of the IEC to provide opinion on the legal implication of adverse event.

5.3 Membership requirements:

• The Chairperson of Ethics Committee is responsible for appointing the SAE Subcommittee members.
• The IEC members can suggest names of potential IEC members but the final decision will remain with the Chairperson.
• Members will be selected in their personal capacities based on their interest, ethical and/or scientific knowledge and expertise, as well as on their commitment and willingness to volunteer the necessary time and effort for the SAE Subcommittee work.

5.4 Tenure of Membership:

• The tenure of Institutional Ethics Committee members will be for a continuous period of two (2) years from the date of appointment.
• The IEC secretariat will initiate the process of filling up the forthcoming vacancies two months prior to the end of tenure of a member of SAE Subcommittee. The IEC members will recommend names of individuals to the Chairperson. The Chairperson will select and appoint a member for the new tenure from the list provided by the IEC or otherwise. The retiring member will be eligible to be appointed for the new tenure consecutively three times.

5.5 Appointment of new members:

a) The SAE Subcommittee members will be appointed by the Chairperson. New members will be appointed under the following circumstances:
1.When a regular member completes his/ her tenure.
2.If a regular member resigns before the tenure is completed.
3.If a regular member ceases to be a member for any reason including death or disqualification.
4.To fulfill the membership requirements as per 5.3 of this SOP. New members will be identified by the Chairperson according to the requirement (i.e. as per the composition specified in Section 5.2 of this SOP), membership requirement (Section 5.3 of this SOP) and provided the potential member fulfils the conditions of appointment as defined in 5.8 of this SOP after discussion by the IEC. The names of new members to be appointed may be suggested by the IEC members to the Chairperson. The final decision regarding appointment of members will be taken by the Chairperson.

5.6 Resignation and Disqualification of Members:

• Resignation: An SAE Subcommittee member may resign from membership by submitting a letter of resignation to the Chairperson. The member may or may not assign reasons for resignation. The resignation will become effective from the day it is accepted by the Chairperson.
• Disqualification for conduct unbecoming of an SAE Subcommittee member: A member may be disqualified from continuance should IEC determine by a three-fourth majority specifically called for the purpose that the member's conduct has been unbecoming of an SAE Subcommittee member. (i) The process will be initiated if IEC Chairperson or Head of SAE Subcommittee receives a communication in writing (provided by IEC member) alleging misconduct by a SAE Subcommittee member.
(ii) The Chairperson will satisfy himself/herself that a prima facie case exists before initiating

action. If, in the opinion of the Chairperson, the matter is of grave significance where integrity of IEC could be questioned, the Chairperson may suspend the membership of the concerned SAE Subcommittee member till final decision is taken by IEC. During the period of suspension, the concerned individual will not have any rights, privileges or responsibilities of an IEC member and will not perform any duties of SAE Subcommittee member.
(iii) The Chairperson may call for a meeting of the IEC specifically to discuss this issue or the matter will be taken up for discussion. The meeting convened will follow the usual rules of quorum. The allegation will be discussed at the IEC meeting and the member alleged of misconduct will be provided adequate opportunity to defend him/ her.
(iv) The member would stand disqualified if members present approve of disqualification by voting (voting by 2/3rd of majority of members present in the meeting and voting). The Chairperson will convey the disqualification to the concerned member through a written communication.
• Disqualification for not attending IEC meetings: A SAE Subcommittee member may be disqualified from SAE Subcommittee membership if the member fails to attend more than 5 regular consecutive SAE Subcommittee meetings without prior intimation. The process conducted will be as follows:

(i) The Head of SAE Subcommittee will inform Chairperson, in writing, if a member has not attended more than five consecutive regular meetings of the SAE Subcommittee.

(ii) The Chairperson will initiate the process of review of membership of such a member by including the matter in the Agenda of the next regular IEC meeting

(iii) A written communication will be sent to the concerned SAE Subcommittee member informing him/her that the issue of disqualification would be discussed at the meeting inviting the member to be present at the meeting to put up his/her case. Alternately, the concerned SAE Subcommittee member will be allowed to state his/ her arguments regarding unauthorized absence in writing by a letter addressed to the Chairperson.

(iv) The matter will be discussed and reviewed at the respective IEC meeting. The concerned member will be provided adequate opportunity to represent his/her case. A written communication, if received from the concerned member will be read and reviewed at the meeting.

• The Chairperson or Head of SAE Subcommittee will inform the IEC members about the cessation of membership by a confidential written communication to other members of IECs or at the next meeting of IECs.

5.7 Conditions of appointment:

Members will be appointed to the SAE Subcommittee if they accept the following conditions.
• Willingness to publicize his/her full name, profession and affiliation.
• Willingness to sign the Confidentiality and Conflict of Interest Agreements regarding meeting, deliberations, applications, information on research participation and related matters.
• Willingness and commitment in terms of time to perform the role and responsibility as SAE Subcommittee member.

5.8 Hierarchy:

• There will be one SAE Subcommittee-Head, one executive Secretary of SAE Subcommittee.

• The executive Secretary will be the guardian of all documents in the possession of the committee. In case of anticipated absence, the head of SAE subcommittee will nominate a SAE subcommittee member as Acting Executive Secretary. The Acting executive secretary will have all the powers of the executive secretary of the SAE subcommittee for that meeting.

• Other SAE Subcommittee members will be regular committee members with equal ranking.

• The Head of the SAE Subcommittee will be appointed by the Chairperson.
• The executive secretary, will be elected by and from amongst the SAE Subcommittee members for 2 years term. The executive secretary may be re-elected any number of times. Should he/she resign or be disqualified, the SAE Subcommittee members will elect a replacement for another term.

5.9 Head of the SAE Subcommittee:

• The Head of the SAE Subcommittee will be appointed by the Chairperson.
• The Head of the SAE Subcommittee will be affiliated to the institution.
• The Head of the SAE Subcommittee will be responsible for conducting SAE subcommittee meetings, and will lead all discussions and deliberations pertinent to the review of All type of adverse event reports [Serious Adverse Event (SAE), Unexpected Adverse Event (UAE), Adverse Event (AE), Suspected Unexpected Serious Adverse Event (SUSAR)].
• The Head of the SAE Subcommittee will sign minutes of the SAE Subcommittee meeting.
• In case of anticipated absence, the head of SAE subcommittee will nominate a SAE subcommittee member as Acting Head. The Acting Head will have all the powers of the Head of SAE subcommittee for that meeting.

5.10 Functions of the Executive secretary of the SAE Subcommittee:

1. To receive All type of adverse event reports (SAE, UAE, AE, SUSAR's).
2. To organize an effective and efficient tracking procedure for each onsite adverse event report received.
3. To inform the adverse events (serious and unexpected) reports to other members of the SAE Subcommittee.
4. To schedule and organize the SAE Subcommittee meetings.
5. To prepare and maintain meeting agenda and minutes.
6. To prepare the communication letters related to the adverse event reports.
7. To communicate with the IEC members and applicants/ investigators.

8. To provide necessary administrative support for SAE Subcommittee related activities.
9. To ensure adherence of the SAE Subcommittee functioning as per SOPs.

5.11 Functions of the IEC Secretariat:

The IEC Secretariat will perform the functions as mentioned in for the SAE Subcommittee.

Functions of the Administrative Manager, Officer/s, Executive Assistant:

1. To support the executive Secretary in executing functions of the SAE Subcommittee.
2. To prepare the agenda of the SAE subcommittee with help of Secretary of the SAE Subcommittee. The agenda of the SAE Subcommittee will include the information on SAE/ UAE at the site in the following format:

Participant ID	Letter no./ and date of reporting	Type of report	Type of SAE/UAE	Date of onset	whether study drug withheld	Outcome	Causality in the opinion of PI

Summary:

Total no. of SAE Reported =xx
Total no. of Death = xx

3. The agenda will also include information about onsite AE reports and SAE/UAE reports for the SAE /UAE occurring at other trial sites.

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4. To prepare the minutes (to be prepared within 5 working days of the meeting) with the help of the Secretary of the Subcommittee The minutes of the SAE Subcommittee will include the information on SAE /UAE at the site in the following format:

Participant ID	Letter no./ and date of reporting	Type of report	Type of AE/SAE/ UAE	Date of onset	whether study drug withheld	SAE Outcome	Causality in the opinion of PI	Recommendation (s) by the SAE Sub Committee

The minutes will also include the notification /recommendation on the onsite AE reports and other site SAE/UAE reports

4. To perform any other functions as instructed by executive Secretary/ Head of the SAE Subcommittee.

5.12 Roles and Responsibilities of the SAE Subcommittee members:

• To attend the SAE Subcommittee Meetings and participate in discussions and deliberations so that appropriate decisions can be arrived at.

• To review, discuss and consider adverse event reports submitted for evaluation.

• To review Serious Adverse Event and unexpected adverse reports and recommend appropriate action(s) as follows:

- The SAE /UAE reports will be reviewed completely in the SAE subcommittee meeting
- with a special focus on relatedness to the clinical trial, medical management and

- financial compensation to be given to the research participant as per Schedule Y (Drugs
- and Cosmetic Act 1940; amendment 20th January 2005, G.S.R 53 (E) dated 30th January
- 2013 amendment, G.S.R 889(E) dated 12th December 2014).

- The SAE subcommittee while reviewing may solicit opinion of one or more independent
- consultant(s) in writing, if the Sub-committee decides to consult experts. The
- information can be provided to expert after he/ she/ they agree(s) to the confidentiality
- cause and abide by the rules and regulations of IEC or the necessary confidentiality
- documents are signed. The independent consultant would be requested to provide an
- opinion in writing within 2-3 working days, depending upon the gravity and seriousness.

- The following decisions/actions including the following but not limited to, are listed below:

1. Note the information about the SAE in records for future reference.
2. To opine on compensation entitled to research participants (as per Drugs and Cosmetic Act 1940, Schedule Y - amendment 20th January 2005, G.S.R 53 (E) dated 30th January 2013, G.S.R 292 (E) dated 24th April 2014, G.S.R 889(E) dated 12th Dec 2014) experiencing Serious Adverse Event and unexpected adverse events and adverse events and recommend appropriate action(s)
3. Request further follow up information and/ or additional details on causality of the event, provision of medical treatment till SAE is resolved and financial compensation.
4. Provide periodic follow-up of the research participant till SAE is resolved or till death occurs (whichever is earlier). In case of pregnancy as SAE to send follow up reports of the child in utero and post-delivery of the baby till 1 year.

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If appropriate to the discussions, the recommendation regarding a specific action or combination of actions to be taken is arrived at by the SAE subcommittee meeting. The recommendations will be communicated to the IEC within 5 working days.

5.13 Quorum Requirements:

• The SAE Subcommittee meeting will be held as scheduled provided there is quorum. For the SAE Subcommittee meeting, a quorum will consist of at least 4 members as follows- one member (preferably pharmacologist), one member (preferably clinician), executive secretary and Head / Acting head of the SAE subcommittee.

5.14 Minutes of the SAE subcommittee meeting:

Minutes of SAE subcommittee meeting will be prepared by SAE subcommittee Executive secretary. These minutes will then be presented in the next Full Board meeting of IEC.

5.15 Responsibilities of the SAE Subcommittee:

• The SAE Subcommittee primary responsibilities will be protection of safety, rights and confidentiality of the research participants.
• The SAE Subcommittee will keep all information submitted to them confidential specially the proprietary information.
• The SAE Subcommittee will maintain concise but clear documentations of its views on each adverse event report.
• The SAE Subcommittee will review the serious adverse event, unexpected adverse event and non-serious adverse event and other site SAE reports (CIOMS, SUSARs) of each research project at appropriate and specified intervals.
• The SAE Subcommittee will ensure that appropriate compensation is paid to the research participant as per (Drugs and Cosmetic Act 1940; Schedule Y amendment 20th January 2005,

G.S.R 53 (E) dated 30th January 2013 amendment, G.S.R 889(E) dated 12th December 2014).

6. References

1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, (Geneva 2000)- *https://www.who.int/tdr/publications/documents/ethics.pdf* (last accessed 22nd October 2020).
2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996-*http://www.ich.org/LOB/media/MEDIA482.pdf* (last accessed 22nd October 2020).
3. National Ethical Guidelines for Biomedical and Health Research involving Human Participants, ICMR 2017

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