# DRAFT
# ICMR GUIDELINES FOR
# COMMON ETHICS REVIEW OF MULTICENTRE RESEARCH

**2019**

**Indian Council of Medical Research**

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**1. Introduction:**

Collaborations in biomedical and health research have gained a great momentum in recent years and provide a great opportunity to present meaningful outcomes for the country. Collaborative research actively engages researches, communities and/ or policy makers in the research process from start to finish. Researchers are increasingly collaborating with colleagues who have the expertise and/or for resources needed to carry out particular research. This could be inter-departmental/ inter-institutional or international and also multicentre involving public and/or private research centres and agencies. Multicentre research collaborations offer opportunities to engage diverse scientific expertise to answer important research questions amongst wider population groups. However, there are ethical issues surrounding collaborations such as those pertaining to sharing techniques, ownership of materials and data, IPRs, joint publications, managing research findings, managing COI and commercializing research outcomes.

Every biomedical and Health Research must be reviewed by an Ethics Committee (EC) before its conduct. At present in India, all centres are required to obtain approval from their respective ECs, which would consider the local needs and requirements of the population and safeguard the dignity, rights, safety and well-being of the participants. In order to streamline the review process and improve coordination in multicenter research, a process for common ethics review has been suggested in the ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017, to be carried out through the Designated Ethics Committees (DEC) and ECs of participating centres (PEC).

**2. Purpose:**

The purpose of this guidance is to describe the process for a common ethics review of a multicentre research proposal. This method can be adopted as an option by ECs overseeing centres engaged in multicentre research. The guidance is intended to address a variety of issues related to common ethics review so that research can proceed expeditiously without compromising ethical principles and ensuring protection for human research participants.

**3. Scope:**

This guidance applies to ECs, investigators, and other stakeholders involved in multicentric biomedical and health research. Clinical trials requiring approval from CDSCO are excluded from common ethical review. These guidelines serve as annexure to the main ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017, the reference document.

**4. Designated Ethics Committee (DEC):**

**4.1** The EC which assumes the responsibility to undertake a common review of the study proposal with mutual agreement of all the ECs of participating centres in a multicentre study shall be called as the Designated Ethics Committee.

**4.2** Each DEC will be research study specific and may be formalized through an agreement/Letter of Understanding (LoU) between the participating institutes.

**4.3** The EC of the Coordinating centre may serve as the DEC.

The EC is required to fulfil the following criteria to be identified as the DEC.

**4.4 Essential criteria:**

- To be one of the centres for the multicentre research.
- To be located in India and be willing to conduct ethical review of study for Indian centres.
- Have minimum 3 years of experience in reviewing research protocols.

**4.5 Desirable criteria:**

- Registered with the regulatory authority such as CDSCO and/or with DHR.
- Accredited by NABH or AAHRPP or have undergone a SIDCER recognition/other ethics committee -Quality Assurance programs.

**4.6 Responsibilities of DEC:**

The National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017 prescribe the roles and responsibilities of the EC under section 4.7. In addition, the following are the responsibilities of DEC:

4.1.1 To conduct a detailed initial review of the proposal which is common for all centres involved in a multicentre research

4.1.2 To review local issues specific to the centre, changes in informed consent document, translations and monitor research as per local requirements.

4.1.3 To review the application form for multicentre research (Annexure 14 part A and part B) received from the participating centres.

4.6.1 To invite representatives from Participating centre Ethics Committees (PECs) to discuss local ethical issues (If required). These special invitees do not have voting rights but can participate in DEC meeting to provide their comments and local perspectives.

4.6.2 To provide recommendations to the participating centres after the review.

4.1.4 To be transparent, accountable, competent, sensitive and consider the local socio-cultural issues.

4.1.5 To review policy for publication/data sharing between centres/benefit sharing/post study results with all participants involved in the study.

4.1.6 To review continuing review reports, annual reports at the DEC centre.

4.1.7 To review serious adverse events related to the study, causality assessment, protocol deviations, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance as reported to DEC from other centres.

**5. Ethics Committees of the participating centres (PEC):**

The Participating Centre ECs in a multicentre research are located at the participating centres (including DEC). They should ensure respect of participants and communities, changes in informed consent document, translations and monitor research as per local requirements.

**5.1 Responsibilities of PECs:**

The National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017 prescribe the roles and responsibilities of the EC under section 4.7. In addition, the following are the responsibilities of PEC:

5.1.1 PEC may primarily review the local issues specific to the centre. However, PEC may also review full proposal submitted by PI at the participating centre through full committee meeting/expedited review.

5.1.2 To identify a representative/nominee to attend the common review at DEC.

5.1.3 Formally endorse recommendations of the DEC, but retain their autonomy to review the proposal through full committee meeting/expedited review/ depending on the importance of

local issues involved specific to the centre and as per SOP of the institute. Member Secretary in consultation with Chairperson may take a call on the above.

5.1.4 To issue the final decision letter for the study at the centre to PIs.

5.1.5 To review serious adverse events related to the study, causality assessment, protocol deviations at the centre, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance.

5.1.6 To decide if serious adverse events related to the study, causality assessment, protocol deviations at the centre, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance must be reported to DEC and inform the PI at the participating centre.

5.1.7 Ensure good and prompt communications to DEC as per requirement or if there are specific concerns that may impact other centres as well.

5.1.8 Member Secretaries of all the participating centres may take initiative to form a network for improved direct communication

**6. Coordinating PI:**

Coordinating PI is the PI at DEC who takes an overall responsibility for the conduct of the multicentre research along with PIs from all the participating centres and is also responsible for ongoing communication between DEC and PIs at other participating centres.

**6.1 Responsibilities of Coordinating PI:**

6.1.1 To submit the study proposal to DEC for review using the ICMR common forms for EC review.

6.1.2 To submit the application form for multicentre research (Annexure 14 - part A and part B) to DEC

6.1.3 To submit the application for multicenter research (Annexure 14 – part B) received from PI at participating centres to DEC

6.1.4 To function as a link between DEC and PIs and communicate the recommendations of DEC to PIs at the PEC.

6.1.5 To submit serious adverse events, causality assessment, protocol deviations at the centre, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance to DEC as per requirement or if there are specific concerns that may impact other centres as well.

6.1.6 To communicate with Steering/Monitoring committee and Technical advisory committee/ sponsors.

6.1.7 To communicate the concerns received at one centre with other centres (if required) depending on the type of concern such as adverse event or specific concerns that may impact other centres as well.

**7. Principal Investigator(PI):**

The PI is the person who takes an overall responsibility for the conduct of multicentre research at their respective centres involved in research. Each centre can have additional co-investigator(s), who may coordinate the study with in the centre (*please refer to glossary for multicentre research*).

**7.1 Responsibilities of PIs of participating centres:**

7.1.1 To submit the study proposal to respective PECs for review using ICMR Common forms for EC review.

7.1.2 To submit the application form for multicentre research (Annexure 14 - part B) to PEC and coordinating PI

7.1.3 To function as a link between PEC and Coordinating PI and communicate the recommendations of PEC to Coordinating PI.

7.1.4 To submit serious adverse events related to the study, causality assessment, protocol deviations, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance to PEC and DEC as per requirement.

7.1.5 In consultation with Coordinating PI, to initiate the study at the local centres as and when the approval from EC is obtained without waiting for EC approvals at other participating centres. *(Please note: For certain types of research, study should be initiated simultaneously at all centres and this has to be decided by PI in accordance to the need.)*

**8. Letter of understanding (LoU) for Common Review of Multicentre Research**

**8.1** A signed document/agreement should be made to support and validate the agreed roles and responsibilities of the DEC and the participating centre ECs

**8.2** This should be in the form of a letter of understanding, documenting the roles, responsibilities and communication plan between the PECs for common review.

**8.3** If any additional centre is added after the initiation of the study, the LoU should be revisited. The additional PEC should be explained the terms and conditions and should be asked to sign the LoU. The copy of revised agreement shall then be circulated to the other PECs.

**8.4** If the EC of the coordinating PI is not serving as the DEC, the relationship of coordinating PI with DEC has to be worked out to address logistic issues.

**8.5** The LoU shall come in to effect on the date of its signature by all centres and shall remain in force for the specified duration of research.

**8.6** If any existing centre is suspended or terminated for any reasons, the other centres should be informed. A template of LoU for common review of multicentre research is given at the Annexure-3 for reference.

**9. Timelines for Review:**

**9.1** Proposals can be submitted simultaneously to all the PECs including DEC.

**9.2** Reasonable and mutually agreed timelines should be allotted for the initial review process. A maximum of 30 days to DEC for common review and 30 days to PEC for local review should be considered appropriate.

**10. Protocol Amendment: Submission and Review Process:**

**10.1** Major amendments in the protocol will be submitted to DEC for review and the decision of which shall be communicated to PEC.

**10.2** Minor amendments in the protocol will be submitted to PEC for review.

~~10.2~~**10.3 The PEC should inform the DEC and other centres any amendments they approve (even minor)**

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**11. Serious Adverse Events, Adverse Events, Deviations and Other Types of Reportable Events, Suspension and Termination of studies:**

**11.1** Reporting of Serious Adverse Events, Adverse Events, Deviations and Other Types of Reportable Events for each centre may be done in accordance with the SOPs of the EC. And ICMR National Ethical Guidelines, 2017.

**11.2** The PEC can suspend or terminate the approval of studies in accordance to its policies and procedures. The DEC may advise the centres regarding the same.

**11.3** If the research as a whole is suspended or terminated, the coordinating PI will promptly notify all the PECs of the suspension or termination.

**12. Record Keeping and archiving**

**12.1** All the records will be retained in an accessible way by PECs and DEC for a minimum period of 3 years following completion or termination of the study.

**12.2** The PIs and PECs should refer to their local institutional SOPs or as per sponsor requirements in record keeping and archiving.

**Glossary:**

**Designated Ethics Committee(DEC):**
The participating EC of a multicentre study which assumes the responsibility to undertake a common initial and continuing review of study proposal with mutual agreement of all the participating centres of a multicentre study is called as the Designated Ethics Committee.

**Participating Centre Ethics Committee (PEC):**
The Participating Centre ECs are located at the participating centres in a multicenter research (including DEC) and are responsible for detailed review of research in accordance to ICMR National Ethical Guidelines, 2017.

**Coordinating PI:**
Coordinating PI is the PI at DEC who takes an overall responsibility for the conduct of the multicentre research along with PIs from all the participating centres and is also responsible for ongoing communication between DEC and PIs at other participating centres.

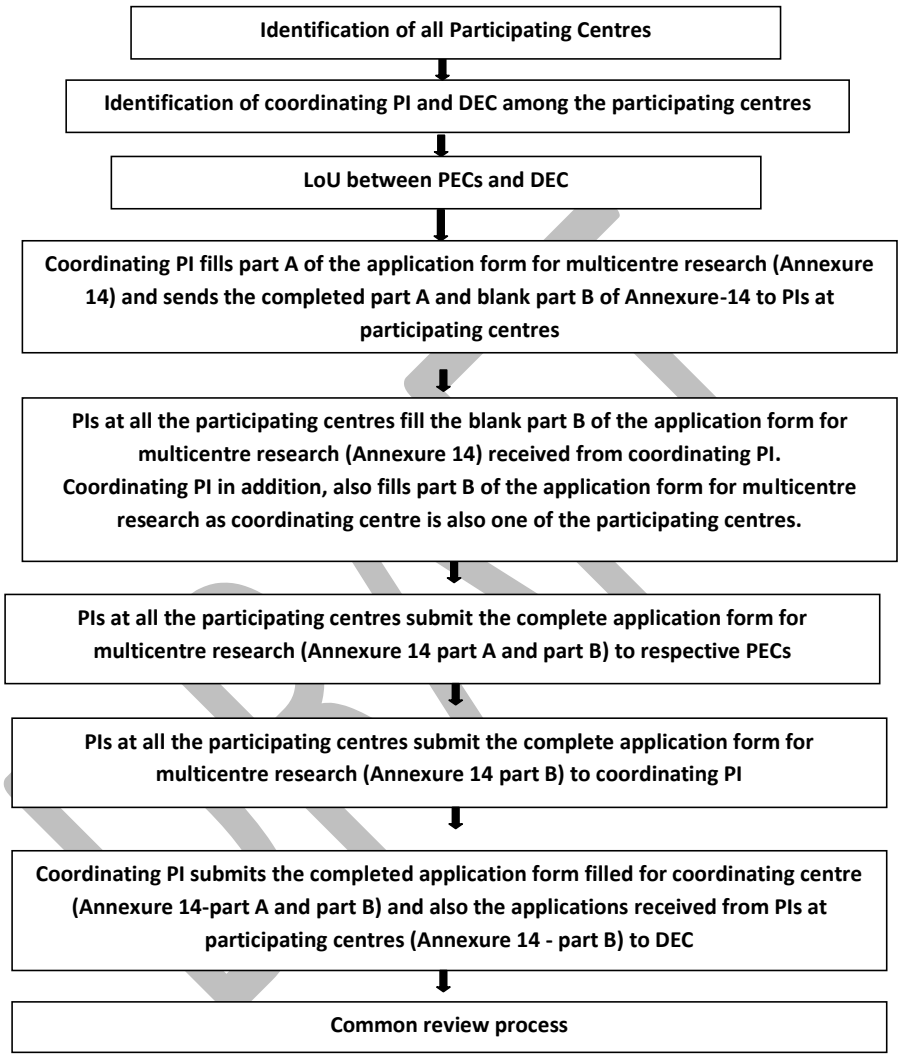
**Principal Investigator:**
The PI is the person who takes an overall responsibility for the conduct of multicentre research at various centres involved in research. Each centre can have additional co-investigator(s), who may coordinate the study with in the centre

**Multicentre research:** Multi-centre study is conducted at more than one centre by different researchers usually following a common protocol. However, certain studies where each centre with a PI is involved in different research roles according to the objective/methodology such as quality control, data management may also be considered as multi centre studies. Each centre can have multiple sites from which participants can be recruited. However, each site should have a responsible nodal person as applicable at the local level. (one PI but different sites)

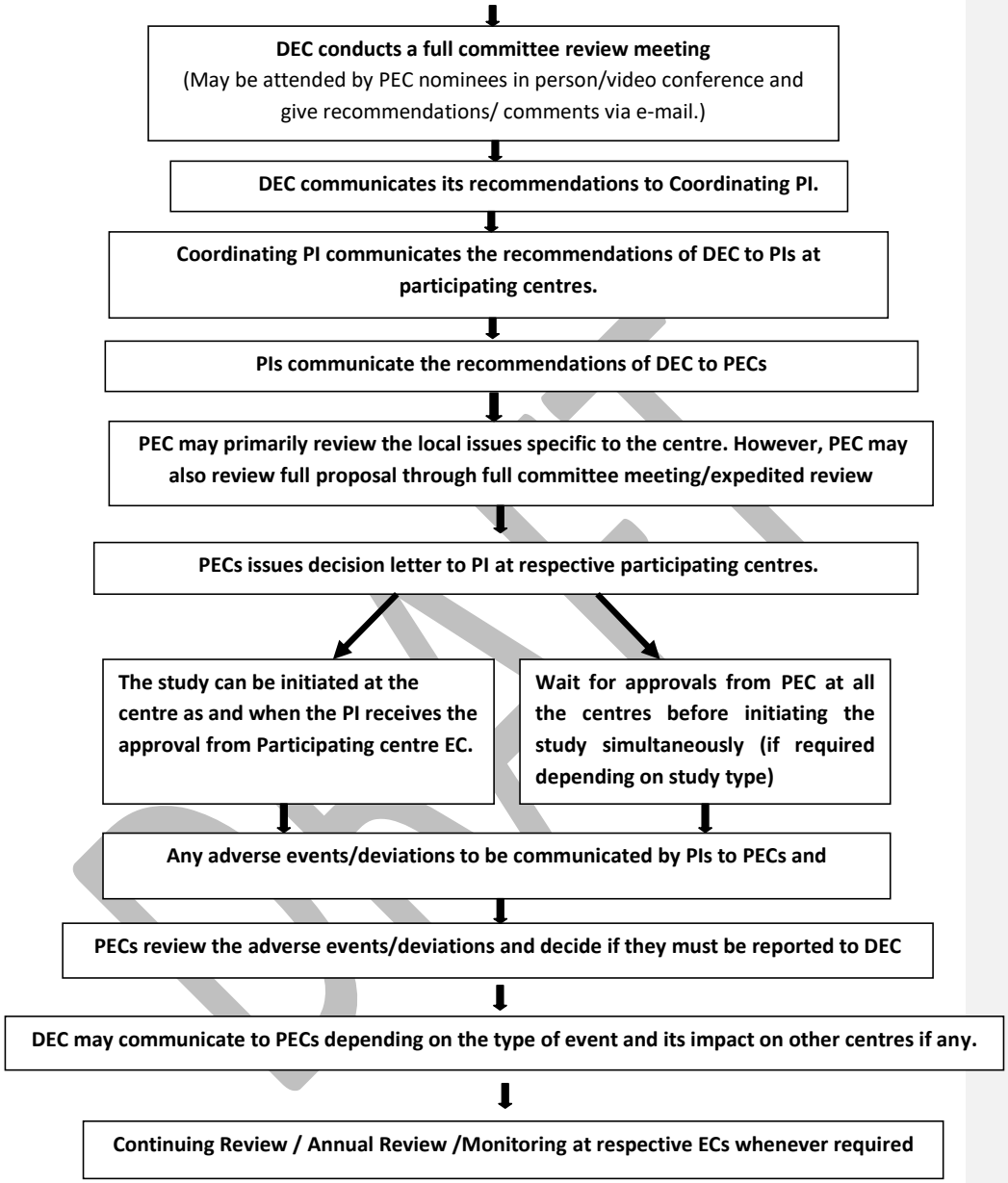
**Steering/Monitoring Committee:** This committee includes experts from funding agencies/sponsors/partners from the centre or region as per requirement. The committee ensures smooth functioning and implementation of the study protocol and monitoring

**Technical (Scientific) Advisory Committee:** This committee includes a group of independent subject experts who are not investigators of the study/ member of funding agencies/sponsors/monitors/representatives. The experts undertake scientific review and provide guidance for the progress of the study.

**Annexure 1: Flow chart for submission process of a multicenter proposal to EC**



**Annexure 2: Flow chart for Common Review Process of Multicentre Research**



**Annexure- 3 Draft - LoU format for Common Review of multicenter research**

**Designated EC**

Name of EC: ……
Name (Institution/ Organization): ……
EC Registration No, if any: ……

**Participating Centre ECs** *(Add additional sheets according to the number of centres involved)*

Name of EC: ……
Name (Institution/ Organization): ……
EC Registration No, if any: ……

The Officials signing below agree that Participating centre EC of **……** (name of the institution) may utilize the services of the Designated EC **……** (name of the institution) for efficient Common Ethics Review of Multicentre Research protocols.

It is understood that Designated Ethics Committee would undertake full ethics committee review. Ethical issues related to local centres may be reviewed by Participating Centre EC in expedited or full review and the final decision may be communicated to Designated Ethics Committee.
This agreement is limited to the following specific Proposal(s):
Title of Research Proposal: ……
……
Name of Principal Investigator/ Coordinating PI:……
Sponsor or Funding Agency: ……
The responsibilities of centres will be fulfilled in accordance with the ICMR Guidelines and they are responsible for ensuring compliance with the Guidelines.

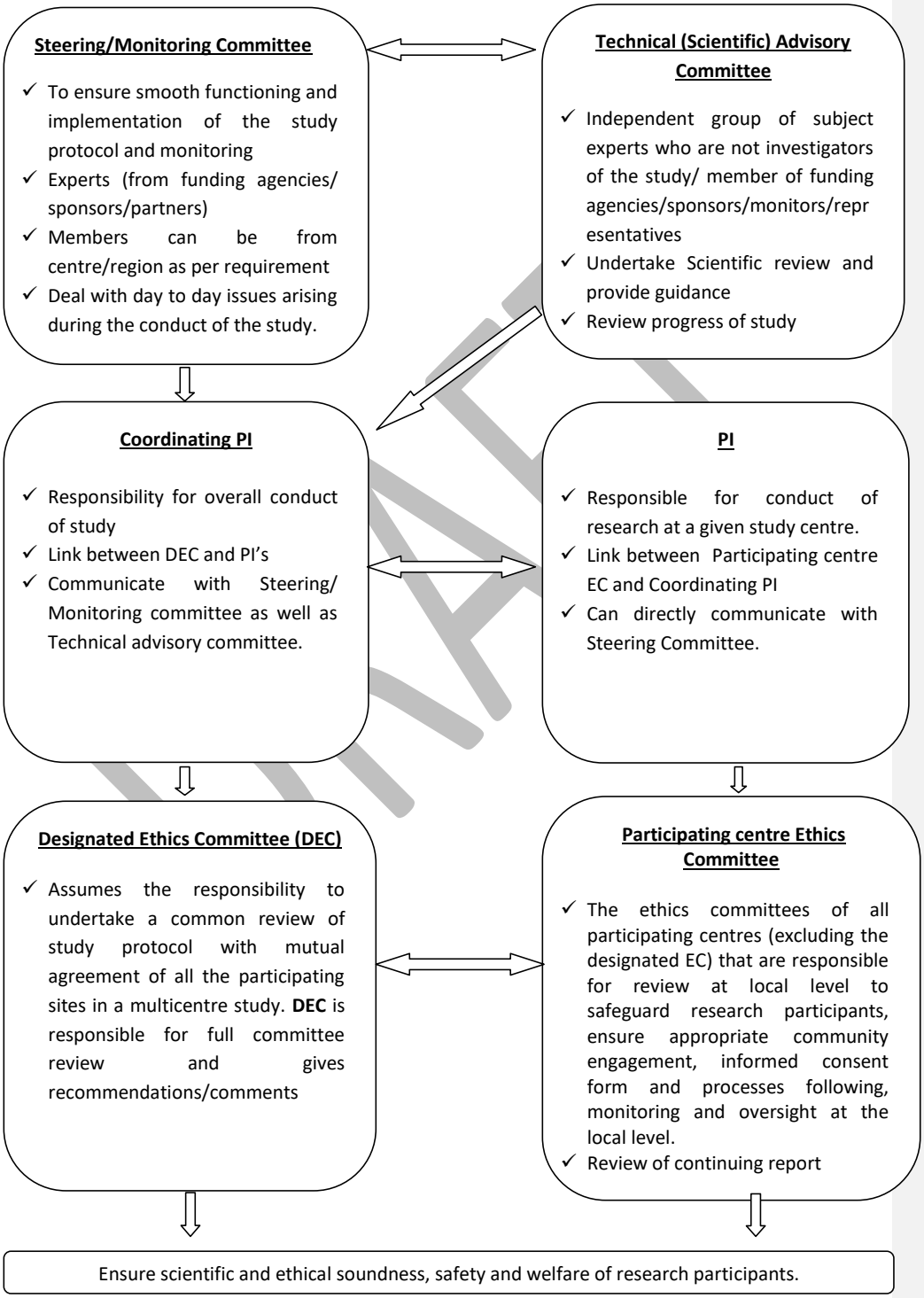
**For Designated Ethics Committee:**

**Signature:…… Date: ……**
**Name: ……**
**Address: ……**
**……**
**……**

**For Participating Centre EC:**

**Signature:…… Date: ……**
**Name: ……**
**Address: ……**
**……**
**……**

**Annexure 4: Suggested Governance mechanism for large Multicentre Research studies**



**Annexure 5: Standard Operating Procedure**

**Title: Common Review of Multicentre Research**

1. **Purpose:**
   The purpose of this SOP is to describe the process for a common ethics review of a multicentre research proposal. This SOP may be adopted by ECs engaged in multicentre research.

2. **Scope:**
   This SOP applies to concerned ECs, investigators, and other stakeholders involved in multicentric, biomedical and health research. It is intended to provide a process for review so that research can proceed expeditiously without compromising ethical principles and protections for human research participants.

3. **Responsibilities:**
   i. **Designated Ethics Committee (DEC):**
      - To conduct a detailed initial review of the proposal which is common for all centres involved in a multicentre research
      - To review local issues specific to the centre, changes in informed consent document, translations and monitor research as per local requirements.
      - To review the application form for multicentre research (Annexure 14 part A and part B) received from the participating centres.
      - To invite representatives from Participating centre Ethics Committees (PECs) s to discuss local ethical issues (If required). These special invitees do not have voting rights but can participate in DEC meeting to provide their comments and local perspectives.
      - To provide recommendations to the participating centres after the review.
      - To be transparent, accountable, competent, sensitive and consider the local socio-cultural issues.
      - To review policy for publication/data sharing between centres/benefit sharing/post study results with all participants involved in the study.
      - To review continuing review reports, annual reports at the DEC centre.
      - To review serious adverse events related to the study, causality assessment, protocol deviations, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance as reported to DEC from other centres.

   ii. **Participating Centre Ethics Committee (PEC):**
      - PEC may primarily review the local issues specific to the centre. However, PEC may also review full proposal submitted by PI at the participating centre through full committee meeting/expedited review.
      - To identify a representative/nominee to attend the common review at DEC.
      - Formally endorse recommendations of the DEC, but retain their autonomy to review the proposal through full committee meeting/expedited review/ depending on the importance of local issues involved specific to the centre and

as per SOP of the institute. Member Secretary in consultation with Chairperson may take a call on the above.

- To issue the final decision letter for the study at the centre to PIs.
- To review serious adverse events related to the study, causality assessment, protocol deviations at the centre, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance.
- To decide if serious adverse events related to the study, causality assessment, protocol deviations at the centre, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance must be reported to DEC and inform the PI at the participating centre.
- Ensure good and prompt communications to DEC as per requirement or if there are specific concerns that may impact other centres as well.
- Member Secretaries of all the participating centres may take initiative to form a network for improved direct communication

**iii. Coordinating PI:**

- To submit the study proposal to DEC for review using the ICMR common forms for EC review.
- To submit the application form for multicentre research (Annexure 14 - part A and part B) to DEC
- To submit the application for multicenter research (Annexure 14 – part B) received from PI at participating centres to DEC
- To function as a link between DEC and PIs and communicate the recommendations of DEC to PIs at the PEC.
- To submit serious adverse events, causality assessment, protocol deviations at the centre, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance to DEC as per requirement or if there are specific concerns that may impact other centres as well.
- To communicate with Steering/Monitoring committee and Technical advisory committee/ sponsors.
- To communicate the concerns received at one centre with other centres (if required) depending on the type of concern such as adverse event or specific concerns that may impact other centres as well.

**iv. Principal Investigator(PI):**

- To submit the study proposal to respective PECs for review using ICMR Common forms for EC review.
- To submit the application form for multicentre research (Annexure 14 - part B) to PEC and coordinating PI
- To function as a link between PEC and Coordinating PI and communicate the recommendations of PEC to Coordinating PI.
- To submit serious adverse events related to the study, causality assessment, protocol deviations, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance to PEC and DEC as per requirement.

- In consultation with Coordinating PI, to initiate the study at the local centres as and when the approval from EC is obtained without waiting for EC approvals at other participating centres.

**4. Review process:**

**i. Review process by DEC:**

- The DEC assumes the responsibility to undertake a common review of study protocol with mutual agreement of all the participating centres in a multicentre study
- The coordinating PI of the study submits the proposal to DEC.
- DEC conducts a detailed initial review of the proposal which is common for all centres involved in a multicentre research and provides its recommendations to the participating centres.
- DEC reviews local issues specific to the centre, changes in informed consent document, translations and monitor research as per local requirements.
- DEC reviews the application form for multicentre research (Annexure 14 part A and part B) received from the participating centres.
- Invites representatives from participating centre Ethics committees to discuss local ethical issues and/or specific requirements. (If required). These special invitees do not have voting rights but can participate in DEC meeting to provide their comments and local perspectives.
- Reviews policy for publication/data sharing between centres/benefit sharing/post study results with all participants involved in the study.
- Reviews continuing review reports and annual reports for DEC
- Reviews serious adverse events, protocol deviations, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance as reported to DEC from other centres.

**ii. Review process by PEC:**

- Member secretary of PEC in consultation with chairperson may take a call to accept the recommendations of the DEC as such or conduct a full committee review/expedited review /review by circulation depending on the local issues specific to each centre.
- Primarily reviews local specific concerns, informed consent document and its translations and monitor research as per local requirements.
- Reviews serious adverse events, protocol deviations, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance at the centre.
- Decides if serious adverse events related to the study, causality assessment, protocol deviations at the centre, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance must be reported to DEC and informs other participating centre.

**5. Communication between ECs, Coordinating PI and PIs:**

- DEC communicates the recommendations to coordinating PI
- Coordinating PI functions as a link between DEC and PI's

- PI communicates with Steering/Monitoring committee and Technical advisory committee.
- PI communicates the recommendations of DEC received from coordinating PI to PEC and functions as a link between both.
- PEC may communicate with DEC as per requirement or if there are specific concerns that may impact other centres as well.

**6. Final decision of the common review process:**

- PECs issue the final decision letter for the study at the centre to PIs.
- In consultation with Coordinating PI, PI to initiate the study at the local centre as and when the approval from PEC is obtained without waiting for PEC approvals at other participating centres.
- For certain types of research, study at all centres should be initiated simultaneously and this has to be decided by PI in accordance to the need.