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 as they provide a great opportunity to present meaningful outcomes for the country and actively engage researchers, 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 resources needed to carry out specific research. This could be inter-departmental/inter-institutional, national or international collaboration, involving public and/or private research centres and agencies. Multicentre research collaborations offer opportunities to engage diverse scientific expertise to address important research questions pertaining to wider population groups. However, there are ethical issues surrounding collaborations such as sharing techniques, ownership of materials and data, IPRs, joint publications, managing research findings, managing COI and research outcomes with commercial potential.

Every biomedical and health research must be reviewed by an Ethics Committee (EC) before it is initiated. 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 the ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017, a process for common ethics review for multicentre research has been suggested. This guideline provides a detailed procedure for common ethics review to be carried out through the Designated Ethics Committees (DEC) and ECs of participating centres (PECs) by improving coordination amongst them in order to affect a shortened review process without compromising quality of that review.

2. Purpose

The purpose of this document is to describe the roles, responsibilities and mechanisms for a common ethics review of a multicentre research proposal. This method can be adopted as an option by ECs engaged in multicentre research. It 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 of human research participants.

3. Scope

3.1. This document applies to ECs, investigators, and other stakeholders involved in multicentric biomedical and health research.

3.2. **Clinical trials** requiring registration with Central Drugs Standard Control Organization (CDSCO) for marketing approvals are **excluded** from common ethical review and should abide by the rules and regulations under Drugs and Cosmetics Act as effected from time to time.

3.3. These guidelines serve as annexure to and should be read in conjunction with the ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017.

4. Structure

4.1. **Coordinating PI:** The PI from the coordinating centre will be the Coordinating PI for the multicenter study. Her/His institutional ethics committee will serve as the Designated Ethics Committee. Coordinating PI shall take overall responsibility for the conduct of the

multicentre research along with PIs from all the participating centres and ongoing communication between DEC and PIs of other participating centres.

4.2. **Principal Investigator (PI):** The PI is the person who is entrusted with responsibility for the conduct of multicentre research at her/his participating centre. Each centre can have additional co-investigator(s), who may conduct the study within the centre (please refer to glossary for multicentre research).

4.3. **Designated Ethics Committee (DEC):** The EC which assumes the responsibility to undertake a common review of the research proposal with mutual agreement of all the ECs of participating centres in a multicentre research shall be called as the Designated Ethics Committee. The existing EC of the Coordinating centre shall serve as the DEC, if agreeable to the participating centres with option to include additional members as per its procedures. Each DEC will be research protocol specific, and may be formalized through Memorandum of Understanding (MoU) between the participating institutes. The DEC shall strive to form a network for improved communication amongst centres involving the authorized representatives of their ethics committees.

4.4. **Ethics committees of the participating centres (PEC):** The Participating Centre ECs in a multicentre research are located at different 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 of their respective Centres.

5. **Responsibilities of Coordinating PI**

5.1. To submit the research protocol to DEC for review using the common forms for EC review.

5.2. To submit the Application Form for Multicentre Research for her/his centre through (Annexure 4 – Form 1A and Form 1B) to DEC.

5.3. To report/channelize reporting from any PEC of serious adverse events, causality assessment, protocol deviations at the centre, unanticipated problems involving risks to participants or others, significant complaints/any potential non-compliance to DEC as per requirement or if there are specific concerns that may impact other centres as well.

Comment [DN1]: Needs to be simplified

5.4. To assess the need and communicate the concerns received from one centre to other centres (if required) depending on the type of concern such as adverse event or specific concerns that may impact other centres as well.

6. Responsibilities of Principal Investigator (PI)

6.1. To submit the research protocol along with any participating centre specific changes/modifications through Annexure 4- Form 1B to respective PECs for review using Common forms for EC review.

6.2. 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 non-compliance to PEC as per requirement.

6.3. To initiate the study at the local centres with approval from PEC of their Centre.

7. **Designated Ethics Committee (DEC)**

7.1. **Qualifying criteria for DEC**

- Should be the coordinating centre for the multicentre research.

- Should be located in India and be willing to conduct ethical review of all participating Indian centres.
- Have minimum 3 years of experience in reviewing research protocols.
- Registered with the regulatory authority such as CDSCO and/or DHR (as per New Drugs and Clinical Trials Rules, 2019)

7.2. **Tenure of DEC**: The tenure of the DEC shall be from the start until the closure of the study.

7.3. **Responsibilities of DEC**

7.3.1. To conduct a detailed initial review of the research protocol which is common for all centres involved in a multicentre research. *(Please note: For certain types of research, study should be initiated simultaneously at all centres and this has to be decided by DEC according to the need.)*

7.3.2. To ensure representation from at least 50% PECs to participate in deliberations of the DEC. This participation can be in person or through electronic means. These special invitees do not have voting rights but can participate in DEC meeting to provide their comments and respective local perspectives. The names of representatives, the PECs represented by them shall be recorded in the minutes of the meeting as well as in the decision letter issued by the DEC. The observations of the PEC representatives shall be minuted in the proceedings of the DEC.

7.3.3. The DEC shall receive regular communications from the PECs (continuing review reports, annual reports, serious adverse events related to the study, causality assessment, protocol deviations, unanticipated problems involving risks to participants or others, significant complaints/any potential non-compliance)

7.3.4. To maintain and update a repository of copies of site specific documents, which include the submissions made by the site PIs to their PECs, the site specific consent forms and decision letters issued by the PECs.

7.3.5. To inform other centres if any existing centre is suspended or terminated for any reasons.

8. Responsibilities of Ethics Committees of the participating centres (PECs)

8.1. To identify representative/nominee who is a member of PEC to attend the common review meeting of DEC who will communicate the specific issues as warranted at their centre, if any.

8.2. To participate in the DEC meeting through video/tele conferencing.

8.3. To document their centre specific information and related modifications in the research protocol through full committee meeting/expedited review including any local consent related issues specific to the centre and as per SOP of the centre.

8.4. Member Secretary in consultation with Chairperson may take a call on these.

8.5. The PEC can recommend/suggest changes in the research protocol to PI at their participating centre who will communicate these to the coordinating PI.

8.6. To communicate the final decision for the study at the centre to PI.

8.7. 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 non-compliance as per protocol and as per prevailing regulations for biomedical and health research.

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

9. Memorandum of Understanding (MoU) for Common Review of Multicentre Research

9.1. A bipartite MoU between the DEC and each PEC will be signed. A template of MoU for common review of multicentre research is given at the Annexure-3 for reference.

9.2. The MoU shall come in to effect on the date of its signature by all centres and shall remain in force till the closure of the study.

10. Timelines for Review:

10.1. Research protocol will be submitted to DEC and all the PECs.

10.2. The protocol may be reviewed by all the Centres as per conditions stipulated in the MoU.

10.3. The DEC will communicate its decision on research protocol including any centre specific changes to the PECs.

10.4. The ethical approval for individual Centres will be issued by their respective PECs.

10.5. Reasonable and mutually agreed upon timelines should be allotted for the review process. A maximum of 30 days to the DEC for review of the research protocol from the date of last submission from PEC as per MoU.

Comment [DN2]: I don't think the D can communicate centre specific change to PEC

11. Protocol Amendment: Submission and Review Process:

11.1. Major amendments in the protocol will be submitted to DEC for review through respective PECs.

11.2. Minor amendments in the protocol that do not significantly affect the study may be submitted to concerned PECs for review.

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

12.1. Reporting of Serious Adverse Events, Adverse Events, Deviations and other types of Reportable Events for each centre may be done in accordance with the prevailing regulations for biomedical and health research.

12.2. The PEC reserves its right to suspend or terminate the approval of studies with due justification.

12.3. If the research as a whole is suspended or terminated by the DEC, the same shall promptly be notified to all the PECs.

13. Record Keeping and archiving

13.1. Access to and control over all the records will be maintained by PECs and DEC for a minimum period of 3 years following closure or termination of the study.

13.2. The PIs and PECs should maintain records and archives as stipulated by the research protocol and the prevailing regulations for biomedical and health research.

Glossary

Designated Ethics Committee (DEC):
The participating EC, which assumes the responsibility of undertaking a common initial and continuing review of the multicentre research proposal with mutual agreement of all the participating centres, shall be called 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 according to the local requirements and dignity, rights, safety and well-being of their research participants.

Research Protocol: The common protocol with uniform core objectives, methods, and measurement tools approved by the DEC. The research protocol is to remain consistent across the sites but site PECs may modify consent form according to local and cultural context and also have the liberty to add objective(s)/ questions for fulfilling essential local requirements.

Principal Investigator (PI):
The PI is the person who takes the responsibility of conducting research at her/his centre as part of multicentre research. Each centre can have additional co-investigator(s), who may conduct the study with in the centre in association and/or in the absence of the PI.

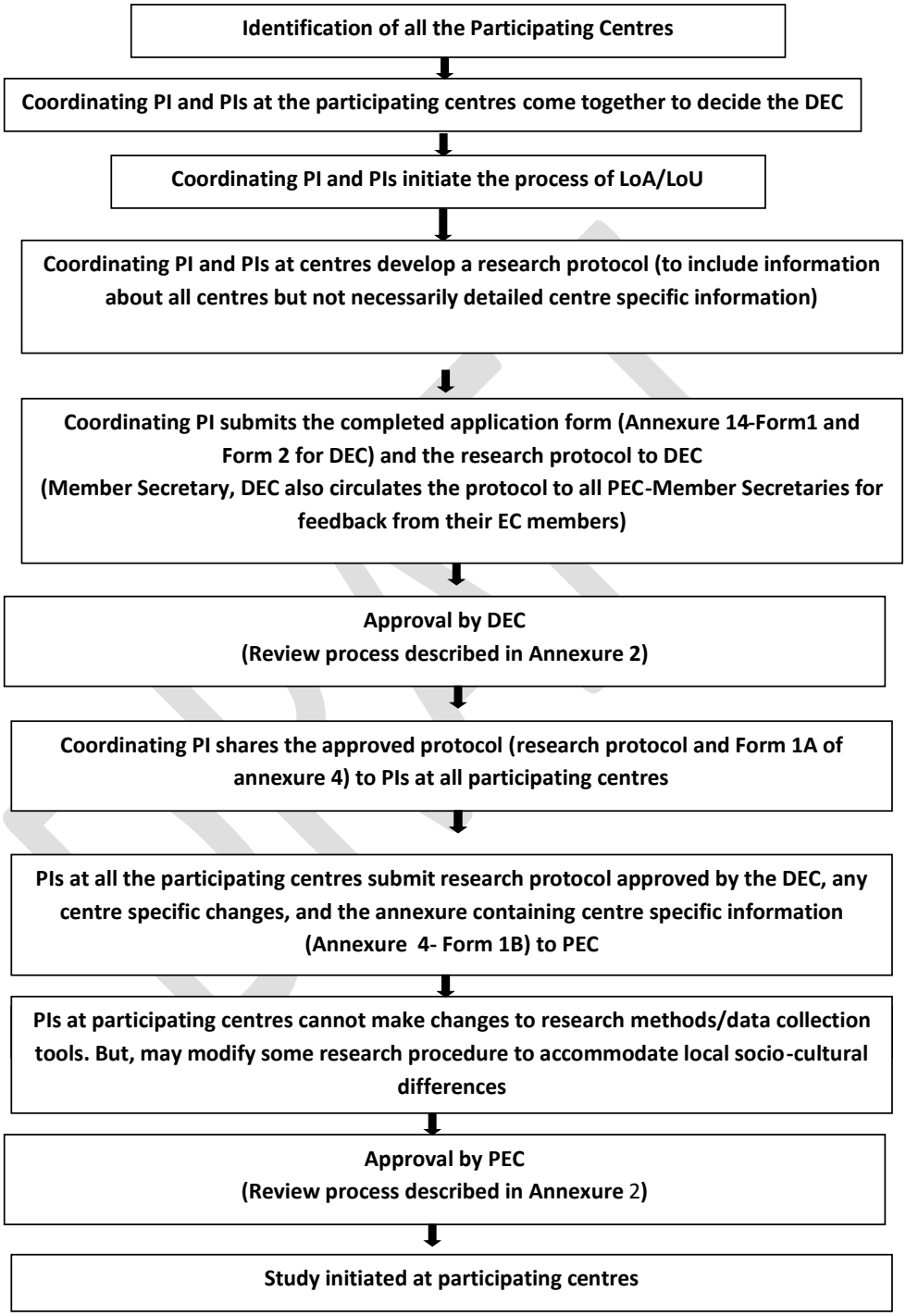
Coordinating Principal Investigator (PI):
Coordinating PI is one who takes an overall responsibility of conducting multicentre research along with PIs from all the participating centres and is also responsible for ongoing communication between DEC and PIs at other participating centres.

Multicentre research: Multi-centre research is conducted at more than one centre by different researchers following a common protocol. However, certain research proposals may also be considered as multi centre research where each centre with a PI is involved in a different defined role as per the objective/methodology such as quality control and data management etc. Each centre can have multiple sites from which participants can be recruited. However, each site should have a responsible nodal person as applicable at local level i.e. one PI for different sites in that centre.

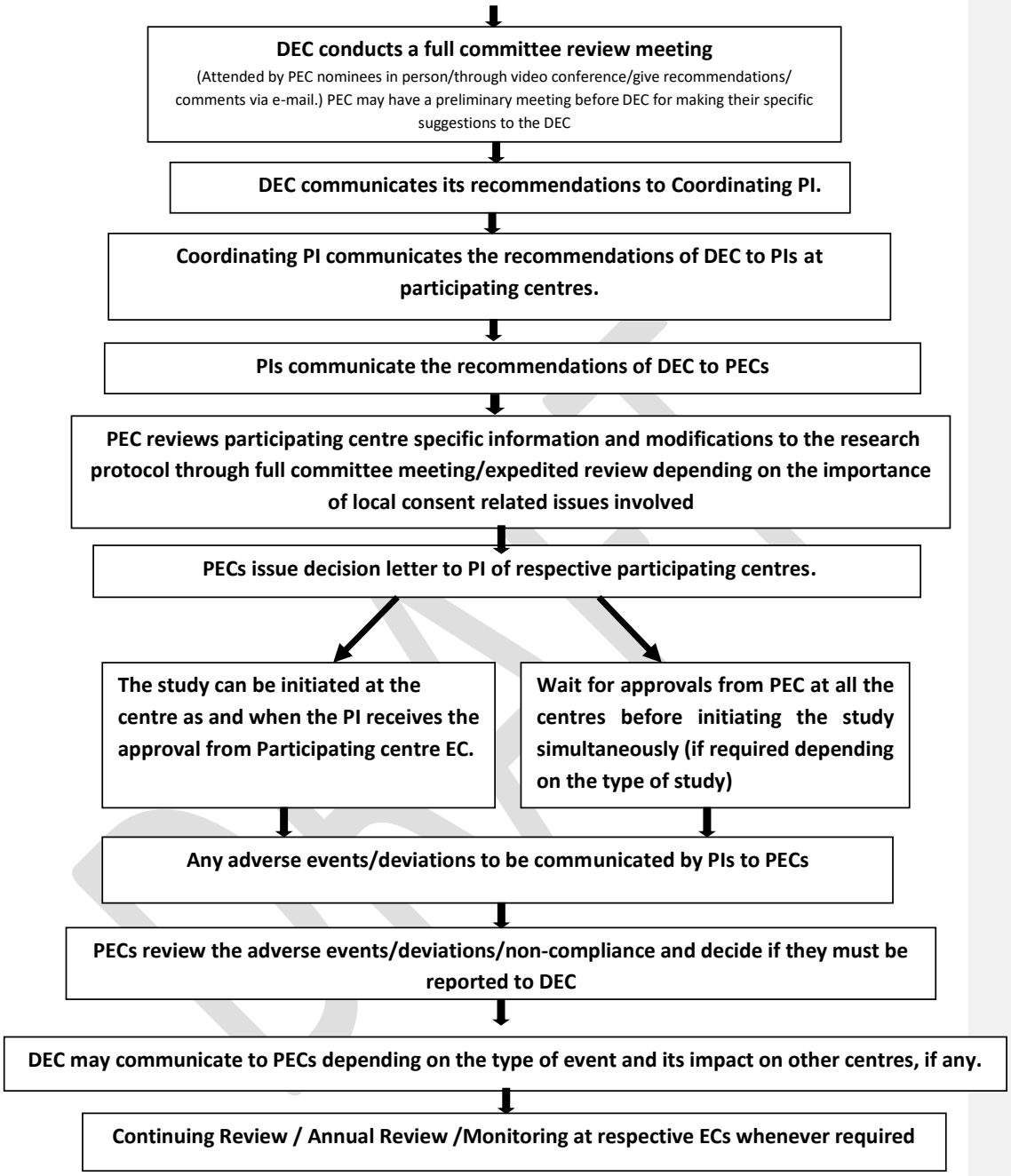
Abbreviations

CDSCO: Central Drugs Standard Control Organization
DEC: Designated Ethics Committee
DHR: Department of Health Research
EC: Ethics Committee
ICMR: Indian Council for Medical Research
MoU: Memorandum of Understanding
PEC: Participating Centre Ethics Committee
PI: Principal Investigator

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 –MoU 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: …….

We, the undersigned are authorised by the Participating centre EC of **……** (name of the institution) to utilize the services of the Designated EC **……** (name of the institution) for Common Ethics Review of Multicentre Research protocols.

It is understood that Designated Ethics Committee would undertake full ethics committee review on behalf of the PEC. Ethical issues related to local centres may be reviewed by PEC and the final decision communicated to Designated Ethics Committee within 30 days of signing this MoU. The PEC shall have the option of participating in person or submitting their comments to the DEC. A decision of the DEC shall be communicated to the PEC in due course. The PEC may represent its concern against the decision of the DEC within _days of receiving the decision, failing which it will be deemed that the PEC concurs with the decision. This MoU is valid from _____ to _____. (Life of this study, i.e., proposed date of common review meeting to tentative date of submission of project completion report to DEC).

This agreement is limited to the following specific Proposal(s):
Title of Research Proposal: ……
……
Name of Principal Investigator/ Coordinating PI:……
Name of Co-investigator:……
Sponsor or Funding Agency: ……
The responsibilities of centres will be fulfilled as per the ICMR Guidelines and related regulations ensuring compliance with the same.

For Designated Ethics Committee

Signature of Chairperson/Member Secretary:…….
Date: ……
Name: ……
Address: ……
……
……

For Participating Centre EC

Signature of Chairperson/ Member Secretary:…….
Date: ……..
Name: ……
Address: ……
……
……

Annexure 4: Standard Operating Procedure

Title: Common Review of Multicentre Research

1. Purpose

The purpose of this guidance is to describe the roles, responsibilities and mechanisms for a common ethics review of a multicentre research proposal. This method can be adopted as an option by ECs 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 of human research participants.

2. Scope

- This guidance applies to ECs, investigators, and other stakeholders involved in multicentric biomedical and health research.
- Clinical trials requiring approval from Central Drugs Standard Control Organisation (CDSCO) are excluded from common ethical review and should abide by the rules and regulations under Drugs and Cosmetics Act as effected from time to time.
- These guidelines serve as annexure to and should be read in conjunction with the ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017, the reference document.

3. Responsibilities

i. Coordinating PI

- To submit the research protocol to DEC for review using the common forms for EC review.
- To submit the Application Form for Multicentre Research for her/his centre through (Annexure 4 – Form 1A and Form 1B) to DEC.
- To report/ channelize reporting from any PEC of serious adverse events, causality assessment, protocol deviations at the centre, unanticipated problems involving risks to participants or others, significant complaints/any potential non-compliance to DEC as per requirement or if there are specific concerns that may impact other centres as well.
- To communicate the concerns received from one centre to other centres (if required) depending on the type of concern such as adverse event or specific concerns that may impact other centres as well.

Comment [DN3]: Needs to be simplified

ii. Principal Investigator(PI)

- To submit the research protocol along with any participating centre specific changes/modifications through Annexure 4- Form 1B to respective PECs for review using Common forms for EC review.
- 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 non-compliance to PEC as per requirement.
- To initiate the study at the local centres with approval from PEC of their Centre.

iii. Designated Ethics Committee (DEC)

- To conduct the research protocol which is common for all centres involved in a multicentre research. *(Please note: For certain types of research, study should be initiated simultaneously at all centres and this has to be decided by DEC according to the need.)*
- To ensure representation from at least 50% or five [5] PECs to participate in deliberations of the DEC. This participation can be in person or through electronic means. These special invitees do not have voting rights but can participate in DEC meeting to provide their comments and respective local perspectives. The names of representatives, the PECs represented by them shall be recorded in the minutes of the meeting as well as in the decision letter issued by the DEC. The observations of the PEC representatives shall be minuted in the proceedings of the DEC.
- The DEC shall receive regular communications from the PECs (continuing review reports, annual reports, serious adverse events related to the study, causality assessment, protocol deviations, unanticipated problems involving risks to participants or others, significant complaints/any potential non-compliance)
- To maintain and update a repository of copies of site specific documents, which include the submissions made by the site PIs to their PECs, the site specific consent forms and decision letters issued by the PECs.
- To inform other centres if any existing centre is suspended or terminated for any reasons.

iv. Participating Centre Ethics Committee (PEC)

- To identify representative/nominee who is a member of PEC to attend the common review meeting of DEC who will communicate the specific issues as warranted at their centre, if any.
- To participate in the DEC meeting through video/tele conferencing.
- To document their centre specific information and related modifications in the research protocol through full committee meeting/expedited review including any local consent related issues specific to the centre and as per SOP of the centre.
- Member Secretary in consultation with Chairperson may take a call on these.
- The PEC can recommend/ suggest changes in the research protocol to PI at their participating centre who will communicate these to the coordinating PI.
- To communicate the final decision for the study at the centre to PI.
- 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 non-compliance as per protocol and as per prevailing regulations for biomedical and health research.
- To ensure good and prompt communications to DEC as per requirement or if there are specific concerns that may impact other centres as well.

4. **Review process**

   i. **Review process by DEC**

   - The DEC assumes the responsibility to undertake a common review of research protocol with mutual agreement of all the participating centres in a multicentre research.
   - The coordinating PI of the study submits the research protocol along with application form (Annexure 4- Form 1A and 1B) 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.
   - Invites representatives from PECs 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.
   - The PECs can participate in the DEC meeting through their representatives or via video/tele conferencing.
   - DEC reviews local issues specific to the centre through form 1B, changes in informed consent document, translations and monitor research as per local requirements.
   - Reviews policy for publication/data sharing between centres/benefit sharing/post research results with all involved participants.
   - 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**

   - PIs at all the participating centres submit research protocol with any centre specific changes and the Annexure 4- Application form 1B containing centre specific information to PEC.
   - PEC reviews participating centre specific information and modifications in the research protocol through full committee meeting/expedited review depending on the importance of local consent related 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. The meeting may be held before ~~or after~~ the DEC meeting.
   - The DEC's final recommendations are reviewed by the PECs trough full committee or expedited review to grant site specific approval for the study.
   - Reviews serious adverse events, protocol deviations, unanticipated problems involving risks to participants or others, significant complaints/any potential noncompliance at the centre and decide about reporting them to DEC.

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

   - DEC communicates the recommendations to coordinating PI and DEC

Comment [DN4]: Needs to be redor

- PEC shall 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.
- For certain types of research, study at all centres should be initiated simultaneously and this has to be decided by DEC according to the need.