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 has gained a great momentum in recent years. It provides a great opportunity to present meaningful outcomes for the country and actively engages 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 a specific research. This could be inter-departmental/inter-institutional or international and also multicentric 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. These guidelines provide 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 effect a timely review process without compromising quality of that review as well as autonomy of individual ECs.

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 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 for ensuring protection of 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 and should abide by the rules and regulations under Drugs and Cosmetics Act and Rules as amended from time to time. 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 research proposal with mutual agreement of all the ECs of participating centres in a multicentre research shall be called as the Designated Ethics Committee.

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

4.3 The EC of the Coordinating centre may serve as the DEC, if agreeable to all participating centres.

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

4.4.1 **Essential criteria:**

- Should be one of the centre for the multicentre research.
- Should be located in India and be willing to conduct ethical review of specific research for 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).

4.4.2 **Desirable criteria:**

- Accredited by NABH or AAHRPP or has undergone SIDCER recognition/ other ethics committee quality assurance programs.

4.5 Responsibilities of DEC:

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

4.5.1 To conduct a detailed initial review of the study proposal/ master protocol which is common for all centres involved in a multicentre research.

4.5.2 To review the study proposal/ master protocol and also application form (Annexure 5 – application form part A and local issues of DEC through part B).

4.5.3 To ensure representation from at least 50% or five [5] (whichever is less) PECs to participate in deliberations of the DEC. This participation can be in person or through electronic means including Skype or other mechanisms. 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 and 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.

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

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

4.5.6 To review policy for publication/data sharing between centres/benefit sharing/post research results with all involved participants.

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

4.5.8 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 non-compliance as reported to DEC from other centres.

4.5.9 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 centre specific consent forms and decision letters issued by the PECs.

4.5.10 To form a network for improved communication amongst centres by involving Member Secretaries of all the participating 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; incorporate changes in informed consent document if necessary, translations in local language and monitor research as per local requirements of their respective Centres.

5.1 Responsibilities of PECs:

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

5.1.1 To identify a representative/nominee to attend the common review meeting of DEC who will communicate the specific concerns at their centre, if any.

5.1.2 To attend the DEC meeting through Skype or any other mechanism whenever possible.

5.1.3 To review participating centre specific information and related modifications in the study proposal/ master 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. PEC also reviews the recommendations of the DEC and suggest modifications, if need be.

5.1.4 If a particular PEC wishes to change the master protocol, the coordinating PI of the project may take a call on the continuation of this centre in the multicentric study.

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

5.1.6 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.

5.1.7 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 non-compliance must be reported to DEC.

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

6. Coordinating PI:

Coordinating PI is the one who takes an 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. In general, the EC of her/his centre becomes the DEC.

6.1 Responsibilities of Coordinating PI:

6.1.1 To submit the study proposal/ master protocol to DEC for review using the common forms for EC review.

6.1.2 To submit the application form for multicentre research for her/his centre through (Annexure 5 – application form - part A and part B) to DEC.

6.1.3 To function as a link between DEC and PIs to communicate the recommendations of DEC to PIs and the PECs.

6.1.4 To submit 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.

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

6.1.6 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.

7. Principal Investigator (PI):

The PI is the person who takes an overall 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*).

7.1 Responsibilities of PI:

7.1.1 To submit the study proposal/ approved master protocol along with any participating centre specific changes/modifications through Annexure 5 – application form - part B to respective PECs for review using Common forms for full committee or expedited EC review.

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

7.1.3 To participate in the DEC meeting along with respective EC representative to communicate the PEC views, if necessary.

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 non-compliance to PEC and DEC as per requirement.

7.1.5 To initiate the study at the local centres as and when the approval from PEC is obtained for their Centre. *(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.)*

8. Letter of Agreement (LOA) /Letter of Understanding (LoU) for Common Review of Multicentre Research

8.1 A signed document/agreement/email should be made to support and validate the agreed roles and responsibilities of the DEC and the PECs. Signature/ affirmation can be obtained from Member Secretaries of ECs of participating institutes on behalf of Chairperson or concerned Chairpersons.

8.2 This should be in the form of LoA/LoU, documenting the roles, responsibilities, communication and publication plans between the PECs for common review.

8.3 If any additional centre is added after the initiation of the study, the LoA/LoU should be revisited. The additional PEC should be explained the terms and conditions and should

be asked to sign the LoA/LoU. The copy of revised agreement shall also be circulated to other PECs for record.

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 LoA/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 LoA/ LoU for common review of multicentre research is given at the Annexure-3 for reference.

9. Timelines for Review:

9.1 Study proposals/master protocol will be submitted to DEC and all the PECs.

9.2 The protocol may be reviewed by all the Centres according to their convenience and procedures.

9.3 The DEC meeting will be attended by representatives of all PECs – PI and or any EC member. The PECs can also participate in the DEC meeting by Skype or any other mechanism so that concerns of individual Centres may also be discussed to arrive at a consensus decision.

9.4 The DEC approved master protocol along with any centre specific changes through Annexure 5 – application form - part B will be submitted to PEC again.

9.5 The final approval for individual Centres will be provided by the concerned PEC.

9.6 Reasonable and mutually agreed timelines should be allotted for the review process. A maximum of 30 days to DEC for approval of study proposal/ master protocol and application form (Annexure 5 – application form - part A and B). A maximum of 30 days to PEC for approval of local participating centre specific review.

10. Protocol Amendment: Submission and Review Process:

10.1 Major amendments in the protocol will be submitted to DEC for review, the decision of which shall be communicated to PECs.

10.2 Minor amendments in the protocol not affecting the study will be submitted to concerned PEC for review.

10.3 All amendments should be communicated to the DEC for information by all Centres at the earliest.

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.

11.3 The PEC can convey their concerns and decision, if any, to DEC for consideration. The DEC may advise the centres regarding the same.

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

12. Record Keeping and archiving

12.1 Access to all the records and its control will be maintained 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 sponsor requirements for record keeping and archiving beyond 3 years.

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, 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 according to the local requirements and dignity, rights, safety and well-being of their research participants.

Study proposal/ Master protocol: The common protocol with uniform core objectives, methods, and measurement tools approved by the DEC. The Master 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.

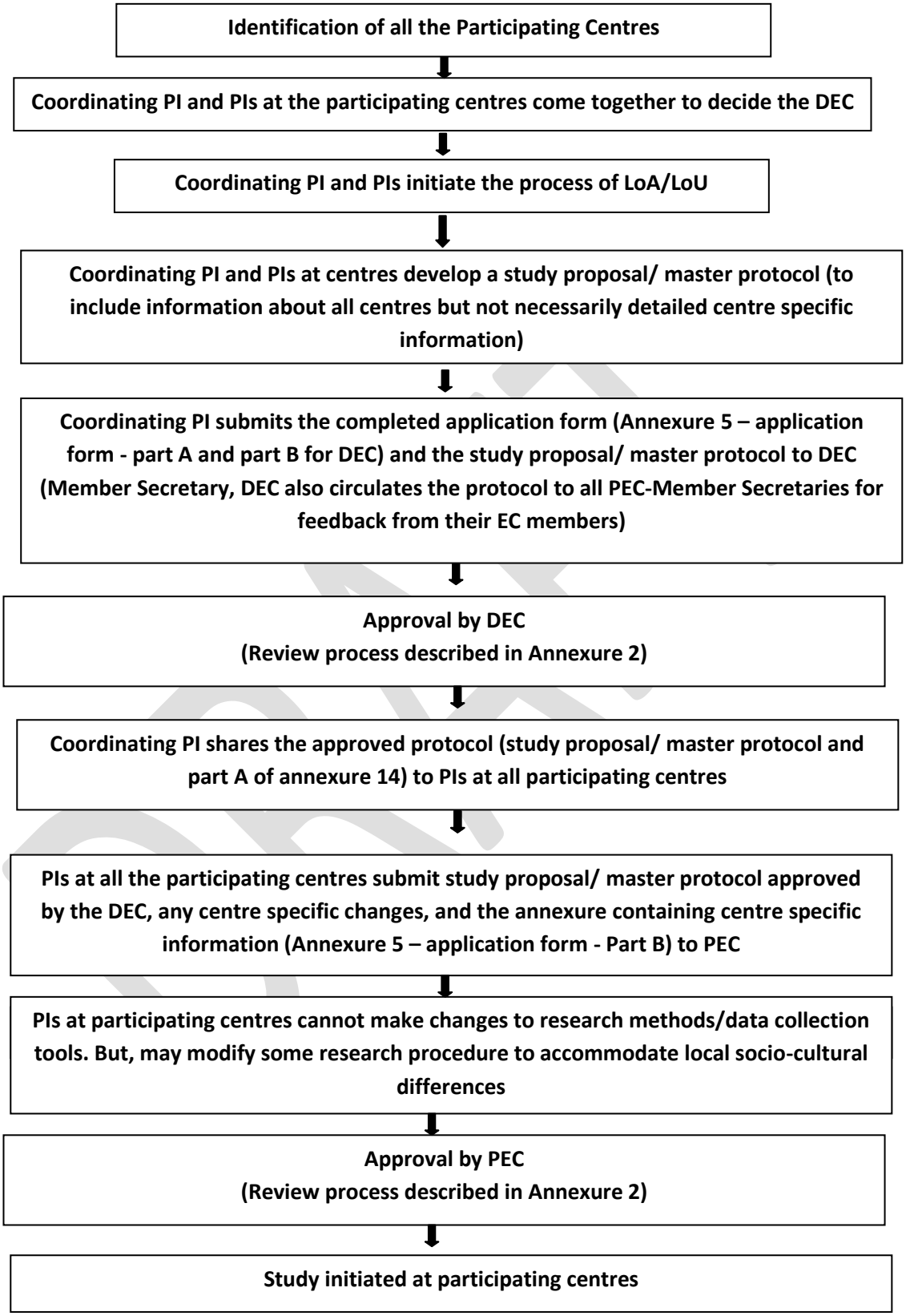
Coordinating Principal Investigator (PI):
Coordinating PI is one who takes an overall responsibility of conducting multicentre research along with PIs from all the participating centres and is also responsible for ongoing communication between DEC and PIs at other participating centres.

Multicentre Research: Multicentre research is conducted at more than one centre by different researchers following a common protocol. However, certain research proposals may also be considered as multicentre 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.

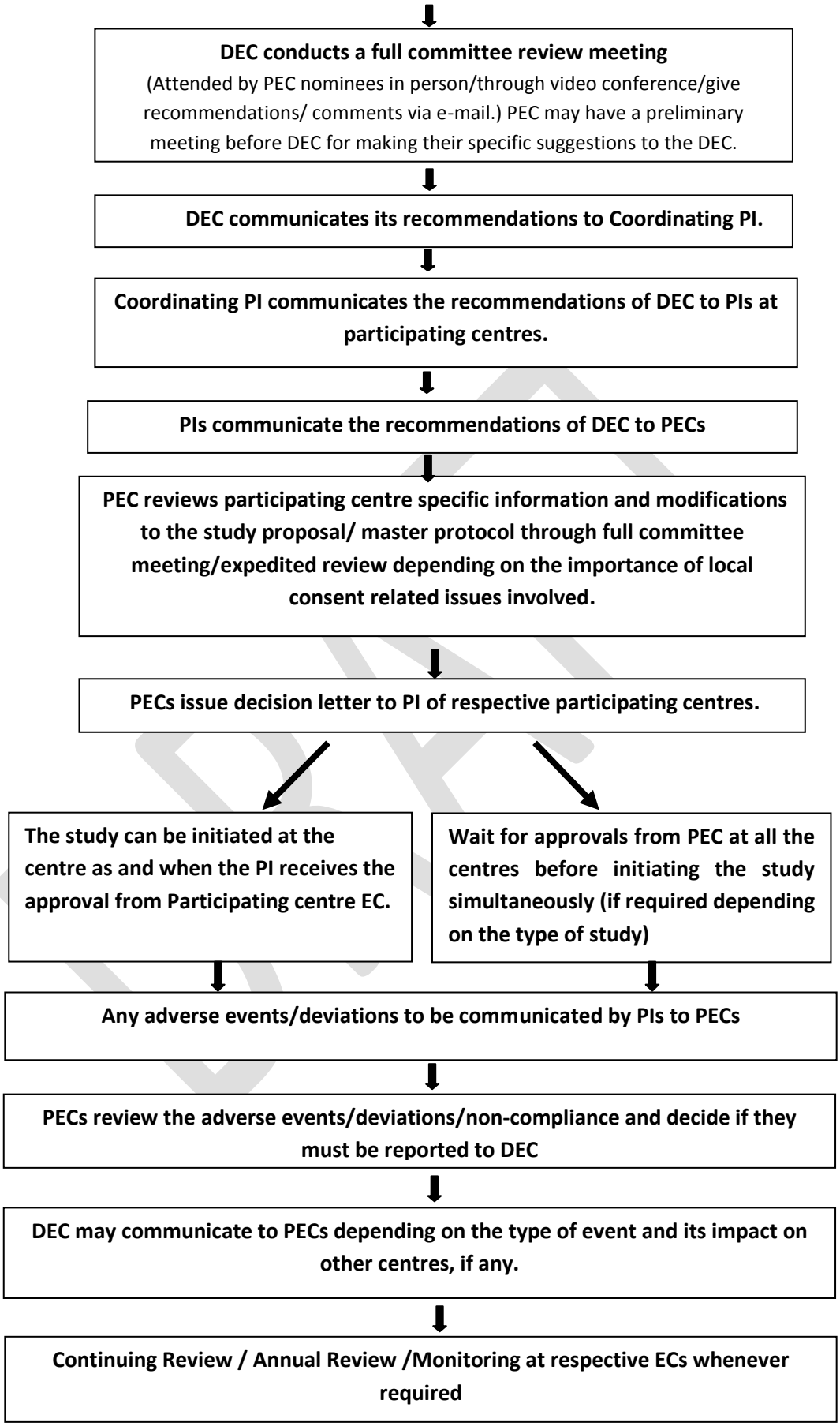
Steering/Monitoring Committee: This committee includes experts from funding agencies/sponsors/partners from the centre or region as per requirement. The committee ensures smooth functioning and implementation of the study protocol and monitoring

Technical (Scientific) Advisory Committee: This committee includes a group of independent subject experts who are not investigators of the research/member of funding agencies/sponsors or its representatives/monitors. 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 – LoA/ 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) will accept the review 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 committee review meetings and communicated to DEC which also participate in DEC meeting through their representatives or any other mechanism and the final decision communicated to Centre with intimation to the Designated Ethics Committee. The LoA/LoU 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 specific to the following Proposal(s):
Title of Research Proposal: ……
……
Name of / Coordinating PI: ……
Name of principal Investigator/ 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.

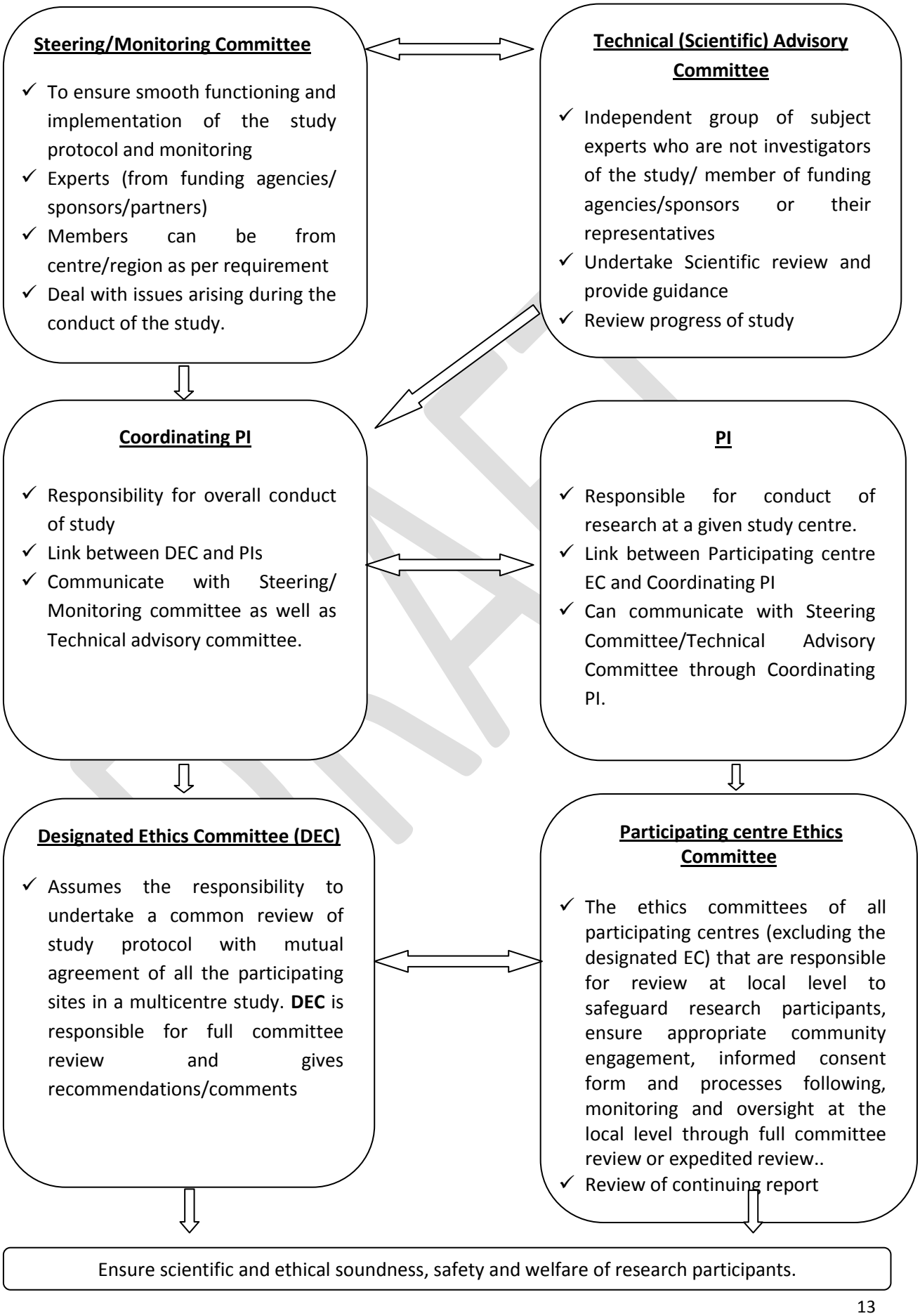
For Designated Ethics Committee:

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

For Participating Centre EC:

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

Annexure 4: Suggested Governance Mechanism for large Multicentre Research



Annexure 5: SOP and Application Form for Common Review of Multicentre Research

Standard Operating Procedure (SOP)

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 common combined review so that review process can be expeditious without compromising ethical principles for protection of human research participants.

3. **Responsibilities:**

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

   - To conduct a detailed initial review of the study proposal/ master protocol which is common for all centres involved in a multicentre research.
   - To review the study proposal/ master protocol and also application form (Annexure 5 – application form - part A and local issues of DEC through part B)
   - 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 respective 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 research results with all involved participants.
   - 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 non-compliance as reported to DEC from other centres.
   - To form a network for improved communication amongst centres by involving Member Secretaries of all the participating centres.

   ii. **Participating Centre Ethics Committee (PEC):**

   - To review participating centre specific information and modifications in the study proposal/ master 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 can be held before or after the DEC meeting.

- To identify a representative/nominee to attend the common review meeting of DEC who will communicate the specific concerns at their centre, if any.
- To issue the final decision letter for the study at the centre to PIs after reviewing the DEC decision.
- 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.
- 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 non-compliance must be reported to DEC.
- To ensure good and prompt communications to DEC as per requirement or if there are specific concerns that may impact other centres as well.

iii. Coordinating PI:

- To submit the study proposal/ master 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 5 – application form - part A and part B) to DEC.
- To function as a link between DEC and PIs to 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 non-compliance 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 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.

iv. Principal Investigator (PI):

- To submit the study proposal/ approved master protocol along with any participating centre specific changes/modifications through Annexure 5 – application form - part B to respective PECs for review using Common forms for EC review.
- To function as a link between PEC and Coordinating PI to 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 non-compliance to PEC and DEC as per requirement.

- To initiate the study at the local centres as and when the approval from EC is obtained. *(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.)*

4. Review process:

i. Review process by DEC:

- The DEC assumes the responsibility to undertake a common review of study proposal/ master protocol with mutual agreement of all the participating centres in a multicentre research.
- The coordinating PI of the study submits the study proposal/ master protocol along with application form (Annexure 5 – application form - part A and B) 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 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 Skype/ video conferencing.
- DEC reviews local issues specific to the centre through part B, 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 study proposal/master protocol with any centre specific changes and the Annexure 5 – application form - part B containing centre specific information to PEC.
- Reviews participating centre specific information and modifications in the study proposal/ master 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 through 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
- Coordinating PI functions as a link between DEC and PI's
- PI communicates the recommendations of DEC received from coordinating PI to PEC and functions as a link between both.
- PI communicates with Steering/Monitoring committee and Technical advisory committee through Coordinating PI.
- 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 participating 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.

Logo of the Institute

Application form for Common Review of Multicentre Research *

.....

Name of the Institute

EC Ref. No*. *(For office use):*

Instructions to fill the form:

- Coordinating Principal Investigator should fill both Part A and part B of the form and submit to DEC
- Principal Investigators at the participating centres should fill Part B of the form and submit to respective PECs and also to coordinating PI
- May attach additional sheets wherever necessary

Protocol number: ..... Version number: .....
Title of study: .....
.....
.....
Coordinating Principal Investigator (Name, Designation and Affiliation) .....
.....
.....

Part A

1. Date of proposal submission: | dd | mm | yy |

2. Please provide details of the partcipating centres in the table below.

S.No	Name and address of the participating centre / Institution	Name and contact details of PI at the participating centre

3. Provide details of Designated Ethics Committee (DEC) identified for common review for this study (Address and contact details of member secretary)
.....
.....
.....

Signature of Coordinating PI ..... | dd | mm | yy |

**This is to be filled in addition to application form for initial review*

Protocol number: ..... Version number: .....
Title of study: .....
.....
.....
Principal Investigator at the participating centre (Name, Designation and Affiliation) .....
.....
.....

Part B

1. Are there any sites involved locally at each study centre for recruitment purposes? If yes, please provide details.

   Yes ☐ No ☐

   .....
   .....
   .....
   .....
   .....

2. Please provide details of the study team involved in research at the centre in the following table:

Type of Role	Number of personnel

3. Are there any local socio - cultural issues that might impact the study at this centre?
   If yes provide details. Yes ☐ No ☐

   .....
   .....
   .....

4. Are there any specific local laws or institutional requirements that apply? Yes ☐ No ☐
   If yes, provide details.

   .....
   .....
   .....

5. Are there any oversight committees at the participating centres to oversee and monitor the research?
   If yes, provide details about the committees and their members. Yes ☐ No ☐

   .....
   .....
   .....

6. Has translations bee done for the informed consent form? Yes ☐ No ☐
   If yes, list the languages in which translations were done. If no, please justify.

   .....
   .....
   .....
   .....

7. Who will be obtaining the informed consent?
   PI ☐ Nurse/counsellor ☐ Research Staff ☐ Other *(please specify)* ☐
   ……

8. Is there local capacity to manage the adverse events? Yes ☐ No ☐

9. What are the local arrangements for emergencies? Please limit your response to 150 words.
   ……
   ……
   ……
   ……

10. Provide details of the person to be contacted during emergencies (in case PI is not available)
    ……
    ……

Signature of PI…… | dd | mm | yy |