Title: Initial Full Board Review of New Research Study Protocols

1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe how the Institutional Ethics Committee (EC) members will perform an initial review on a new research study protocol using the Assessment Form.

2. Scope

This SOP applies to the initial review and assessment of all research study protocols submitted for review and approval from the EC. All research studies presented with more than minimal risk and which do not qualify for exemption (See SOP 7C/V4) or expedited review (See SOP 7B/V4), are covered in this SOP.

3. Responsibility

- The Member Secretary is responsible, after categorisation of the studies (as per SOP 07/V4), to forward the studies to the Secretariat.
- The EC Secretariat is responsible for creation of a study specific file, distribution of the packages along with study assessment forms to the EC members for review (If the study is categorised for Full Board review), and communicate the review results to the investigators.
- EC members (including Member Secretary) will be responsible for reviewing the research protocols and related documents within the given time frames.
- It is the responsibility of all the EC members to fill the Assessment form along with comments and recommendation they have after reviewing each study protocol.
- The EC members are responsible for attending and participating actively in the discussion at the full Board Meeting
- The Member Secretary is responsible for setting up the Full Board Meeting (SOP 07A/V4)
- The EC Secretariat is responsible for recording and filing the decision, relevant points and deliberation about a specific protocol, including the reasons for that decision.

- The Chairman is responsible to sign and date the decision in the EC Decision Form *AX 03A/SOP 7A/V4.*

4. Detailed instructions

4.1 Appointment of primary reviewers

- The Member Secretary/Chairman will appoint two or more primary reviewers for each study on the basis of expertise in the related field and experience. They should include one clinician and one non technical person as applicable. More than two may be appointed if necessary.

4.2 Distribute the protocol package

- The Secretariat will fill in the required details in the cover letter to the EC Members requesting initial review (*AX 01/SOP 7A/V4*) and in the study assessment form *AX 02/SOP 7A/V4.*
- The Secretariat will send a packet *(soft copy)* to the EC members.
    - Letter to EC Members requesting Initial Review with study assessment form *AX 01/SOP 7A/V4*
    - Covering letter (AX 01/SOP 06/V4) and Checklist (AX 02/SOP 06/V4)
    - Research Study Application Form Submission *to EC (AX 03/SOP 06/V4)*
    - Protocol and related documents
    - Study assessment form *AX 02/SOP 7A/V4* in case it is to the Primary reviewer.

4.3 Receive the distributed protocol package

- The EC members will receive the protocol package with the Study Application Form as soft copy or as hard copy (for primary reviewer, if desired so).
- Designated primary reviewers will also receive the Study Assessment Form for Initial Review AX 02/SOP 7A/*V4*

4.4 Verify the contents of the package

- The EC member will verify all the contents.

- The EC member will check the meeting date to see if it is convenient to attend the meeting.
- The EC member will notify the EC Secretariat if any documents are missing or if the specified date of the EC meeting is not convenient to attend.

4.5 Review by the EC members

Review of the protocol

- The protocol will be reviewed by each member as per guidelines to review a study protocol described in *AX 06/SOP 7A/V4*.
- The EC member will consider the following criteria when performing the review of the study protocol and the study related documents:
  - Scientific design and conduct of the study
  - Risks and potential benefits
  - Selection of study population and recruitment of research participants
  - Inducements, financial benefits and financial costs
  - Protection of research participants' privacy and confidentiality
  - Community considerations
  - Qualifications of Investigators and assess adequacy of study sites
  - Disclosure or declaration of potential conflicts of interest
- The EC member will consider the following criteria when performing the review of the Informed Consent Document (as per *AX 06/SOP 7A/V4*)
  - Voluntary, non-coercive recruitment, participation/ withdrawal
  - Procedures for obtaining informed consent
  - Contents of the patient information sheet - title, objective, study design and procedures
  - Contents and language of the informed consent document
  - Translation of the informed consent document in the local languages
  - Language used – plain and easy to understand by general public

- Contact persons with address and phone numbers for questions about research participants rights and study or injury
- Privacy and confidentiality
- Risks and discomforts – physical / mental / social
- Alternative treatments
- Benefits – to participants, community, institution and society
- Compensation for participation: (Whether it will act as undue inducement)
- Involvement of vulnerable participants
- Provisions for medical/ psychosocial support
- Treatment for study related injuries
- Compensation for study-related injuries: as per applicable local regulations
- Use of biological materials
- Check for provision for signatures with dates of participant, person conducting informed consent discussion, investigator and witness
- Provision for audiovisual recording of consent process in case of regulatory drug trials

4.6 Use of study assessment form for reviewers

- The assessment form is designed to standardize the review process.
- All reviewers will fill out the form (AX 01/SOP 7A/V4 - letter to EC members requesting initial review with study assessment form) and write their comments related to review of the research proposal.
- In addition, primary reviewers will use the study assessment form (AX 02/SOP 7A/*V4*) to ensure that all elements of research study are reviewed and are accordingly documented during the discussion / meeting.
- The duly filled, signed and dated assessment forms will be returned along with the research protocols to the Secretariat 7 days prior to the meeting.

4.7 Gather the assessment reports

- The EC Secretariat will collect the Assessment Forms, comments from each reviewer and file in the original study file and converted into a soft copy for discussion at the meeting. If the comments come as a soft copy, these will be collated for discussion at the meeting.
- During the discussion at the meeting, the primary reviewer shall brief the members about summary of the study protocol and read out the comments and evaluation provided on the assessment form.
- The comments of an independent consultant (if applicable) will be discussed by the member secretary.
- The other EC members shall give their comments right after the presentation.
- The investigator/sub-investigator may be called in to provide clarifications on the study protocol that he/she has submitted for review to the EC.
- The EC members will discuss and clarify the comments and suggestions.
- The Member secretary (assisted by the Secretarial staff) shall record the discussions
  - The final decision on the study will be recorded as: "Approved/ Disapproved/ Suggested recommendations (minor or major modifications) or any other in the meeting shall be made by voting or by majority consensus and will be recorded in the EC Decision Form (AX 03A/SOP 7A*/V4)* by the Member Secretary. The EC decision will be communicated to the PI in the intimation letter (AX 03B/SOP 7A*/V4)*
  - A majority vote for approval, disapproval or request for modifications of a study suspension or termination of an ongoing study is defined as 2/3rd of the voting members present at the meeting.
  - The following will not be eligible to vote
    - Member(s) of the committee who is/are listed as investigator(s) on a research proposal
    - An investigator or study team member invited for the meeting.

- An independent consultant invited for the meeting to provide opinion
- Specific patient groups invited for the meeting will not vote or participate in the decision making procedures of the committee.
- The Committee will decide whether the query responses and (if applicable) revised protocol will go only to Member Secretary, to primary reviewers or to Full Board before final approval.
- The response and changes carried out may be considered for discussion at a future EC meeting.
- If the EC decision is 'Disapproved' or any other, the decision should be made on the basis of specific reasons, which are communicated by the EC to the principal investigator in the letter of notification.
- The Secretariat will obtain the signature of all the members and of the Chairman of the EC on the EC Decision Form *AX 03/SOP 7A/V4*.
- If the study is approved, the Committee will recommend monitoring for a study if it is so determined at the meeting depending on factors like risk is high in the protocol, the PI has a history of repeated protocol violations, PI has many protocols and any other reason so deemed.
- The Secretariat will list participating members in the meeting and summarize the guidance, advice and decision reached by the EC members.
- With the study protocol, the Assessment Form from all members and EC Decision Form will be filed in the study file by the Administrative Officer.
- The Administrative Officer will return the file and the protocol to the appropriate shelves.

4.9 Final communication of the EC decision taken on the study to the Principal Investigator

- The Secretariat will prepare an approval letter as *AX 04/SOP 7A/V4* to be sent to the Principal Investigator when the study is approved at an EC meeting.
- The letter contains, at a minimum:
  - Study reference number

- Study title
- A listing of each document approved, the date set by the Committee for frequency of continuing review, and a review of other obligations and expectations from the investigator throughout the course of the study.
- The approval is provided for the entire duration of the study.
- List of EC members present at the meeting when the study was approved.
- The Chairman / Member Secretary will sign the approval letter and the Secretariat will send it to the Principal Investigator within 14 days.

- If the Committee disapproves a study, the Secretariat immediately notifies the investigator in writing about the decision and the reason/s for not approving the study within 7 working days.
- A notifying letter to the investigator should state the following:

  "If you wish to appeal to this decision, please contact the EC and submit your appeal in writing within twelve (12) weeks of the receipt of the committee's decision, addressed to the EC Chairman with justification as to why the appeal should be granted. In absence of appeal, the study will be declared closed for the EC office records."

- If the Committee requires modifications to any of the documents, the Secretariat will send a written request for carrying out specific changes to the investigator asking him or her to make the necessary changes and resubmit the documents to the EC. The Principal Investigator will be asked to respond to the letter of comments/queries within 10 days of the receipt of the letter by the investigator. In the absence of any response, the study will be declared closed for the EC office records.
- The Secretariat will verify the correctness of the wordings and spelling in all the letters and process all the above tasks within 14 days after the meeting.

4.10 Storage of Documents

- The Secretariat will keep a copy of the Approval letter/Query letter/Disapproval letter in the study file along with all the reviewed documents.

- The Administrative Officer will store the file on an appropriate shelf in the designated cabinet.

5. References to Other Applicable SOPs

SOP 6/V4.: Management of Research Study Protocol and Study Related Documents Submitted for Ethics Review

SOP 07/V4: Categorization of Submitted Protocols for Ethics Review

SOP 07B/V4: Expedited Review of Research Study Protocols

SOP 07C/V4: Exemption from Ethics Review of Research Study Protocols

SOP 08/V4: Agenda Preparation, Meeting Procedures and Recording of Minutes

SOP 09/V4: Review of Amended Protocol, Protocol-related Documents and Resubmitted protocol

6. Annexures

Annexure 1 AX 01/SOP 7A/V4 - Letter to the EC Members requesting initial review with study assessment form

Annexure 2 AX 02/SOP 7A/V4 - Study assessment form for primary reviewer

Annexure 3A AX 03A/SOP 7A/V4 - EC decision form

Annexure 3B AX03B/SOP 7A/V4- Intimation letter to PI (Intimation of EC decision to PI)

Annexure 4A AX 04A/SOP 7A/V4 - Format of regulatory clinical trial approval letter (as per NDCT rules 2019)

Annexure 4B AX 04B/SOP 7A/V4 - Format of Interventional Research Study approval letter

Annexure 4C AX 04C/SOP 7A/V4 - Format of Observational Research Study approval letter

Annexure 5 AX 05/SOP 7A/V4- Undertaking by the investigator for regulatory clinical trials (As per NDCT rules 2019)

Annexure 6 AX 06/SOP 7A/V4 Guidelines for reviewing a study protocol

Annexure 1: ***AX 01/SOP 7A/V4***

Letter to EC Members requesting Initial Review with study assessment form

Dear member,

The next meeting of the EC will be held on XXX at XXX in XXXX.

Please note that the package of research proposals is to be circulated in the following order. You are requested to review the same preferably within 5 working days of receiving the package. Please review the protocol and related documents as per the guidelines attached with Annex 1 and provide your comments below and fill the study assessment form (for primary reviewers only) provided with the package (*AX 02/SOP 7A/V4*). Kindly confirm your availability for the meeting.

Name of Member	Date of Receipt	Signature	Attending meeting (Y/N)

Protocol Number : (as per EC records)	Date of receipt at EC office after review by E member (DD/MM/YY):	
Protocol Title :		
Name of the Principal Investigator	Designation	Department
Name of the Reviewer:		

Comments:

Signature of EC member reviewing the study:		Date:

Annexure 2: ***AX 02/SOP 7A/V4***

Study Assessment Form to be used by the Primary Reviewer

IEC code number of Protocol :		Date (DD/MM/YY):	
Protocol Title :			
Principal Investigator:			
Department :			
No. of Participants:		No. of Study site (s) :	

Mark and comment on whatever items are applicable to the study.

S. No	Item	Comments (if any)
1.	Objectives of the Study ☐ clear ☐ unclear	
2	Need for Human Participants ☐ Yes ☐ No	
3	Methodology: (comment on sample size) ☐ clear ☐ unclear	
4 a.	Background Information and Data ☐ Sufficient ☐ Insufficient	
4 b.	Risk Assessment: A. Type of Risk anticipated to study participant: ☐ Psychological ☐ Physical ☐ Social ☐ Economical ☐ Legal B. ICMR Risk Categorization: ☐ Less than minimal risk ☐ Minimal risk ☐ Minor increase over minimal risk	

	☐ More than minimal risk	
4 c.	Benefit Assessment Yes No For participant ☐ ☐ For society / community ☐ ☐ Improvement in science ☐ ☐ If Yes, mention Direct/Indirect type of benefit for each category Direct Indirect For participant ☐ ☐ For society / community ☐ ☐ Improvement in science ☐ ☐	
4 d.	Exclusion Criteria ☐ Appropriate ☐ Inappropriate	
4 e.	Discontinuation and Withdrawal Criteria ☐ Appropriate ☐ Inappropriate ☐ NA	
5	Involvement of Vulnerable Participants: Yes ☐ No ☐	
6	Control Arms (placebo, if any) Yes ☐ No ☐ NA ☐	
7	Contents of the Informed Consent Document: ☐ clear ☐ unclear	
8	Language of the Informed Consent Document: ☐ clear ☐ unclear	
9	Inducement for Participation Unlikely ☐ Likely ☐	
10	Provision for Compensation for Participation	

	☐ Appropriate ☐ inappropriate ☐ NA	
11	Provision for Treatment for Study-Related Injuries ☐ Appropriate ☐ inappropriate ☐ NA	

Any other comments:

Reviewer's Signature with date:

Annexure 3A: ***AX 03/SOP 7A/V4***

Decision Form

Date of EC meeting: _____

Protocol number: _____

EC Protocol No. and Title:	
Principal Investigator:	Department:
Final Decision at the meeting:	☐ Approved ☐ Approved with modifications ☐ Resubmission ☐ Disapproved ☐ Reviewed at the Full Board meeting ☐ Review by any 2 / more EC members ☐ Monitoring required Reason:_____

Disapproved, Reasons:

_____

_____

_____

No.	Names of Members present	AP	AM	RS	DA	Signature

Note: *AP: Approved; AM: Approved with modification [(either primary reviewer/full board) if reviewed by full board again a decision form has to be filled; RS: Resubmission; DA: Disapproved.*

Comments:
No. of members voting for the decision:
No. of members voting against the decision:
No. of members abstaining from voting:

_____
Signature of Chairman **Date:** _____

Annexure 3 B: AX03B/SOP 7A/V4

Intimation letter to PI (Intimation of EC decision to PI)

To **SMVMCH –EC code no:**

Dear Dr.

SMVMCH Ethics Committee processed your research protocol entitled ""

Comments of the reviewers:

You are informed that you have to rectify your proposal based on the comments given by the members of the Ethics Committee and resubmit it for review by the Ethics Committee on or before Date: XXXX. One hard copy of the revised proposal addressed to the chairman should be submitted to the office of the Ethics Committee. Kindly note that the edited items must be highlighted by yellow colored highlighter.

Above entitled research work can be initiated only after SMVMCH-EC approval letter. SMVMCH-EC approval letter will be issued only after verification of edited copy of the protocol.

MEMBER SECRETARY

Annexure 4A: ***AX 04A/SOP 7A/V4***

Format of regulatory clinical trial approval letter (as per NDCT rules 2019)

To

Dr.

Dear Dr._____

The SMVMCH Institutional ethics committee (SMVMCH-EC) reviewed and discussed your application to conduct the clinical trial entitled "……."

on……..….(date).

The following documents were reviewed:

(a) Trial protocol (including protocol amendments), dated…….version No.(s) ……

(b) Patient information sheet and informed consent form (including updates, if any) in English or vernacular language.

(c) Investigator's brochure, dated ..... , Version no..... Proposed methods for patient accrual including advertisements etc. proposed to be used for the purpose.

(d) Principal investigator's current Curriculum Vitae.

(e) Insurance policy or compensation for participation and for serious adverse events occurring during the study participation.

(f) Investigator's agreement with the sponsor.

(g) Investigator's undertaking (AX 05/SOP 7A/V4).

The following members of the ethics committee were present at the meeting held on (date, time, place).

.....Chairperson of the ethics committee;

.....Member-Secretary of the ethics committee;

.....Name of each member with designation;

We approve the trial to be conducted in its presented form.

The ethics committee to be informed about the progress of the study, any Serious Adverse Events (SAE) occurring in the course of the study, any changes in the protocol and patient information or informed consent and to be provided with a copy of the final report.

Yours sincerely,

Member Secretary/ Chairman, EC
(Signed and dated by the EC Chairman or Member Secretary)

Annexure 4B: *AX 04B/SOP 7A/V4*

Format of Interventional Research Study Approval letter

Date XX/XX/XXXX

To,
Dr. xxxxxxxxxxxx,
Dept. of xxxxxxxxxxxxx.

Ref: The study no. EC/xxx/20xx entitled, "xxxxxxxxxx".
Sub: Letter no.

Dear Dr. XXXXx,
The meeting of the Institutional Ethics Committee (EC) was held on xxxxx at xxxx, in the xxxxxxxxxxxxx with xxxxx as Chairman.
xxxx members attended the meeting held on xxxx. The list of members who attended the meeting is as follows

Name of Members	Position on EC	Designation & Affiliation	Qualification	Gender

It is hereby confirmed that neither you nor any of the study team members have participated in the voting/decision making procedures of the committee.

The EC reviewed the above mentioned clinical study and approved the following documents submitted for this clinical study at the meeting.

1. Xxx
2. Xxx
3. xxx

The EC hereby approves the proposal entitled, "xxxxxxxxxxxxx".

It is understood that the study will be conducted under your direction, in a total of xxxx research participants, at XXXXXXXXXXXXX as per the submitted protocol.

This approval is valid for the entire duration of the study.

It is the policy of EC that, it be informed about any onsite serious adverse event or the unexpected adverse event report within 24 hours as per the formats specified in SOP 09/V4 to the EC or by email if there is holiday. The report of SAE or death after due analysis shall be

forwarded by the Investigator to chairman of the EC and the head of the institution where the trial is been conducted within 10 calendar days of SAE or death.

In case of injury or death occurring trial subject the sponsor (whether a pharmaceutical company or an institution) or his representative, whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial shall make payments for medical management of the subject and also provide financial compensation for the clinical trial related injury or death.

No deviations from, or changes of the protocol and Informed Consent Document should be initiated without prior written approval by EC of an appropriate amendment. The EC expects that the investigator should promptly report to EC any deviations from, or changes of, the protocol to eliminate immediate hazards to the research participants and about any new information that may affect adversely the safety of the research participants or the conduct of the trial.

For studies which will continue for more than a year, a continuing review report needs to be submitted (within 1 month of the due date i.e. 11 months from the date of approval) on or before XXXXXXXXXXX.

A copy of the final report should be submitted to the EC for review.

The EC functions in accordance with ICH GCP, Schedule Y, ICMR guidelines and other applicable regulatory requirements.

Sincerely yours

Member Secretary/ Chairman,
EC
(Signed and dated by the EC Chairman or Member Secretary)

Date of approval of the study: XX/XX/20XX

Annexure 4C: *AX 04C/SOP 7A/V4*

Format of Observational Research Study Approval letter

Date XX/XX/XXXX
To,
Dr. xxxxxxxxxxxx,
Dept. of xxxxxxxxxxxxx.

Ref: The study no. EC/xxx/20xx entitled, "xxxxxxxxxx".
Sub: Letter no.

Dear Dr. XXXXx,

The meeting of the Institutional Ethics Committee (EC) was held on xxxxx at xxxx, in the xxxxxxxxxxxxx with xxxxx as Chairman.

xxxx members attended the meeting held on xxxx. The list of members who attended the meeting is as follows.

Name of Members	Position on EC	Designation & Affiliation	Qualification	Gender

It is hereby confirmed that neither you nor any of the study team members have participated in the voting/decision making procedures of the committee.

The EC has reviewed and approved the following documents submitted for the above – mentioned clinical study.

1. Xxx
2. Xxx
3. xxx

The EC hereby approves the proposal entitled, "xxxxxxxxxxxxx".

It is understood that the study will be conducted under your direction, in a total of xxxx research participants, at Dept. of xxxx, _____ as per the submitted protocol.

This approval is valid for the entire duration of the study.

No deviations from, or changes of the protocol and Informed Consent Document should be initiated without prior written approval by the EC of an appropriate amendment. The EC expects that the investigator should promptly report to the EC any deviations from, or changes of, the protocol to eliminate immediate hazards to the research participants and about any new information that may affect adversely the safety of the research participants or the conduct of the trial.

For studies which will continue for more than a year, a continuing review report needs to be submitted (within 1 month of the due date i.e. 11 months from the date of approval) on or before XXXXXXXXXXX.

A copy of the final report should be submitted to the EC for review.
The EC functions in accordance with ICH GCP, Schedule Y, ICMR guidelines and other applicable regulatory requirements.

Sincerely yours

Member Secretary/ Chairman,
EC
(Signed and dated by the EC Chairman or Member Secretary)
Date of approval of the study: XX/XX/20XX

Annexure 5: AX 05/SOP 7A/V4
Undertaking by the investigator for regulatory clinical trials (As per NDCT rules 2019)

1. Full name, address and title of the Principal Investigator (or Investigators when there is no Principal Investigator).
2. Name and address of the medical college, hospital or other facility where the clinical trial will be conducted: Education, training & experience that qualify the Investigator for the clinical trial (Attach details including Medical Council registration number, or any other statements of qualifications)
3. Name and address of all clinical laboratory facilities to be used in the study.
4. Name and address of the Ethics Committee that is responsible for approval and continuing review of the study.
5. Names of the other members of the research team (Co-or sub-Investigators) who will be assisting the Investigator in the conduct of the investigations.
6. Protocol Title and Study number (if any) of the clinical trial to be conducted by the Investigator.
7. Commitments:

(i) I have reviewed the clinical protocol and agree that it contains all the necessary information to conduct the study. I will not begin the study until all necessary ethics committee and regulatory approvals have been obtained.

(ii) I agree to conduct the study in accordance with the current protocol. I will not implement any deviation from or changes of the protocol without agreement by the Sponsor and prior review and documented approval or favourable opinion from the ethics committee of the

amendment, except where necessary to eliminate an immediate hazard to the trial subject or when the changes involved are only logistical or administrative in nature.

(iii) I agree to personally conduct or supervise the clinical trial at my site.

(iv) I agree to inform all trial subject, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent and ethics committee review and approval specified in the New Drugs and Clinical Trials Rules, 2019 and Good Clinical Practices guidelines are met.

(v) I agree to report to the Sponsor all adverse experiences that occur in the course of the investigation(s) in accordance with the regulatory requirements and Good Clinical Practices guidelines.

(vi) I have read and understood the information in the Investigator's brochure, including the potential risks and side effects of the drug.

(vii) I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are suitably qualified and experienced and they have been informed about their obligations in meeting their commitments in the trial.

(viii) I agree to maintain adequate and accurate records and to make those records available for audit or inspection by the Sponsor, ethics committee, Central Licencing Authority or their authorised representatives, in accordance with regulatory provisions and the Good Clinical Practices guidelines. I will fully cooperate with any study related audit conducted by regulatory officials or authorised representatives of the Sponsor.

(ix) I agree to promptly report to the ethics committee all changes in the clinical trial activities and all unanticipated problems involving risks to human subjects or others.

(x) I agree to inform all serious adverse events to the Central Licencing Authority, sponsor as well as the ethics committee within twenty-four hours of their occurrence. In case, of failure to do so, I shall furnish the reason for the delay to the satisfaction of the Central Licencing Authority along with the report of the serious adverse event.

(xi) The report of the serious adverse event, after due analysis, shall also be forwarded by me to the Central Licencing Authority, the Chairperson of the ethics committee and the Head of the institution where the trial has been conducted within fourteen days in accordance with the regulatory requirements.

(xii) I will maintain confidentiality of the identification of all participating subjects and assure security and confidentiality of study data.

(xiii) I agree to comply with all other requirements, guidelines and statutory obligations as applicable to clinical Investigators participating in clinical trials.

8. Signature of Investigator with date.

Annexure 6: AX 06/SOP 7A/V4

Guidelines for reviewing a study protocol

Reviewers should make use of the following points while reviewing research studies which relate to scientific validity, informed consent documents, placebo justification, suitability and feasibility of the study, advertisements review.

1. How will the knowledge, result or outcome of the study contribute to human well-being?
   - ❑ Knowledge from the basic research may possibly benefit.
   - ❑ A new choice of method, drug or device that benefits the research participants during the study and others in the future.
   - ❑ Provide safety data or more competitive choices.
2. Does the study design will be able to give answers to the objectives? Whether
   - ❑ The endpoints are appropriately selected.
   - ❑ The participating duration of a study participant is adequate to allow sufficient change in the endpoints.
   - ❑ The control arm is appropriately selected for best comparison.
   - ❑ The placebo is justified.
   - ❑ The number of study participants in non-treatment (or placebo) arm is minimized.
   - ❑ Unbiased assignment (e.g. randomization, etc.) is in practice.
   - ❑ Inclusion and exclusion criteria are carefully selected to eliminate confounding factors as much as possible.
   - ❑ The sample group size appropriate with the given statistical assumptions.
   - ❑ Predictable risks are minimized.
   - ❑ The tests and procedures that are more than minimal risk are cautiously used.
   - ❑ Research participants deception is avoid.
   - ❑ Instruction and counseling for study participants are included (if needed) when deception is integral to the study design.
   - ❑ The study participants are adequately assessed and provided follow-up care, if needed.
3. Who will be the participants in the study? Whether
   - ❑ The described population is appropriate for the study.

- Predictable vulnerabilities are considered.
- It is completely necessary to conduct the study in a vulnerable population. If not, is there any other way to get the study answers?
- There will be secondary participants.

4. Do the inclusion and exclusion criteria
   - Selectively include participants most likely to serve the objective of the study?
   - Equitably include participants?
   - Properly exclude participants who can predictably confound the results?
   - Properly exclude participants who may predictably be at increased risk in the study due to coexisting conditions or circumstances?
5. Does the study design have adequate built-in safeguards for risks?
   - Appropriate screening of potential participants?
   - Use of a stepwise dose escalation with analysis of the results before proceeding?
   - Does the frequency of visits and biological samplings reasonably monitor the expected effects?
   - Are there defined stopping (discontinuation) / withdrawal criteria for participants with worsening condition?
   - Is there minimized use of medication withdrawal and placebo whenever possible?
   - Will rescue medications and procedures be allowed when appropriate?
   - Is there a defined safety committee to perform interim assessments, when appropriate?
   - Is appropriate follow-up designed into the study? For instance, gene transfer research may require following the participants for years or for their entire lifetime after they receive the gene transfer agent.
6. Is pre-clinical and/or early clinical studies sufficiently performed before this study?
   - The animal study and *in vitro* testing results?
   - Previous clinical results, if done?
   - Whether the proposed study is appropriately built on the pre-clinical and/or early clinical results.
   - The selected dose based on adequate prior results?
   - Monitoring tests designed to detect expected possible risks and side effects?
7. Do the study and the informed consent process include issues of special concern, such as:
   - Waiver or alteration of consent?
   - Delayed consent (e.g., emergency treatment, etc.)?
   - Deception?
   - Sensitive information of participants that may require a confidentiality statement?

Guidelines to review Informed Consent Document/Patient Information Sheet The actual process of informed consent should:

- Give the participants significant information about the study.
- Make sure the participants have enough time to carefully read and consider all options.
- Answer all questions of the participants before making decision to participate.
- Explain risks or concerns to the participants.
- Make sure that all information is understood and satisfied by the participants.
- Make sure the participants understand the study and the consent process.
- Obtain voluntary informed consent to participate.
- Make sure the participants can freely consent without coercion, pressure or other undue influences.
- Consent should be informally verified on a continuing basis.
- Continue to inform the participants throughout the study.
- Continue to re-affirm the consent to participate throughout the study.

Guidelines to Placebo Justification

Background conditions, such as benefits of standard treatment, risk of using placebo, risk management and disclosure should be considered.

I. Benefits of standard treatment

1) Is there a standard treatment?
2) Is the standard treatment widely accepted?
3) Has efficacy of the treatment been consistently proven?
4) Are all newly diagnosed patients with this condition put in standard treatment (versus observed or other)?
5) Does the treatment act on the basic mechanism of the disease (vs. symptoms)?
6) Are most (≥85%) of the patients with this condition responsive to standard treatment alternatives (vs. resistant or refractory)?

   If the answers of (1) to (6) are "yes", placebo is not recommended.

   If any one or more answers are "no", placebo may be possible.
7) Are the side effects of the standard treatment severe?
8) Does standard treatment have many uncomfortable side effects?
9) Does standard treatment have contraindications that prevent some research participants from being treated?
10) Is there substantial (≤25%) placebo response in this disease or symptom?

    If the answer of (7) *to* (10) *are "no", placebo is not recommended.*

    If any one or more answers are "yes", placebo may be possible.

II. Risks of placebo

1) Is the risk of using placebo instead of treatment life threatening? *If yes, placebo is not acceptable.*
2) Is the use of placebo instead of treatment likely to lead to permanent damage? *If yes, placebo is not acceptable.*
3) Is the risk of using placebo instead of treatment likely to cause irreversible disease progression?
   If yes, placebo is not acceptable.
4) Can the use of placebo instead of treatment lead to an acute emergency?
5) Is the risk of using placebo instead of treatment the persistence of distressing symptoms?
6) Is the risk of using placebo instead of treatment severe physical discomfort or pain?
   If answers of (4) *to* (6) *are "yes", placebo is not acceptable unless risk management is adequate.*

III. Risk management

1) Is there benefit in the overall management of the research participants?
   - ☐ *Yes, consider placebo*
   - ☐ *No, placebo not recommended.*
2) Will the discontinuation of previous treatment put the participant in danger of acute relapse when transferred to placebo?
   - ☐ *No, consider placebo*
   - ☐ *Yes, placebo not recommended.*
3) Are research participants at high risk for the use of placebo excluded?
   - ☐ *Yes, consider placebo*
   - ☐ *No, placebo not recommended.*
4) Is the duration of the study the minimum necessary in relation to the action of the drug?
   - ☐ *Yes, consider placebo*
   - ☐ *No, placebo not recommended.*
5) Are there clearly defined stopping rules to withdraw the research participants in case he/she does not improve?
   - ☐ *Yes, consider placebo*
   - ☐ *No, placebo not recommended.*
6) Is risk monitoring adequate to identify progression of the disease before the research participants experience severe consequences?
   - ☐ *Not applicable.*
   - ☐ *Yes, consider placebo*

☐ *No, placebo not recommended.*

7) Are there clearly defined stopping rules to withdraw the research participants before the advent of severe disease progression?
   - ☐ *Yes, consider placebo*
   - ☐ *No, placebo not recommended.*

8) If the risk of placebo is an acute emergency, are rescue medication and emergency treatment available?
   - ☐ *Not applicable.*
   - ☐ *Yes, consider placebo*
   - ☐ *No, placebo not recommended.*

9) If the risk of placebo is the persistence of distressing symptoms, is concurrent medication to control them allowed?
   - ☐ *Not applicable.*
   - ☐ *Yes, consider placebo.*
   - ☐ *No, placebo not recommended.*

10) If the risk of placebo is severely physical discomfort or pain, is there rescue medication?
   - ☐ *Not applicable.*
   - ☐ *Yes, consider placebo.*
   - ☐ *No, placebo not recommended.*

IV. Risk disclosure in the consent form

1) Are the risks of getting placebo instead of active treatment fully disclosed?
   - ☐ *Yes, consider placebo.*

2) Are the risks of the test drug disclosed?
   - ☐ *Yes, consider placebo.*

3) Are the advantages of alternative treatments explained?
   - ☐ *Yes, consider placebo.*

Conclusions:

The use of placebo is ethically acceptable when

- ☐ Research participants are not exposed to severe or permanent harm by the use of placebo.
- ☐ Research participants under placebo will benefit from the overall treatment of the disease.
- ☐ Risks of the use of placebo are minimized.

☐ Risks are adequately disclosed in the consent form.

Guidelines to review advertisements

- Advertisements are limited to the information prospective participants need to determine their eligibility and interest, such as:
  - The name and address of the researcher or research facility.
  - The purpose of the research or the condition under study.
  - In summary form, the criteria that will be used to determine eligibility for the study.
  - A brief list of benefits to participants, if any.
  - The time or other commitment required of the participants.
  - The location of the research and the person or office to contact for further information

- The EC reviews advertising to ensure that advertisements **DO NOT**:
  - State or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.
  - Include exculpatory language.
  - Emphasize the payment or the amount to be paid, by such means as larger or bold type
  - Promise "free treatment" when the intent is only to say participants will not be charged for taking part in the investigation.

7. Flow Chart

No.	Activity	Responsibility
1	Receive package or research proposal and research related documents package	Secretariat
2	Verify contents and distribute	Secretariat
3	Appointment of primary reviewers	Member Secretary/Chairman
4	Initial review of documents, Fill review assessment form	EC members
5	EC board meeting, discussion and decision	EC members, Member Secretary, Chairman
6	EC decision communicated to PI	Secretariat
7	Storage of study related documents with relevant correspondence	Secretariat

8. References

1. Forum for Ethics review Committees in India (FERCI). Standard Operating Procedures of Institutional Ethics Committee (cited 22nd October 2018). Available from: http:// www.ferci.org/sops/
2. Ethical guidelines for biomedical research on human participants. (2017). Indian Council of Medical Research. Available from: http://www.icmr.nic.in/guidelines/ICMR_Ethical_Guidelines_2017.pdf
3. Ministry of Health and Family Welfare. New Drugs and Clinical Trials Rules, 2019. Available from: https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/NewDrugs_CTRules_2019.pdf

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