Title: ***Initial Full Board Review of New Research Study Protocols***
SOP Code: KIMS/SOP-08A/V3
Effective Date: 10/07/2019

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Table of Contents:

1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe how the Institutional Human Ethics Committee (IHEC) 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 IHEC. All research studies presented with more than minimal risk and which do not qualify for exemption (See KIMS/SOP-8C/V2) or expedited review (See KIMS/SOP-8B/V2), are covered in this SOP.

3. Responsibility

- The Member Secretary is responsible, after categorization of the studies (as per KIMS/SOP-08/V2), to forward the studies to the Secretariat.
- The IHEC Secretariat is responsible for creation of a study specific file, distribution of the packages along with study assessment forms to the IHEC members for review (If the study is categorized for Full Board review), and communicate the review results to the investigators.
- IHEC 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 IHEC members to fill the Assessment form along with comments and recommendation they have after reviewing each study protocol.
- The IHEC 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 (KIMS/SOP-08A/V3)
- The IHEC Secretariat is responsible for recording and filing the decision, relevant points and deliberation about a specific protocol, including the reasons for that decision.
- The Chairperson is responsible to sign and date the decision in the IHEC Decision Form *ANX-03/KIMS/SOP-8A/V3.*

4. Detailed instructions

4.1 Appointment of reviewers

The Member Secretary/Chairperson will appoint one primary reviewer or one secondary reviewer 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 send a packet *(hard)* to the IHEC members.

- Letter to IHEC Members requesting Initial Review and specifying their role
- Study Submission Application Form *ANX-01/KIMS/SOP-07/V2*
- Protocol and related documents
- Study assessment form *ANX-02/KIMS/SOP-8A/V3* to the Primary reviewer and secondary reviewer. The same form will be given to all members for facilitating the review process.

4.3 Receive the distributed protocol package

- The IHEC members will receive the protocol package with the Study Application Form ANX-01/KIMS/SOP-07/*V2*as hard copy.
- Designated reviewers will also receive the Study Assessment Forms ANX-02/KIMS/SOP-8A/*V3*

4.4 Review by the IHEC members

Review of the protocol

- The protocol will be reviewed by each member as per guidelines
  - 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
  - Recruitment strategy (Direct recruitment of potential study participants/ in-hospital Advertisements, flyers, information sheets, and notices/referrals from non-investigator health care providers).

The IHEC member will consider the following criteria when performing the review of the Informed Consent Document Annexure (*ANX-08/SO- 8A* /V3- checklist for reviewing Informed Consent may be used).

- 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
- Provision for unique code number for the patients

4.5 Use of study assessment form for reviewers

- The assessment form is designed to standardize the review process.
- All reviewers will be sent a letter (ANX-01/KIMS/SOP-8A/V2) requesting initial review with study assessment form and write their comments related to review of the research proposal.
- The duly filled, signed and dated assessment forms will be returned on the day of the programme
- *The risk and benefit of the proposed study will be evaluated by using ANX-09/KIMS/SOP-8A/V3*

4.6 Gather the assessment reports

The IHEC Secretariat will collect the Assessment Forms, comments from each reviewer and file in the original study file. If the comments come as a soft copy these will be collated for discussion at the meeting.

4.7. Review by the Legal Representative

The Legal Representative will review ICD along with translations, Memorandum of Understanding (MOU), Clinical Trial Agreement (CTA), regulatory approval, insurance document, other site approvals, researcher's undertaking, protocol specific other permissions, such as, stem cell committee for stem cell research, Health Ministry's Screening Committee (HMSC) for international collaboration, compliance with guidelines etc. The Legal Representative will consider the following items when reviewing the Clinical Trial Agreement.

- Statement of work
- Obligations and Responsibilities of the Principal Investigator
- Obligation and Responsibilities of the Institute
- Obligation and Responsibilities of the Sponsor
- Financial compensation for trial related injury such as injury or death as per the notification of the Drug Controller General of India (DCGI) & Government of India
- Undertaking and Representation of Principal Investigator
- Undertaking and Representation of Institute
- Undertaking and Representation of Sponsor
- Administration
- Trial Drug; Materials Transfer; Records Retention; Inspection
- Representation and Warranties
- Confidentiality
- Return of Confidential Information
- Trial Results and Inventions
- Payment
- Screen Failures/ Drop-outs
- Set-Up Fees
- Hospitalization costs

- Institutional Ethics Committee Fees
- Payments by Sponsor to Institute
- Tax deduction
- Use of other parties' names
- No joint venture etc
- Insurance and Indemnification
- monitoring; audit; regulatory inspections
- Term; Waiver; Severability (The trial on its time extended)
- Effect of termination
- Recordkeeping
- Publication
- Miscellaneous
- Governing Law
- Jurisdiction
- Arbitration
- Amendment

The legal expert has to record his opinion on the CTA or other agreements or MOUs reviewed by him and it will be documented in the concerned study file.

4.8. IHEC 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 IHEC 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 IHEC.
- The IHEC 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 or any other (as per IHEC policy" in the meeting shall be made by voting or by majority consensus (as per the IHEC policy) and will be recorded in the IHEC Decision Form

ANX-03/KIMS/SOP-8A*/V3* by the Member Secretary.

- 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 IHEC meeting.
- If the IHEC decision is 'Disapproved' or any other, the decision should be made on the basis of specific reasons, which are communicated by the IHEC to the principal investigator in the letter of notification.
- The Secretariat will obtain the signature of the Chairperson of the IHEC on the IHEC Decision Form *ANX-03/KIMS/SOP-8A/V3*.
- 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 IHEC members.
- With the study protocol, the Assessment Form from all members and IHEC 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 IHEC decision taken on the study to the Principal Investigator

- The Secretariat will prepare an approval letter as *ANX-04/KIMS/SOP-8A/V3* to be sent to the Principal Investigator when the study is approved at an IHEC 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 or for a certain duration
    - List of IHEC members present at the meeting when the study was approved.
    - The Chairperson / 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 IHEC and submit your appeal in writing within twelve (4) weeks of the receipt of the committee's decision, addressed to the IHEC Chairperson with justification as to why the appeal should be granted. In absence of appeal, the study will be declared closed for the IHEC 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 IHEC. 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 IHEC 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.
- All letters should have KIMS emblem and address
- Date of the first patient recruitment should be notified to the Ethics committee.

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

KIMS/SOP-7/V2: Management of Research Study Protocol and Study Related Documents Submitted for Ethics Review

KIMS/SOP-08/V2: Categorization of Submitted Protocols for Ethics Review

KIMS/SOP-08B/V2: Expedited Review of Research Study Protocols

KIMS/SOP-08C/V2: Exemption from Ethics Review of Research Study Protocols

KIMS/SOP-09/V2: Agenda Preparation, Meeting Procedures and Recording of Minutes

KIMS/SOP-10/V2: Review of Amended Protocol, Protocol-related Documents and Resubmitted protocol

6. Annexures

Annexure 1 *ANX-01/SOP 8A*/V3 - Letter to the IHEC Members requesting initial review with study assessment form

Annexure 2 *ANX-02/SOP-8A*/V3 - Study assessment form for primary reviewer

Annexure 3 *ANX-03/SOP-8A*/V3- IHEC decision form

Annexure 4 *ANX-04/SOP-8A*/V3 - Format of Interventional research study approval letter

Annexure 5 *ANX-05/SOP-8A*/V3 - Format of observational research study approval letter

Annexure 6 *ANX-06/SOP-8A* /V3- Guidelines for reviewing a study protocol

Annexure 7 *ANX-07/SO- 8A* /V3- checklist for reviewing a CTA

Annexure 8 *ANX-07/SO- 8A* /V3- checklist for reviewing a Informed consent

Annexure 1: ***ANX-01/KIMS/SOP-8A/V3***

Letter to IHEC Members requesting Review

KIMS/IHEC/Review/Ref.No./year
Date:

From,
IHEC Member Secretary

Sub: Appointment of Primary/Secondary Reviewer
Refer: Study …….

Dear member,
The next meeting of the IHEC will be held on XXX at XXX in XXXX.

I hereby appoint you as the Primary/Secondary review of the above referenced study and you are therefore requested to review the protocol and related documents as using the study assessment form provided with the package (*ANX-02/KIMS/SOP-7A/V2*) and bring the form when you come for the meeting with your comments.

You are requested to do the needful.

Yours sincerely,

IHEC Member Secretary

Annexure 2: ***ANX-02/KIMS/SOP-8A/V3***

Study Assessment Form to be used by the Reviewer

Protocol Number :		Date (DD/MM/YY):	
Protocol Title :			
Principal Investigator:			
Department :			
No. of Participants at the site:		No. of Study site(s):	

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

1	Objectives of the Study ☐ clear ☐ unclear	What should be improved?
2	Need for Participants ☐ Yes ☐ No	Comments:
3	Methodology: ☐ clear ☐ unclear	What should be improved?
4a	Background Information and Data ☐ sufficient ☐ insufficient	Comments:
4b	Risks and Benefits of Assessment ☐acceptable ☐ unacceptable	Comments:
4c	Inclusion Criteria ☐ appropriate ☐ inappropriate	Comments:
4d	Exclusion Criteria ☐ appropriate ☐ inappropriate	Comments:
4e	Discontinuation and Withdrawal Criteria ☐ appropriate ☐ inappropriate	Comments:
5	Involvement of Vulnerable Participants: ☐ Yes ☐ No	Comments:
6	Voluntary, Non-Coercive	Comments:
	Recruitment of Participants ☐ Yes ☐ No	
7	Sufficient number of participants? ☐ Yes ☐ No	Comments:
8	Control Arms (placebo, if any) ☐ Yes ☐ No	Comments:
9	Are Qualifications and experience of the Participating Investigators appropriate? ☐ Yes ☐ No	Comments:
10	Disclosure or Declaration of Potential Conflicts of Interest ☐ Yes ☐ No	Comments:

11	Facilities and infrastructure of Participating Sites ☐ Appropriate ☐ Inappropriate	Comments:
12	Community Consultation: ☐ Yes ☐ No ☐ NA	Comments:
13	Benefit to Local Communities ☐ Yes ☐ No	Comments:
14	Contribution to development of local capacity for research and treatment ☐ Yes ☐ No	Comments:
15	Availability of similar Study / Results: ☐ Yes ☐ No	Comments:
16	Are blood/tissue samples sent abroad? ☐ Yes ☐ No	Comments:
17	Are procedures for obtaining Informed Consent appropriate? ☐ Yes ☐ No	Comments:
18	Contents of the Informed Consent Document: ☐ clear ☐ unclear	Comments:
19	Language of the Informed Consent Document: ☐ clear ☐ unclear	Comments:
20	Contact Persons for Participants ☐ Yes ☐ No	Comments:
21	Privacy & Confidentiality ☐ Yes ☐ No Assigning unique code number for the patients ☐ Yes ☐ No	Comments:
22	Inducement for Participation ☐ Unlikely ☐ Likely	Comments:
23	Provision for Compensation for Participation ☐ appropriate ☐ inappropriate	Comments:
28	Provision for Treatment for Study-Related Injuries ☐ appropriate ☐ inappropriate	Comments:
25	Provision for Compensation for Study Related Injuries ☐ appropriate ☐ inappropriate	Comments:

Reviewer's Signature with date: _____

Annexure 3: ***ANX-03/KIMS/SOP-8A/V3***

Decision Form

Date of IHEC meeting: _____

Protocol number: _____

IHEC 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 IHEC members ☐ Monitoring required Reason:_____ **Disapproved,** **Reasons:**

No.	Names of Members present	AP	AM	RS	DA	Remarks if any

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 Chairperson **Date:** _____

Annexure 4: ***ANX-04/KIMS/SOP-8A/V3***

Format of Interventional Research Study Approval letter

Date XX/XX/XXXX
To,
Dr. xxxxxxxxxxx,
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 (IHEC) was held on xxxxx at xxxx, in the xxxxxxxxxxxxx with xxxxx as Chairperson.

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

Name of Members	Position on IHEC	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 IHEC 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 IHEC 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 XXXXXXXXXXXXXX as per the submitted protocol.

This approval is valid for **ONE YEAR** duration and the approval should be renewed before the date of expiry of the approval.

It is the policy of IHEC that, date of the recruitment of the first patient should be informed to the IHEC and it be informed about any onsite serious adverse event or the unexpected adverse event report within 28 hours as per the formats specified in SOP 09/V2 to the IHEC or by email if there is a holiday to the IHEC member secretariat. The report of SAE or death after due analysis shall be forwarded by the Investigator to chairman of the IHEC 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 to the subject the sponsor (whether a pharmaceutical or company), who 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 IHEC of an appropriate amendment. The IHEC expects that the investigator should promptly report to IHEC 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 IHEC for review.

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

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

Sincerely yours

Member Secretary
IHEC
(Signed and dated by the IHEC Chairperson or Member Secretary)

Annexure 5: ANX-05/KIMS/SOP-8A/V3
Format of Observational Research Study Approval letter

Date XX/XX/XXXX
To,
Dr. xxxxxxxxxxx,
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 (IHEC) was held on xxxxx at xxxx, in the xxxxxxxxxxxxx with xxxxx as Chairperson.
xxxx members attended the meeting held on xxxx. The list of members who attended the meeting is as follows.

Name of Members	Position on IHEC	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 IHEC has reviewed and approved the following documents submitted for the above – mentioned clinical study.

1. Xxx
2. Xxx
3. xxx

The IHEC 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 one year duration and the approval should be renewed before the expiry of the date.

Date of the recruitment of the first patient should be informed to the IHEC. No deviations from, or changes of the protocol and Informed Consent Document should be initiated without prior written approval by the IHEC of an appropriate amendment. The IHEC expects that the investigator should promptly report to the IHEC 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 IHEC for review.

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

Sincerely yours

Member Secretary
IHEC
(Signed and dated by the IHEC Chairperson or Member Secretary)
Date of approval of the study: XX/XX/20XX

Annexure 6: ANX-06/KIMS/SOP-8A/V3

Guidelines for reviewing a study protocol

Reviewers should make use of the following points as sited below:

1. How will the knowledge, result or outcome of the study contribute to human well-being?
2. Does the study design fulfill the following:
   - The endpoints are appropriately selected.
   - The participating duration of a study participant is adequate
   - 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
   - Deception of the participant is avoided
   - The study participants are adequately assessed and provided follow-up care, if needed
2. 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?
   - will there be secondary participants?.
3. Do the inclusion and exclusion criteria
   - Selectively include participants most likely to serve the objective of the study?
   - Properly exclude participants who can predictably confound the results?
   - Properly exclude participants
4. Does the study design have adequate built-in safeguards for risks?
   - Appropriate screening of potential participants?
   - Use of dose wise escalation.
   - Does the frequency of visits and collection of biological sampling reasonably monitor the expected outcome.
   - Are there discontinuation / withdrawal criteria for participants with worsening condition?
   - Is there precaution for withdrawal of medication or placebo?
   - 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?

6. Do the study and the informed consent process include issues of special concern, such as:
   - Waiver of consent?
   - Delayed consent (e.g., emergency treatment, etc.)?
   - 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.
- How, when and where and what regarding the participation of the study participant should be clearly given
- 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 without coercion, pressure or other undue influences.

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) Does the treatment act on the basic mechanism of the disease (vs. symptoms)?
4) 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.

5). Are the side effects of the standard treatment severe?

6). Does standard treatment have many uncomfortable side effects?

7). Does standard treatment have contraindications that prevent some research participants from being treated?

8. 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 or lead to threatening, permanent irreversible disease progression?

   If yes, placebo is not acceptable.

2) Can the use of placebo instead of treatment lead to an acute emergency/distressing symptoms?

3) Is the risk of using placebo instead of treatment the persistence of distressing symptoms/severe physical discomfort or pain?

   If answer is "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 there clearly defined stopping rules to withdraw the research participants in case he/she does not improve?

   ☐ *Yes, consider placebo*

   ☐ *No, placebo not recommended.*

4) 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.*

5) 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.

☐ 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 that the prospective participants should have to determine their eligibility and interest, such as:
  - The name and address of the researcher or details of the research facility.
  - Details of the research study
  - In summary form, the criteria that will be used to determine eligibility for the study.
  - The time or other commitment required of the participants.
  - The location of the research and the person to contact for further information with name, phone number and email address.
- The IHEC 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.
  - Do not emphasize the payment or the amount to be paid
  - Do not promise "free treatment" when the intent is only to say participants will not be charged for taking part in the investigation.

Checklist for reviewing CTA

Sl.No.	Item	Remarks
1	Statement of work Yes ☐ No ☐ NA ☐	
2	Obligations and Responsibilities of the Principal Investigator Yes ☐ No ☐ NA ☐	
3	Obligation and Responsibilities of the Institute Yes ☐ No ☐ NA ☐	
4	Obligation and Responsibilities of the Sponsor Yes ☐ No ☐ NA ☐	
5	Financial compensation for trial related injury such as injury or death as per the notification of the Drug Controller General of India (DCGI) & Government of India Yes ☐ No ☐ NA ☐	
6	Undertaking and Representation of Principal Investigator Yes ☐ No ☐ NA ☐	
7	Undertaking and Representation of Institute Yes ☐ No ☐ NA ☐	
8	Undertaking and Representation of Sponsor Yes ☐ No ☐ NA ☐	
9	Administration Yes ☐ No ☐ NA ☐	
10	Trial Drug; Materials Transfer; Records Retention; Inspection Ye ☐ No ☐ NA ☐	
11	Representation and Warranties Yes ☐ No ☐ NA ☐	
12	Confidentiality Yes ☐ No ☐ NA ☐	
13	Return of Confidential Information Yes ☐ No ☐ NA ☐	
14	Trial Results and Inventions Yes ☐ No ☐ NA ☐	
15	Payment Yes ☐ No ☐ NA ☐	
16	Screen Failures/ Drop-outs Yes ☐ No ☐ NA ☐	
17	Set-Up Fees Yes ☐ No ☐ NA ☐	
18	Hospitalization costs Yes ☐ No ☐ NA ☐	

19	Institutional Ethics Committee Yes☐ No☐ NA☐	
20	Payments by Sponsor to Institute Yes ☐ No☐ NA☐	
21	Tax deduction Yes ☐ No☐ NA☐	
22	Use of other parties' names Yes ☐ No☐ NA☐	
23	No joint venture etc Yes☐ No☐ NA☐	
28	Insurance and Indemnification Yes☐ No☐ NA☐	
25	monitoring; audit; regulatory inspections Yes☐ No☐ NA☐	
28	Term; Waiver; Severability (The trial on its time extended) Yes☐ No ☐ NA☐	
28	Recordkeeping Yes ☐ No☐ NA☐	
28	Effect of termination Yes ☐ No ☐ NA☐	
29	Governing Law Yes☐ No ☐ NA☐	
30	Jurisdiction Yes☐ No ☐ NA☐	
31	Arbitration Yes☐ No ☐ NA☐	
32	Amendment Yes☐ No ☐ NA☐	
33	Miscellaneous Yes☐ No ☐ NA☐	
	General Opinion of the expert:	

Checklist for reviewing Informed consent

Sl.No.	Item	Remarks
	ESSENTIAL ELEMENTS	
1	Statement that the study involves research and explanation of the purpose of the research. Yes☐ No☐	
2	Expected duration of the participation of subject Yes☐ No☐	
3	Description of the procedures to be followed, including all invasive procedures Yes☐ No ☐	
4	Description of any reasonably foreseeable risks or discomforts to the Subject Yes☐ No ☐	
5	Description of any benefits to the Subject or others reasonably expected from research. If no benefit is expected Subject should be made aware of this. Yes ☐ No ☐	
6	Disclosure of specific appropriate alternative procedures or therapies available to the Subject. Yes ☐ No ☐	
7	Statement describing the extent to which confidentiality of records identifying the Subject will be maintained and who will have access to Subject's medical records. Yes ☐ No ☐	
8	Trial treatment schedule and the probability for random assignment to each treatment (for randomized trials) Yes ☐ No☐	
9	Statement describing the financial compensation and the medical management Yes ☐ No ☐	
10	An explanation about whom to contact for trial related queries, rights of Subjects and in the event of any injury Yes ☐ No ☐	
11	The anticipated prorated payment, if any, to the subject for participating in the trial. Yes ☐ No☐	
12	Statement that participation is voluntary, that the subject can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the subject is otherwise entitled. Yes ☐ No ☐	

13	Statement that there is a possibility of failure of investigational product to provide intended therapeutic effect. Yes ☐ No ☐	
14	Statement that in the case of placebo controlled trial, the placebo administered to the subjects shall not have any therapeutic effect. Yes ☐ No ☐	
15	Any other pertinent information. Ye☐ No☐	
	ADDITIONAL ELEMENTS, WHICH MAY BE REQUIRED:	
1	Statement of foreseeable circumstances under which the participation of the subject may be terminated by the Investigator without his or her consent. Yes ☐ No☐ NA ☐	
2	Additional costs to the subject that may result from participation in the study. Yes☐ No ☐ NA ☐	
3	Statement that the Subject or Subject's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect the Subject's willingness to continue participation will be provided. Yes☐ No ☐ NA ☐	
4	A statement that the particular treatment or procedure may involve risks to the Subject (or to the embryo or foetus, if the Subject is or may become pregnant), which are currently unforeseeable. Yes ☐ No ☐ NA ☐	
5	Approximate number of Subjects enrolled in the study. Yes ☐ No ☐ NA ☐	
	Any other comment Reviewed by:	

Annexure 8: ANX-09/KIMS/SOP-8A/V3

Check list for risk and benefit assessment of protocols*

Sl.No.	Question	Yes	No	Remarks
	Risks			
1	Is the target group or population's participation justified?			
2	Is the target group or population a vulnerable population and if so, is it absolute necessary for them to participate to answer the research question? Are adequate protective measures being taken to ensure risks are minimized?			
3	If the research involves children, is their participation essential to answer the research question? Has the research previously been undertaken in adults and do the results of the adult research indicate that children will benefit from the research, or will it at least not be harmful to the child participants? Will the parent be present during the research intervention to support the child emotionally? Will it be possible for the parent to terminate the child's participation at any time during the research?			
4	Does the research cause physical (bodily harm or simple inconvenience), psychological (emotional suffering or any other related problems), social (employment or social discrimination) or economic risks (financial costs) to the patients			
5	Have the investigators taken into account the participant's previous experience of illness and medical interventions?			
6	What method did the investigator use to determine the number of participants to be enrolled for the study, and is the number justified (keeping in mind that the sample size should involve the critical number of participants necessary to obtain statistically significant and valid results)?			
7	Are the proposed interventions the least invasive (both physically and psychologically) that can be used to obtain the information required for the study?			
8	Have the investigators described in detail how the assent/consent should be obtained?			
	Benefits			
1	Does the research provide physical (improvement of disease), psychological (comfort from suffering) and economic (financial support) benefit to the patients.			
2	Benefits to society (generalizable knowledge, effective interventions in the future, and change in practice standards decreasing morbidity and mortality)			
	How do you categorize the risk (Refer the category given below: Any comments	☐ **Less than minimal risk:** ☐ **Low risk** ☐ **High risk**		
	How do you rate the benefit of the research Beneficial to individual Beneficial to society Any comments	**Yes** ☐ **No** ☐ **Yes** ☐ **No** ☐		

** Chi PC, Horn L, Kruger M. Risk-benefit Assessment. In 2014. p. 63–70.*

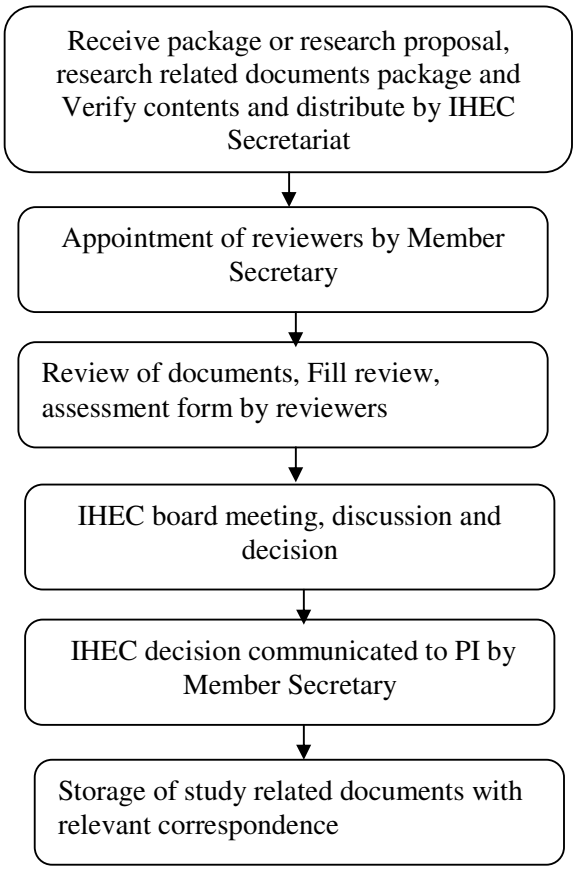
- *(www.icmr.nic.in Ethical Guidelines for Biomedical Research on Human Participants, Indian Council of Medical Research, October 2017)*

a. Less than minimal risk: Probability of harm or discomfort anticipated in the research is nil or not expected. For example, research on anonymous or non-identified data/samples, data available in the public domain, meta-analysis, etc.

b. Minor increase over minimal risk or Low risk: Increment in probability of harm or discomfort is only a little more than the minimal risk threshold. This may present in situations such as routine research on children and adolescents; research on persons incapable of giving consent; delaying or withholding a proven intervention or standard of care in a control or placebo group during randomized trials; use of minimally invasive procedures that might cause no more than brief pain or tenderness, small bruises or scars, or very slight, temporary distress, such as drawing a small sample of blood for testing; trying a new diagnostic technique in pregnant and breastfeeding women, etc. Such research should have a social value. Use of personal identifiable data in research also imposes indirect risks. Social risks, psychological harm and discomfort may also fall in this category etc.

c. More than minimal risk or High risk: Probability of harm or discomfort anticipated in the research is not greater than that ordinarily encountered in routine daily life activities of an average healthy individual or general population or during the performance of routine tests where occurrence of serious harm or an adverse event (AE) is unlikely.

7. Flow Chart


Receive package or research proposal, research related documents package and Verify contents and distribute by IHEC Secretariat
Appointment of reviewers by Member Secretary
Review of documents, Fill review, assessment form by reviewers
IHEC board meeting, discussion and decision
IHEC decision communicated to PI by Member Secretary
Storage of study related documents with relevant correspondence