7A1. **Purpose**

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

7A2. Scope

This SOP applies to the initial review and assessment of all research study protocols submitted for review and approval from the IEC. All research studies presenting with more than minimal risk and which do not qualify for exemption (See SOP 7C/V1) or expedited review (See SOP 7B/V1), are covered in this SOP.

7A3. Responsibility

7A.3.1. The Member Secretary is responsible, after categorisation of the studies (as per SOP 07/V1), to forward the studies to the Secretariat.

7A.3.2. The IEC Secretariat is responsible for creation of a study specific file, distribution of the packages along with study assessment forms to the IEC members for review (If the study is categorised for Full Board review), and communication of the review results to the investigators.

7A.3.3. IEC members (including Member Secretary) will be responsible for reviewing the research proposals and related documents within the given time frames.

7A.3.4. It is the responsibility of reviewer to fill the Assessment form along with comments and recommendation they have after reviewing each study protocol.

7A.3.5. The IEC members are responsible for attending and participating actively in the discussion at the full Board Meeting

7A.3.6. The Member Secretary is responsible for setting up the Full Board Meeting (SOP 07A/V1)

7A.3.7. The IEC Secretariat is responsible for recording and filing the decision, relevant points and deliberation about a specific protocol, including the reasons for that decision.

7A.3.8. The Chairperson is responsible to sign and date the decision in the IEC Decision Form *AX 03/SOP 7A/V1*.

7A4. Detailed instructions

7A.4.1. *Appointment of primary reviewers*

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

7A.4.2. *Distribute the protocol package*

a. The Secretariat will fill in the required details in the cover letter to the IEC Members requesting initial review (*AX 01/SOP 7A/V1*) and in the study assessment form *AX 02/SOP 7A/V1*.

b. The Secretariat will send a packet *(hard or soft copy)* to the IEC members.

   i. Letter to IEC Members requesting Initial Review
   ii. Study assessment form *AX 01/SOP 7A/V1*
   iii. Study Submission Application Form *AX 01/SOP 06/V1*
   iv. Protocol and related documents
   v. Study assessment form *AX 02/SOP 7A/V1* in case it is to the Primary reviewer.

7A.4.3. ***Receive the distributed protocol package***

a. The IEC members will receive the protocol package with the Study Application Form AX 01/SOP 06*/V1*, in a CD or pen-drive or as hard copy (if desired so).

b. Designated primary reviewers will also receive the Study Assessment Form for Initial Review AX 02/SOP 7A*/V1*

7A4.4. Verify the contents of the package

a. The IEC member will verify all the contents.

b. The IEC member will check the meeting date to see if it is convenient for most of the members to attend the meeting.

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

7A4.5 Review by the IEC members

***7A4.5.1*. Review of the protocol**

a. The proposal will be reviewed by each member as per guidelines to review a research proposal described in *AX 05/SOP 7A/V1*.

b. The IEC member will consider the following criteria when performing the review of the study protocol and the study related documents:

i. Scientific design and conduct of the study

ii. Risks and potential benefits

iii. Selection of study population and recruitment of research participants

iv. Inducements, financial benefits and financial costs

v. Protection of research participants' privacy and confidentiality

vi. Procedures for voluntary, informed consent

vii. Risk to participants

viii. Needs of dependent persons

ix. Community considerations

x. Qualifications of Investigators and assess adequacy of study sites
xi. Disclosure or declaration of potential conflicts of interest
xii. Ensuring that photographs or other information that may reveal the individual's identity are not published. A specific re-consent would be required for publication, if this was not previously obtained.
xiii. Permission for access to participants from other institutions or bodies

- The IEC member will consider the following criteria when performing the review of the Informed Consent Document (as per *AX 05/SOP 7A/V1*)
    - 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 the research project, participants' rights and 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 and compensation for study related injuries as per applicable regulations
    - Use of biological materials

- Check for provision for signatures with dates of participant, person conducting informed consent process (investigator/investigator designee and witness (if applicable)
- Provision for audio-visual recording of consent process in case of regulatory clinical trials

7A4.6 Use of study assessment form for reviewers

- The assessment form is designed to standardise the review process.
- All reviewers will fill out the form (AX 01/SOP 7A/V1 - letter to IEC 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/*V1*) 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 proposals to the Secretariat 7 days prior to the meeting.

7A4.7 Gather the assessment reports

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

4.8 IEC meeting

- At the commencement of the meeting itself members having conflict of interest, if any, on the proposals coming up for discussion shall disclose the same and be absent at the time when the particular proposal is taken up for consideration. Such absentees shall not be considered for the required quorum for the particular proposal. The minutes of the meeting shall also include details of such abstention.
- During the discussion at the meeting, the primary reviewer shall brief the members about summary of the study proposal and read out the comments and evaluation provided on the assessment form.
- The comments of independent consultant (if applicable) will be discussed by the member secretary.
- The other IEC 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 she/he has submitted for review to the IEC.
- The IEC 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/ Approved with recommendations/Revision with minor amendments/Revision with major amendments/ Disapproved either by broad consensus or by voting (majority considered as 50%+1). Decision in the meeting shall be made by consensus or by majority votes and will be recorded in the IEC Decision Form AX 03/SOP 7A/*V1* by the Member Secretary.
    - The following will not be eligible to participate in decision making or vote -
        - Absentee members who have declared conflict of interest
        - 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.

- In the case of decision to raise any query as a prelude to further consideration of the proposal, the Committee will specify whether the query responses and (if applicable) revised proposal will go only to the Chairman, Member Secretary, a specified subcommittee, to primary reviewers or to Full Committee before final approval. In case the sanction is granted taking into account the response by the Chairman or Secretary the fact will be reported to the IEC at the next meeting.
- The response and changes carried out may be considered for discussion at a future IEC meeting.
- If the IEC decision is 'Disapproved' or calling for further details, clarifications or documents, the decision shall be communicated by the Secretary to the Principal Investigator through appropriate letter within 7 days.
- The Secretariat will obtain the signature of all the members and of the Chairperson of the IEC on the IEC Decision Form AX 03/SOP 7A/V1.
- If the study is approved, the Committee may, in appropriate cases, recommend monitoring of a study depending on the degree of risk involved.
- The Secretary shall prepare the minutes of the meetings of the IEC with all relevant details including the list of participating members, and get it approved by the Chairman.
- The Secretary shall implement the decisions taken by the IEC and maintain all required registers and records.

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

- When the study is approved by the IEC, the Secretariat will prepare an approval letter *AX 04/SOP 7A/V1* in the prescribed format which is to be sent to the Principal Investigator within 14 days of the meeting.
- 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 are aggrieved by this decision, you may address the Chairman pointing out specific reasons if any, for concluding that the decision was erroneous or that it requires re-review. This will be done within four (4) weeks of the receipt of the committee's decision. "
- If the Committee has directed modifications to the scheme of research or sought for further documents, the Secretariat will send a written request to the investigator asking for the same. In such cases the Principal Investigator shall provide such additional details within six weeks.
-

4.10 Storage of Documents

1.1. Records can be maintained in hard copies as well as soft copies.

1.2. All records must be archived for a period of at least 3 years after the completion/ termination of the study.

1.3. Documents related to regulatory clinical trials must be archived for 5 years after the completion/termination of the study or as per regulations.

1.4. Records may be archived for a longer period, if required by the sponsors/regulatory bodies or the subject matter is involved in litigation.

7A.5 annexures

Annexure 1: AX 01/SOP 7A/VI-letter to IEC members requesting initial review with study assessment form

Annexure 2: AX 02/SOP 7A/VI-study assessment form to be used by the primary reviewer

Annexure 3:AX 03/SOP 7A/VI-decision form

Annexure 4:AXO4/SOP 7A/VI-format of full/expedicted committee approval letter

Annexure5:AX05/SOP 7A/V1-format of observational research study approval letter

Annexure 6: AX O6/SOP 7A/VI:guide lines for reviewing a study protocol

Annexure 1: ***AX 01/SOP 7A/V1***

Letter to IEC Members requesting Initial Review with study assessment form

Dear member,

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

You are requested to review the proposals in the package especially the ones marked to you as primary reviewer preferably within 5 working days of receiving the package. Please review the proposal and related documents as per the guidelines attached with Annexure 1 and provide your comments below and fill the study assessment form (for primary reviewers only) provided with the package (*AX 02/SOP 7A/V1*). Kindly confirm your availability for the meeting.

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

Protocol Number : (as per IEC records)	Date of receipt at IEC 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 IEC member reviewing the study:		Date:

Annexure 2: ***AX 02/SOP 7A/V1***

Study Assessment Form to be used by the Primary Reviewer

Date of IEC Meeting									
	D	D	M	M	M	Y	Y	Y	Y

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 Human Participants □ Yes □ No	Comments:
3	Methodology: □ clear □ unclear	What should be improved?
4a	Background Information and Data □ sufficient □ insufficient	Comments:
4b	Risks and Benefits Assessment □acceptable □ unacceptable	Comments:
4c	Inclusion Criteria □ appropriate □ inappropriate	Comments:
4d	Exclusion Criteria	Comments:

	□ appropriate □ inappropriate	
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:	Comments:

	□ Yes □ No □ NA	
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	Comments:
22	Inducement for Participation □ Unlikely □ Likely	Comments:

23	Provision for Compensation for Participation □ appropriate □ inappropriate	Comments:
24	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: ***AX 03/SOP 7A/V1***

Decision Form

Date of IEC meeting: _____

Protocol number: _____

IEC Protocol No. and Title:	
Principal Investigator:	Department:
Final Decision at the meeting:	Approved (AP) Approved with modifications (AM) Revision with minor/major amendments (RS) Disapproved with reasons (DA) Review by any 2 / more IEC members Monitoring required Reason:_____
	Comments: _____ _____

No.	Names of Members present	AP	AM	RS	DA	Signature

Note: *AP: Approved; AM: Approved with modification [(either primary reviewer/full committee). If reviewed by full committee again one more 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: ***AX 04/SOP 7A/V1***

Format of Full Committee/Expedited Committee Approval letter

Date.....

To,

Dr/Mr./Mrs/Smt/. .....

Dept. of .....

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

Sub: Letter no.

Dear Dr. XXXXx,

The meeting of the Institutional Ethics Committee (IEC) was held on..... at .....in the..... with ..... as Chairperson.

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

Name of Members	Position on IEC	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 IEC 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 IEC hereby approves the proposal entitled, ".....".

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

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

It is the policy of IEC 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/V1 to the IEC 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 IEC and the head of the institution where the trial is being conducted within 14 calendar days of SAE or death.

In case of occurrence of death or injury during the period of research, 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 participant and also provide financial compensation for the clinical trial related injury or death.

No deviations from or changes in the proposal and Informed Consent Document should be initiated without prior written approval by IEC of an appropriate amendment. The IEC expects that the investigator should promptly report to IEC any such events 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 .....

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

Any publications during the approved period should be submitted to the IEC.

The IEC functions in compliance with applicable guidelines and regulatory requirements.

Sincerely yours,

Chairperson,

IEC

(Signed and dated by the IEC Chairperson)

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

Annexure 5: AX 05/SOP 7A/V1

Format of Observational Research Study Approval letter

Date ...../..../....

To,

Dr. .....,

Dept. of .....

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

Sub: Letter no.

Dear Dr. .....,

The meeting of the Institutional Ethics Committee (IEC) was held on .....at ....., in the..... with ..... as Chairperson.

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

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

1. Xxx
2. Xxx

3. xxx

The IEC hereby approves the proposal entitled, "....".

It is understood that the study will be conducted under your direction, in a total of ..... number of research participants, at Dept. of ....., _____ 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 IEC of an appropriate amendment. The IEC expects that the investigator should promptly report to the IEC 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 IEC for review.

The IEC functions in compliance with applicable guidelines and regulatory requirements.

Sincerely yours

Member Secretary/ Chairperson,

IEC

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

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

Annexure 6: AX 06/SOP 7A/V1

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.
   - Will the study design 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 or could be replaced by those, which have lesser risk without compromising the scientific logic..
- Deception of Research participants is avoided.
- Instruction and support systems such as counselling 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.

- 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.
- 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?
- Does the study design have adequate built-in safeguards for risks?
  - Appropriate screening of potential participants?
  - 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.

- 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?

- 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 about the research and consent process is understood to the satisfaction of 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 verified on a continuing basis especially when changes in design of the research or new information are available.
- If participant is illiterate than her/his legally authorized/acceptable representative should sign consent on her/his behalf in the presence of impartial witness.
- Permission for access to participants from other institutions or bodies

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 at minimum necessary level 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.
- If it is used for a self limited disease likely to be of a short duration

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 IEC reviews advertising to ensure that advertisements

  DO NOT:

  - State or imply a certainty of favourable outcome or other benefits beyond what is outlined in the consent document and the protocol.
  - 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/Chairperson
4	Initial review of documents, Fill review assessment form	IEC members
5	IEC board meeting, discussion and decision	IEC members, Member Secretary, Chairperson
6	IEC decision communicated to PI	Secretariat
7	Storage of study related documents with relevant correspondence	Secretariat