Title: Initial Full Review of Research Study Protocols

SOP Code: SOP7A/v2:

Effective date: 01/08/2016

Prepared by:

Dr. Uma Kulkarni Jt Secretary, YUEC	Signature with date: 30/07/2016

Reviewed by

Dr. Vina Vaswani Member-Secretary, YUEC	Signature with date: 30/7/2016

Approved by

Dr. Sayeegeetha Hegde Chairperson, YUEC	Signature with date: 3/8/16

Notified by:

Registrar Yenepoya University vide notification no. YUReg/ACA/YUEC/FERCAP/01/2016	Signature with date: 01/8/16 Dr. G. Shreekumar Menon Registrar Yenepoya University Mangaluru - 675 018

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Notified by:

Registrar Yenepoya University vide notification no. YU/REG/ACA/YEC-1/FERCAP/01/2016 dated 01/08/2016	Signature with date:

Table of Contents:

1. Purpose

The purpose of this SOP is to describe in detail the method of 'full review' of a research protocol submitted to the YEC-1 for ethical clearance.

2. Scope:

This SOP applies to the initial review of all research protocols submitted to the YEC-1 for ethical clearance categorized under "full review" as per the ICMR guidelines for research on human participants, fulfilling the criteria for "full review" as per SOP07/v2, and/or as decided by the Member-Secretary.

3. Responsibility:

3.1 Member-Secretary/Jt Secretary:

3.1.1 Member-Secretary/Jt Secretary will do an initial screening of the protocol and categorize the protocols into 'full review' as per the ICMR guidelines for research on human participants keeping the Chairperson informed as per SOP07/v2

3.1.2 Member-Secretary/Jt Secretary will assign two reviewers for each study protocol, based on matching expertise of the reviewers to the broad research area of the protocol. If needed, one or two additional reviewers may be assigned on the discretion of the Member-Secretary (including independent consultants).

3.1.3 If any of the YEC-1 members assigned to review the protocol declares a conflict of interest or declares inability to complete the assessment of the protocol within 7 calendar days, the Member-Secretary/Jt Secretary will assign an alternative member to review the protocol.

3.1.4 If the Member-Secretary/Jt Secretary feels the additional need to refer the protocol to an independent consultant, expert in the area of the protocol research, he/she can do so with approval of the Chairperson. Alternately, a YEC-1 member who is assigned the protocol may recommend for an additional review by independent consultant, in which case the Member-Secretary/Jt Secretary in consultation with the Chairperson can do so, as per the SOP03/v2.

3.1.4 Member-Secretary/Jt Secretary will set up the agenda, date and venue of the YEC-1 meeting as per SOP08/v2.

3.2 YEC-1 Secretariat:

3.2.1 YEC-1 Secretariat will create a file for each research protocol as soon as the complete protocol submission is received and checked.

3.2.2 YEC-1 Secretariat will distribute the completed protocol submission to the reviewers assigned by the Member-Secretary/Jt Secretary via the email id of YEC-1 ethcom@yenepoya.edu.in or as a hard copy, as per the preference declared by the YEC-1 members.

3.2.3 YEC-1 Secretariat will distribute the review assessment form along with the protocol to each reviewer, as assigned by the Member-Secretary/Jt Secretary.

3.2.4 YEC-1 Secretariat will list the 'full review' protocols in the agenda for the next YEC-1 meeting, if the protocol is received 28 calendar days prior to the date of the meeting. If later, then in the agenda of the YEC-1 meeting after the next.

3.2.5 YEC-1 Secretariat will inform the Member-Secretary/Jt Secretary of any communication from the assigned reviewer regarding the completed assessment form, inability to complete the review process in 7 calendar days or issues of conflict of interest as communicated by the members.

3.2.6 If the reviewer does not return the assessment form within 7 calendar days, the YEC-1 Secretariat will send a reminder to the reviewer by mail/telephonic call.

3.2.7 YEC-1 Secretariat will record and file the assessment forms and the decisions of the reviewers in the protocol file.

3.2.8 YEC-1 Secretariat will communicate the observations of the reviewers after masking the name of the reviewer to the principal investigator thorough an email with a request to respond within 14 calendar days.

3.3 YEC-1 members:

3.3.1 The YEC-1 member(s) will declare any conflict of interest with the protocol received for initial review, within 2 calendar days after receiving the protocol for review.

3.3.2 If the YEC-1 member(s) is unable to do the initial review process, he/she will declare it within 2 calendar days of receiving the protocol for review.

3.3.3 The YEC-1 member(s) assigned to review a protocol will do the review as per the assessment form (Ann02/SOP7A/v2).

3.3.4 The YEC-1 member(s) will record their observations and comments in detail on the assessment forms

3.3.5 The YEC-1 member(s) after reviewing the protocol will enter their comments

3.3.6 The YEC-1 members after reviewing the protocol will sign and date the assessment form.

3.3.7 The YEC-1 members will return the completed assessment form as soft copy by email to ethcom@yenepoya.edu.in or as hard copy to the YEC-1 Secretariat, as the case may be.

3.3.8 The YEC-1 members will complete the review process within the time frame of 7 calendar days from receiving the protocol for review. This deadline is extendable by 7 calendar days, if on account of unforeseeable delay.

3.4 Independent Consultant:

3.4.1 An independent consultant if called upon to do 'full review', shall follow the same timelines as for YEC-1 reviewers, as per the SOP04/v2

4 Detailed instructions:

4.1 Procedure for appointment of lead discussants:

4.1.1 The Member-Secretary/Jt Secretary will assign two lead discussants for each protocol categorised as requiring 'full review'. These lead discussants will be based on the study topic, the expertise of the members in reviewing such studies and relation to the field of study.

4.1.2 If necessary, the Member-Secretary/Jt Secretary will assign one independent consultant, depending on the merit and complexity of each protocol. Or if a member so feels during the review process, he/she may suggest the same to the Member-Secretary.

4.1.3 The Member-Secretary/Jt Secretary will communicate the names of the lead discussants to the YEC-1 Secretariat within 4 calendar days of protocol submission.

4.2 Distribution of protocols for review:

4.2.1 The YEC-1 Secretariat will record the names of the discussants for each protocol in the assessment forms and also in the database.

4.2.2 The YEC-1 Secretariat will send the duly completed request letter to the discussant(s) with details of the protocol and the time frame during which the review has to be completed (Ann01/SOP7A/v2).

4.2.3 The YEC-1 Secretariat will send the complete submission to the discussants along with the assessment forms

4.2.4 If the discussants have opted for soft copies of the protocols, they will be emailed to them at their official email id from the official email id of YEC-1 ethcom@yenepoya.edu.in

4.2.5 If the discussants have opted for hard copies of the protocols, then they will be reviewed by the reviewers in the YEC-1 archive room or in the office of the reviewer, maintaining the strictest confidentiality.

4.2.6 The following documents will be sent to the discussants:

- The request letter for reviewing the protocol
- The protocol submission form and related documents
- The assessment form
- Form for declaring conflict of interest

4.3 Receiving the complete protocol submission for review

4.3.1 The discussants and the other members will receive the complete protocol submission and verify the contents

4.3.2 The discussant/member will notify the YEC-1 Secretariat, immediately, if any of the documents are found missing

4.3.3 The discussant/member will inform the YEC-1 Secretariat if he/she has a conflict of interest within 2 calendar days of receiving the protocol

4.3.4 The discussant will inform the YEC-1 Secretariat within 2 calendar days if he/she is unable to complete the assignment of reviewing the protocol within the given time frame.

4.4 Reviewing of the protocol:

4.4.1 The protocol will be reviewed as laid down in the ICMR guidelines.

4.4.2 All reviewers will consider the following criteria while reviewing the protocol and the submitted documents

- Scientific design and methodology with respect to ethical issues
- Potential risks to participants
- Potential benefits to participants
- Selection of participants and method of recruitment especially for studies involving vulnerable population
- Justification for involving the vulnerable participants
- Inducements, financial benefits and compensation
- Protection of privacy of the participants and their data
- Methods of ensuring confidentiality of the data especially in case of genetic studies
- Disposal/storage/reuse of samples
- Community considerations
- Qualification of the investigators and adequacy of site facilities
- Disclosure of conflicts of interest from members of the research study team

4.5 Reviewing of the informed consent form and participant information sheet:

The YEC-1 member(s) while performing the initial review will look at the informed consent forms (ICF) and the participant information sheets (PIS) (submitted as separate documents) for the following items within them:

4.5.1 Procedure of informed consent process (ICF, PIS)

4.5.2 Translation of the informed consent and participant information sheet in the local language (ICF, PIS)

4.5.3 Back translation to English (in case of regulatory clinical trials) (ICF, PIS).

4.5.4 Content should include details of methodology and the risks and benefits associated. The language used in the participant information sheet should be simple, without jargon and should be written as if addressing a student of standard eight (PIS).

4.5.5 Statement confirming voluntariness, or freedom from coercion on the participant (ICF, PIS).

4.5.6 Statement of choice of refusal or withdrawal from study without prejudice to healthcare rights (ICF, PIS)

4.5.7 Statement of comprehension of the information provided and ample opportunity for clarification of doubts from the Principal Investigator (ICF, PIS)

4.5.8 Contact person(s) from the study team and their phone numbers (ICF, PIS)

4.5.9 Statement assuring maintenance of participant privacy (ICF, PIS)

4.5.10 Statement assuring participant data confidentiality (ICF, PIS)

4.5.11 Compensation for participation, whether there is a chance of undue inducement (PIS)

4.5.12 Provision of medical and psychosocial support (PIS)

4.5.13 Medical management of study related injuries, if any (PIS)

4.5.14 Compensation of study related injuries, if any (PIS)

4.5.15 Use of biological material, its use, its storage and possibility of future use (PIS)

4.5.16 Appropriate and responsible disposal of tissues/samples used in the study (PIS)

4.5.17 Possibility of deriving sensitive information from the biological samples, if any and the possible harm (PIS)

4.5.18 Provision of signatures of participants, investigator or the person conducting the informed consent process, the independent witness with dates (ICF)

4.5.19 Provision for audio-visual recording of consent in case of clinical trials involving vulnerable populations (except HIV and leprosy – in which case audio consent maybe added if participant agrees) (ICF, PIS)

The non-medical person assigned as reviewer will specifically look at the informed consent form and participant information sheet.

4.6 Use of reviewer assessment forms:

4.6.1 The reviewer assessment form is designed to ensure a standard review process by each reviewer

4.6.2 The assessment form will help in ensuring that all the elements of research protocol are reviewed and documented

4.6.3 Each discussant will go through the protocol and make comments/suggestions and recommendations in the assessment form. The other members can raise their points in the meeting discussion.

4.6.4 The duly filled, signed and dated assessment forms filled by the lead discussants will be returned to the YEC-1 Secretariat along with the complete protocol submission

4.7 Compilation of the assessment reports:

4.7.1 The YEC-1 Secretariat will collect the assessment forms from each of the lead discussants/independent consultants (soft or hard copy forms) and file the copies in the respective file

4.7.2 The file along with the lead discussants' reports is used for deliberation during the YEC-1 meeting

4.8 **The YEC-1 meeting**:

4.8.1 The protocol listed under the 'full review' category in the agenda of the YEC-1 meeting will be taken up for discussion during the meeting.

4.8.2 The lead discussants will brief the members about the study, read out the summary of the study and read out the comments and recommendation from the assessment forms

4.8.3 The other YEC-1 members will deliberate on the comments and recommendation of the lead discussants and add their own reflections.

4.8.4 If necessary, a subject expert can be invited to the meeting, by the Member-Secretary/Jt Secretary in advance (SOP06/v2)

4.8.5 If necessary, a community representative can be invited to the meeting, by the Member-Secretary/Jt Secretary, in advance (SOP05/v2)

4.8.6 If necessary, clarifications may be sought by inviting the principal investigator of the protocol.

4.8.7 The Member-Secretary/Jt Secretary assisted by another YEC-1 member or the YEC-1 Secretariat will minute the proceedings of the discussions of each protocol.

4.9 The making of the final decision:

4.9.1 The final decision on the ethical approval of the protocol is recorded as

- Approved
- Approved with minor changes (resubmit for expedited)
- Resubmit (for full review)
- Disapproved

4.9.2 The final decision is made by voting by each YEC-1member present in the meeting, except the subject expert (independent consultant), community representative (if any) or members who have declared conflict of interest

4.9.3 The decision is made by the majority consensus.

4.9.4 In case of a tied vote among the members, the Chairperson has an additional vote to make the final decision.

4.9.5 If any member has a vote against the majority, his **dissent** is recorded in the minutes of the meeting.

4.9.6 If the decision is "**Approved with suggestions**', the committee will also decide about the following:

- The review process to be followed by YEC-1 for resubmission of protocols: full review or expedited
- Need for frequent or annual continuing review
- The principal investigator has to submit the modified protocol within 180 calendar days, failing which the protocol will be considered as cancelled.

4.9.7 If the protocol has been **'Approved'** during the YEC-1 meeting, the committee will decide about the following depending on the risk assessment and on the research record of the principal investigator and this will be communicated to the principal investigator in the approval letter:

- The duration of the validity of the ethics committee approval (this will be based on the risk-benefit analysis with higher risk studies getting proportionately shorter validity periods)
- Whether the protocol requires site monitoring (SOP16/v2)
- Need for frequent or annual continuing review (SOP10/v2)

4.9.8 If a protocol has been **'Disapproved'** during the YEC-1 meeting, the reasons for the same must be listed with justification and communicated as a letter of notification to the principal investigator.

4.10 The communication of the final decision:

4.10.1 The approval letter is sent to the principal investigator within 7 calendar days after the YEC-1 meeting

4.10.2 The approval letter will contain the following matter

- Study reference number
- Study title
- A list of the versions of the protocol documents approved
- Validity period of the approval
- List of participating members in the meeting
- Summary of the guidance, advice and decision that the YEC-1 members have reached in the meeting
- Site monitoring and its frequency
- Other expectations from the principal investigator, if any
- Need for submission of status report, closure report at the end of the period of validity
- Signature of the YEC-1 Member-Secretary/Jt Secretary with date
- While handing over the YEC-1 approval letter to the PI or another research team member, an acknowledgment signature will be taken by the Secretariat on a copy of the YEC-1 approval letter and archived with the remaining documents.

The YEC-1 Secretariat will verify the correctness of the wordings and spelling. The letter will be communicated to the principal investigator within 7 calendar days as a hard copy.

4.11 Storage of documents:

4.11.1 The YEC-1 Secretariat will maintain all documents related to the protocol review (assessment forms by both reviewers, statements of the subject expert, decision form, and the copy of the Approval letter/Query letter/Disapproval letter in the study file along with all the reviewed protocol.

4.11.2 The YEC-1 Secretariat will store the file on an appropriate shelf in the designated cabinet.

5 Reference to other SOPs

5.1 SOP 6/v2: Management of Research Study Protocol and Study Related documents submitted for Ethics Review

5.2 SOP 07/v2: Categorization of Submitted Protocols for Ethics Review

5.3 SOP 07B/v2: Expedited Review of Research Study Protocols

5.4 SOP 07C/v2: Exemption from Ethics Review of Research Study Protocols

5.5 SOP 08/v2: Agenda Preparation, Meeting Procedures and Recording of Minutes

5.6 SOP 09/v2: Review of Amended Protocol, Protocol- Documents and Resubmitted protocol

6 Annexures

Ann01/SOP7A/v2: Letter to the YEC-1 Members requesting initial review with study assessment form for full review

Ann02/SOP7A/v2: Study assessment form for primary reviewer

Ann03/SOP7A/v2: YEC-1 decision form

Ann04/SOP7A/v2: Format of study approval letter

Ann05/SOP7A/v2: Guidelines for reviewing a study protocol

Ann01/SOP7A/v2

Letter to YEC-1 Members requesting Initial Review with study assessment form

To

Name of the Reviewer:

Dear Sir/Madam,

You are requested to review and return the protocol and related documents as per the guidelines attached (refer Ann06/SOP7A/v2, and return the completed and signed assessment form (Ann02/SOP7A/v2), to the YEC-1 Secretariat, within 7 calendar days. This protocol is being kept for full review in the upcoming YEC-1 (details below) and as lead discussant you will be expected to make a brief presentation on this protocol before the members start the discussion.

Thank you,

Signature of the YEC-1 member reviewer (with date):

The next meeting of the YEC-1 will be held on

Date: Time: Venue:

Kindly confirm your availability for the YEC-1 meeting.

Attending Yes / No

Details of the protocols for initial full review

Protocol No.

Title of the study:

Principal investigator:

Department:

Date of receipt of protocol for review:

Last date for submission of review report:

If you have any conflict of interest in reviewing the protocol, kindly inform within 2 calendar days.

If you are unable to complete the review process due to other engagements, kindly inform within 2 calendar days.

Ann02/SOP7A/v2

Reviewer's Assessment Form	
Protocol Number:	
Date:	
Protocol Title:	
Principal Investigator:	
Department:	
Institution:	
Number of study sites:	
Number of participants in the site:	
Name of the reviewer	
Date assigned for review	

Declaration of conflict of interest by reviewer: Yes / No

If yes, please specify and return document package to YEC-1 Secretariat within 2 calendar days of receipt. Please maintain confidentiality.

Mark and comment on the following items as applicable

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?
4	**Background Information and Data** ☐ Sufficient ☐ Insufficient	Comments:

1.	**Risks and Benefits Assessment** □Acceptable □ Unacceptable	Comments:
2.	**Inclusion Criteria** □ Appropriate □ Inappropriate	Comments:
3.	**Exclusion Criteria** □ Appropriate □ Inappropriate	Comments:
4.	**Discontinuation and Withdrawal Criteria** □ Appropriate □ Inappropriate	Comments:
5.	**Involvement of Vulnerable Participants:** □ Yes □ No	Comments:
6.	**Voluntary, non-coercive recruitment of participant**s □ Yes □ No	Comments:
7.	**Sufficient number of participants?** □ Yes □ No	Comments:
8.	**Control Arms (placebo, if any)** □ Yes □ No	Comments:
9.	**Are qualifications and experience of the 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 and participant information sheet:** □ Clear □ Unclear	Comments:
20.	**Contact persons for participants** □ Yes □ No	Comments:

21.	**Privacy & Confidentiality adequately maintained** □ **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:

Ann03/SOP7A/v2

Decision Form for Full Review

Date of YEC-1 meeting:

Protocol number:

Title:

Principal investigator: Department:

Final decision at the YEC-1 meeting:

□ Approved

□ Minor modifications (approval pending)

□ Major modifications requiring resubmission (with reasons):

□ Disapproved (with reasons):

Decision regarding further type of review:

□ Full review □ Expedited review

Continuing review:

Frequency: Annual / Other (specify)

Comments:

Names of members and decision

S.No.	Members present	Approved	Modification	Revision	Disapproved	Signature
1						
2						
3						
4						
5						
6						
7						

Comments:

No. of members voting 'FOR' the decision:

No. of members voting 'AGAINST' the decision:

No. of members abstaining from voting:

Signature of the Member-Secretary/Chairperson Date:

Ann04/SOP7A/v2

Approval letter format for regulated clinical trial (interventional)

Date:

To

Dr.

Department:

Ref: The study protocol no. YEC-1/ titled, " ".

Dear Dr./Mr./Ms.,

The ___ meeting of Yenepoya Ethics Committee - 1 (YEC-1) was held on at , in the . Dr./Mr./Ms. chaired the meeting.

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

1. Name of the member and role in YEC-1
2.
3.
4.
5.
6.
7.
8.
9.
10.

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 YEC-1 reviewed the above mentioned clinical study and approved the following documents submitted for this clinical study at the meeting.

1. Xxx (Title of the document and the version number)

2. Xxx

3. xxx

The YEC-1 hereby approves the proposal No. titled,

"_____".

It is understood that the study will be conducted under your direction, on a total of ____ research participants, at *(Insert name of centre here)* as per the submitted protocol.

This approval is valid for the entire duration of the study, or one calendar year from the date of this approval, whichever is earlier.

It is the policy of YEC-1 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 SOP12/v2 to the YEC-1 Secretariat or by email if there is holiday. The report of SAE or death after due analysis shall be forwarded by the Investigator to the YEC-1 Secretariat and the head of the institution where the trial is being conducted within ~~10~~ 14 calendar days of SAE or death.

In case of injury, the sponsor (whether a pharmaceutical company or an institution) or their representative, whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial shall make necessary arrangements or 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 YEC-1 of an appropriate amendment. YEC-1 expects that the investigator should promptly report to YEC-1 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 of approval expiry i.e. 11 months from the date of approval) on or before _____.

A copy of the final report should be submitted to the YEC-1 for review.

YEC-1 functions in accordance with ICH GCP, Schedule Y, ICMR guidelines and other applicable regulatory requirements and is ~~registered with the DCGI (CDSCO) vide their letter No. ECR/521/Inst/KA/2014 dated 04 September 2014,~~ re-registered with the DCGI (CDSCO) vide their letter no. ECR/892/Yenepoya/Inst/KA/2013/Re-Registration- 2017 dated 03 October 2017, valid for three years.

Member-Secretary/Jt Secretary/ Chairperson, YEC-1

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

Ann05/SOP7A/v2

Approval letter format for Observational Research Study

Date

To,

Dr./Mr./Ms.

Department:

Ref: The study protocol no. YEC-1/ entitled, "_____".

Dear Dr./Mr./Ms.

YEC-1 meeting number:

Date:

Venue:

Chairperson:

Number of members present:

Members present:

1.
2.
3.
4.
5.
6.
7.
8.
9.
10.

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 YEC-1 has reviewed and approved the following documents submitted for the above mentioned clinical study.

1. Xxx
2. Xxx
3. xxx

The YEC-1 hereby approves the proposal entitled,

"_____".

It is understood that the study will be conducted under your direction as per the submitted protocol.

Number of participants:

Site:

Period of validity of ethics approval:

No deviations from, or changes of the protocol and Informed Consent Document should be initiated without prior written approval by the YEC-1 of an appropriate amendment.

The YEC-1 expects that the investigator should promptly report to the YEC-1 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 _____.

A copy of the final report should be submitted to the YEC-1 for review.

The YEC-1 functions in accordance with ICH GCP, Schedule Y, ICMR guidelines and other applicable regulatory requirements and is ~~registered with the DCGI (CDSCO) vide their letter No. ECR/521/Inst/KA/2014 dated 04 September 2014,~~ re-registered with the DCGI (CDSCO) vide their letter no. ECR/892/Yenepoya/Inst/KA/2013/Re-Registration- 2017 dated 03 October 2017, valid for three years..

Member-Secretary/Jt Secretary/ Chairperson, YEC-1

(Signed and dated by the YEC-1 Chairperson or Member-Secretary/Jt Secretary)

Ann06/SOP7A/v2

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?**

a. Knowledge from the basic research may possibly benefit.
b. A new choice of method, drug or device that benefits the research participants during the study and others in the future.
c. Provide safety data or more competitive choices.

2. **Will the study design be able to give answers to the objectives? Whether the endpoints are appropriately selected?**

a. The participating duration of a study participant is adequate to allow sufficient change in the endpoints.
b. The control arm is appropriately selected for best comparison.
c. The placebo is justified.
d. The number of study participants in non-treatment (or placebo) arm is minimized.
e. Unbiased assignment (e.g. randomization, etc.) is in practice.
f. Inclusion and exclusion criteria are carefully selected to eliminate confounding factors as much as possible.
g. The sample group size appropriate with the given statistical assumptions.
h. Predictable risks are minimized.
i. The tests and procedures that are more than minimal risk are cautiously used.
j. Research participants deception is avoid.
k. Instruction and counselling for study participants are included (if needed) when deception is integral to the study design.
l. 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?**

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

4. Do the inclusion and exclusion criteria:

a. Selectively include participants most likely to serve the objective of the study?
b. Equitably include participants?
c. Properly exclude participants who can predictably confound the results?
d. 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?

a. Appropriate screening of potential participants?
b. Use of a stepwise dose escalation with analysis of the results before proceeding?
c. Does the frequency of visits and biological samplings reasonably monitor the expected effects?
d. Are there defined stopping (discontinuation) / withdrawal criteria for participants with worsening condition?
e. Is there minimized use of medication withdrawal and placebo whenever possible?
f. Will rescue medications and procedures be allowed when appropriate?
g. Is there a defined safety committee to perform interim assessments, when appropriate?
h. 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?

a. The animal study and in vitro testing results?
b. Previous clinical results, if done?
c. Whether the proposed study is appropriately built on the pre-clinical and/or early clinical results.
d. The selected dose based on adequate prior results?
e. 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:

a. Waiver or alteration of consent?
b. Delayed consent (e.g., emergency treatment, etc.)?
c. Deception?
d. 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:

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

1. Benefits of standard treatment

a. Is there a standard treatment?
b. Is the standard treatment widely accepted?
c. Has efficacy of the treatment been consistently proven?
d. Are all newly diagnosed patients with this condition put in standard treatment (versus observed or other)?
e. Does the treatment act on the basic mechanism of the disease (vs. symptoms)?
f. Are most (More than 85%) of the patients with this condition responsive to standard treatment alternatives (vs. resistant or refractory)?
g. 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.
h. Are the side effects of the standard treatment severe?
i. Does standard treatment have many uncomfortable side effects?
j. Does standard treatment have contraindications that prevent some research participants from being treated?
k. Is there substantial (less than 25%) placebo response in this disease or symptom?
l. **If the answer of (g) to (h) are "no", placebo is not recommended.** If any one or more answers are "yes", placebo may be possible.

2. Risks of placebo

a. Is the risk of using placebo instead of treatment life threatening?
b. If yes, placebo is not acceptable.
c. Is the use of placebo instead of treatment likely to lead to permanent damage?

If yes, placebo is not acceptable.

d. Is the risk of using placebo instead of treatment likely to cause irreversible disease progression?

If yes, placebo is not acceptable.

e. Can the use of placebo instead of treatment lead to an acute emergency?

f. Is the risk of using placebo instead of treatment the persistence of distressing symptoms?
g. Is the risk of using placebo instead of treatment severe physical discomfort or pain?
h. If answers of (d) to (f) are "yes", placebo is not acceptable unless risk management is adequate.

3. Risk management for placebo study:

a. Is there benefit in the overall management of the research participants?

If Yes, consider placebo

If No, placebo not recommended.

b. Will the discontinuation of previous treatment put the participant in danger of acute relapse when transferred to placebo?

If No, consider placebo

If Yes, placebo not recommended.

c. Are research participants at high risk for the use of placebo excluded?

Yes, consider placebo

No, placebo not recommended.

d. Is the duration of study the minimum necessary in relation to the action of the drug?

Yes, consider placebo

No, placebo not recommended.

e. 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.

f. 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.

g. 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.

h. 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.

i. 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.

j. If the risk of placebo is severely physical discomfort or pain, is there rescue medication?

Not applicable.

Yes, consider placebo.

No, placebo not recommended.

4. Risk disclosure in the consent form

a. Are the risks of getting placebo instead of active treatment fully disclosed?

Yes, consider placebo.

b. Are the risks of the test drug disclosed?

Yes, consider placebo.

c. Are the advantages of alternative treatments explained?

Yes, consider placebo.

5. Conclusions:

The use of placebo is ethically acceptable when

i. The research participants are not exposed to severe or permanent harm by the use of placebo.

ii. The research participants under placebo will benefit from the overall treatment of the disease.

iii. The risks of the use of placebo are minimized.

iv. The 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:

b. The name and address of the researcher or research facility.
c. The purpose of the research or the condition under study.
d. In summary form, the criteria that will be used to determine eligibility for the study.
e. A brief list of benefits to participants, if any.
f. The time or other commitment required of the participants.
g. 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:

a. State or imply a certainty of favourable outcome or other benefits beyond what is outlined in the consent document and the protocol.
b. Include exculpatory language.
c. Emphasize the payment or the amount to be paid, by such means as larger or bold type
d. 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	YEC-1 Secretariat
2	Verify contents and distribute	YEC-1 Secretariat
3	Identify lead discussants and/or independent consultant(s)	Member-Secretary/Chairperson
4	Initial review of documents Full review assessment form	YEC-1 members
5	YEC-1 board meeting, discussion and decision	YEC-1 members/Member-Secretary/Chairperson
6	YEC-1 decision communicated to PI	YEC-1 Secretariat
7	Storage of study related documents with relevant correspondence	YEC-1 Secretariat