Standard Operating Procedures

Institutional Human Ethics Committee

Version No. 1

Effective Date: March 01, 2020

Chennai Fertility Centre and Research Institute

New No.79 / Old No. 129, Nelson Manickam Road, Aminjikarai,

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Standard Operating Procedures

Version 1.0 (final)

Institutional Human Ethics Committee
Chennai Fertility Centre & Research Institute
Chennai, India.

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List of Abbreviations / Acronyms

Abbreviation/Acronym	Full Title/Description
ADR	Adverse Drug Reaction
AE	Adverse Event
BA	Bio-availability
BE	Bio-equivalence
CDSCO	Central Drugs Standard Control Organization
CFR	Code of Federal Regulations
CFC & RI	Chennai Fertility Centre and Research Institute
CIOMS	Council for International Organizations of Medical Sciences
CIMS	Chennai Institute of Medical Sciences
CoI	Conflict of Interest
Co-I	Co-Investigator
CRF	Case Record Form
CRO	Contract Research Organization
CTA	Clinical Trial Agreement
DBT	Department of Biotechnology
DCGI	Drug Controller General of India
DCR	Drugs and Cosmetic Rules, 1945
DGFT	Directorate General of Foreign Trade
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
ELSI	Ethical, Legal and Social Issues
FDA	Food and Drug Administration
FDC	Fixed Dose Combination
FERCAP	Forum for Ethical Review Committees in Asia and the Western Pacific Region
FWA	Federal wide Assurance
GCP	Good Clinical Practice
HMSC	Health Ministry's Screening Committee
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Committee on Harmonization
ICMJE	International Committee of Medical Journal Editors
ICMR	Indian Council of Medical Research
IMA	Indian Medical Association
IND	Investigational New Drug
IHEC	Institutional Human Ethics Committee
IRB	Institutional Review Board
IORG	IRB Organization
ISI	Indian Standards Institute

LAR	Legally Acceptable/ Authorized Representative
MoU	Memorandum of Understanding
MTA	Material Transfer Agreement
NCE	New Chemical Entity
NDA	New Drug Application
NIH	National Institutes of Health
NOC	No-objection Certificate
OHRP	Office for Human Research Protections
PI	Principal Investigator
RCT	Randomized Controlled Trial
SAE	Serious Adverse Event
SOPs	Standard Operating Procedures
SUSAR	Suspected Unexpected Serious Adverse Reaction
WHO	World Health Organization
WMA	World Medical Association

Approval of SOPs with signatures

The below mentioned SOPs are part of IHEC SOP Manual V 1.0

SOP 01-V 1.0
SOP 02-V 1.0
SOP 03-V 1.0
SOP 04-V 1.0
SOP 05-V 1.0
SOP 06-V 1.0
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SOP 34-V 1.0

Prepared by:

Name and Position in the IHEC	Signature with date
Dr. L. Krishnavignesh (Member-Secretary, IHEC)	01/03/2020

Reviewed and Approved by:

Name and Position in the IHEC	Signature with date
Dr. N. Pandiyan (Chairperson, IHEC)	01/03/2020

Accepted by:

Name and Position in the IHEC	Signature with date
Dr. VM. Thomas, Chairman & Institute Director	01/03/2020

List of Members of the IHEC

S.no.	Name of the Member of IHEC	Area of Expertise	Affiliated to CFC & RI or not	Sex
1	Dr. N. Pandiyan (Chairperson)	Reproductive Medicine, Clinician (Obstetrics &Gynaecology)	Non-Affiliated	M
2	Dr. L. Krishnavignesh (Member-Secretary, IHEC)	Embryologist	Affiliated	M
3	Dr. SmishaSridevBarathan (Clinician)	Basic medical ScientistReproductive Medicine, Clinician (Obstetrics &Gynaecology)	Affiliated	F
4	Dr. S. Swarnalakshmi(Social Scientist)	Ethicist / NGO representative	Non-Affiliated	F
5	Dr. C.B. Tharani(Basic Medical Scientist)	Pharmacologist	Non-Affiliated	F
6	Dr. R. Satishkumar (Basic medical scientist)	Plant Molecular Biology, Biotechnology	Non-Affiliated	M
7	Dr. ChitraRamanathan (Clinician)	Clinician (Obstetrics & High-risk pregnancies)	Affiliated	F
8	Dr. T. Puvithra(Clinician)	Reproductive Medicine, Clinician (Obstetrics &Gynaecology)	Non-Affiliated	F
11	Dr. N. Punithavathi (Clinician)	Clinician (Obstetrics &Gynaecology)	Affiliated	F
9	Dr. Malar K.T(Clinician)	Reproductive Medicine, Clinician (Obstetrics &Gynaecology)	Affiliated	F
10	O. Deepa (Scientific Member)	Embryologist	Affiliated	F
12	Mr. K.S. Karthik Raja	Legal expert	Non-Affiliated	M
13	Mr. S.Maruthavijayan	Legal expert	Non- affiliated	M
14	Mr. R. Prabakaran	Lay person	Non-affiliated	M

List of Independent Consultants

Name	Department
Dr. K. Hari Prasad	Anaesthesiology

1. Introduction:

The Chennai Fertility Centre and Research Institute (CFC & RI), is a tertiary fertilitycenter involved in the treatment, education and research in the field of reproductive medicine and it is recognized as one of the leading fertility center in Asia.

It is dedicated to helping childless couples by providing high quality diagnosis and treatments procedures to correct various infertility issues. Its academic, research and development wing focus on interdisciplinary and multi-disciplinary high-quality innovative programs in the field of reproductive medicine to help the society to have a better understanding on various fertility issues and treat them efficiently with an advanced procedure.

The Institutional Human Ethics Committee(IHEC) is established to ensure the safety, well-being and rights of human participants in research conducted by any of the institutions under the administrative authority of the Chairman, Managing director, Chennai Fertility Centre and Research Institute, Chennai, India.

2. Objective:

The objective of this Standard Operating Procedures of the Institutional Human Ethics Committee (IHEC) of Chennai Fertility Centre and Research Institute (CFC & RI) is to maintain effective functioning of the IHEC so that to ensure quality and consistent ethical review of all the submitted health and biomedical research proposals and ongoing approved research studies involving human participants in accordance with the ICMR ethical guidelines for biomedical research on human participants 2017 and New Drugs and Clinical Trial Rules 2019, Government of India.

3. Jurisdiction of the Institutional Human Ethics Committee, CFC & RI

The Institutional Human Ethics Committee (IHEC) of CFC & RIshall receive, review, approve (or otherwise) and monitor research proposals involving human study volunteers in the following Institutions

1. All branches of Chennai Fertility Centre and Research Institute,
2. Fertility Society of India(FSI),
3. Chennai Institute of Medical Sciences (CIMS)
4. Dr. Thomas Fertility Center, Puducherry.

This includes both intramural and extramural research by faculties and students. All studies including clinical trials proposed to be conducted in CFC & RI must obtain approval from the IHEC of CFC & RI. Approval given by ethics committee of another institution to carry out a study shall not be valid for carrying out the same study in CFC & RI.

4. Functions of Institutional Human Ethics Committee (IHEC)

IHEC should provide an independent, competent and timely review of the ethics of proposed studies within the ethical norms laid down by the latest revisions of the Ethical Guidelines for Biomedical Research on Human Subjects of the Indian Council for Medical Research (ICMR) and other relevant guidelines before the commencement of a study and should regularly monitor the ongoing studies. In addition, it will ensure that all research it approves will also confined to applicable central, state and local laws and regulations.

The IHEC take care of all the cardinal principles of research ethics viz. autonomy, beneficence, non-malfeasance and justice are taken care of in planning, conduct and reporting of the proposed research. The committee will also examine compliance with all regulatory requirements, applicable guidelines and laws. The

mandate of the IHECs will be to review all research projects involving human subjects to be conducted at the Institute.

5. Constitution of IHEC

The Institutional Human Ethics Committee will be multidisciplinary and multi-sectorial in composition. The committee is composed of a minimum of 7 and maximum of 15 members. It includes scientific and non-scientific, clinicians and non - clinicians, clinical pharmacologist, a social scientist, lawyer, expert in ethics, Scientific member, layperson needed to represent different point of view.

The committee should have adequate representation of age, gender and community to safeguard the interests and welfare of all sections of the community / society. Members are expected to be aware of local, social and cultural norms, as this is the most important social control mechanism.

5.1. Structure of IHEC

The composition should be as follows: -

1. Chairperson (non-affiliated)
2. Member-secretary (affiliated)
3. 1-2 clinicians
4. Basic medical scientist
5. Clinical Pharmacologist
6. One legal expert or retired judge or medico-legal expert
7. One social scientist / representative of non-governmental voluntary agency
8. One philosopher / ethicist / theologian
9. Scientific Member
10. Lay person from the community.

6. Authority under which IHEC is constituted:

The Chairman of Chennai Fertility Centre and Research Institute constitutes the IHEC and has the authority to dissolve the IHEC.

7. IHEC Membership

a. The duration of appointment will be initially for a period of 3 years.

b. The membership can be renewed for another term of 3 years. There will be no bar on the members serving for more than one term but it is desirable to have around one third of fresh members every three years.

c. At the end of 3 years, the committee is to be reconstituted, and one third of the members can be replaced by a defined procedure.

d. A member can be replaced in the event of death or long-term non-availability or for any action not commensurate with the responsibilities laid down in the guidelines deemed unfit for a member.

e. A member can tender resignation from the committee with proper reasonsto do so.

f. All members should maintain absolute confidentiality of all discussionsduring the meeting.

g. Conflict of interest should be declared by members of the IHEC.

h.If a regular member resigns, or ceases to be a member due to disqualification, or death, a new member will be appointed for the remaining term as per the Conditions of appointment.

7.1. Resignation / Replacement procedure

a. The members who have resigned may be replaced at the discretion of the appointing authority for the same. IHEC members (includingMember- Secretary) who decide to resign must inform the Chairman, CFC& RI and Chairperson,

IHEC in writing about their intention to resign by citing reasons for the same at least 30 calendar days prior to the next scheduled meeting.

b. In case of resignation of the Chairperson, he/she is required to inform the Chairman 30 calendar days prior to his/her resignation. If there is a situation which warrants an emergency resignation of a member wherehe/she could not give a 30-day notice, her/his resignation may beaccepted.

c. In case of resignation, Chairman, CFC & RI would appoint a newmember, falling in the same category of membership if it is a mandatedcategory as per New Drugs and Clinical Trial Rules 2019, Government of India. Chairman appoints Member-Secretary and Chairperson as per the procedure described in this SOP.

7.2. Termination / Disqualification procedure

A member may be relieved or terminated of his/her membership in case of:

a. Conduct unbecoming for a member of the Ethics Committee, inability to participate in the meetings on any grounds

b. If a regular member fails to attend more than 3 meetings of IHEC. The membership shall be reviewed by the IHEC and a letter of reminder will be sent to the concerned member. If deemed necessary, the IHEC may decide to terminate the membership and recommend to the Chairman, CFC & RI, by the Chairperson IHEC for necessary action

c. Relocate to another city

d. In any such situation/circumstances, Chairman, CFC & RI will serve a letter of termination to the member citing the reason.

e. Documentation of the termination will be recorded in the meeting minutes of the next duly constituted IHEC meeting and IHEC membership circular/ roster will be revised.

7.3. Members going on long leave

Long leave refers to duration of leave that is taken as three months (90 days) or above. If a situation occurs when a member is required to go on long leave for professional and personal reasons the following will befollowed.

a. If the period of leave is less than or equal to 6 months and the IHEC appointment term is valid for more than 6 months.

b. He/she can continue as the member of IHEC if he/she wants to do so. If not, the member should tend her/his resignation from IHEC prior to going on leave as per the clause described in 7.1. If the member intending togo on leave is an office bearer (see 8.1 below for definition of office bearers) the same rules will be implemented. In addition, any suitable,consenting member of the IHEC can hold the post of the office bearer untilshe/he returns.

c. If the member is going on leave for more than one year she/he should tend herresignation from the IHEC as per clause 7.1 even if the term of the member is valid. This is to ensure efficient and uninterrupted functioning of IHEC review mechanism. A suitable replacement of the member in the same/similar specialty will be inducted to IHEC. This will be applicable to all the office bearers of the IHEC too.

8. Conditions of Appointment

a. Name, age, sex, profession, and affiliation of IHEC members will be publicized through the CFC & RI website and notice boards (and that of the CFC & RI for whom CFC & RI reviews study protocols).

b. Members must accept the appointment in writing.

c. Submit a CV and training certificates in Ethics and / or GCP.

d. Disclose any Conflict of interest.

e. Members must apprise themselves of the relevant documents, codes, GCP,ICH guidelines and the ICMR code & IHEC, CFC & RI SOPs.

f. All Members (including Chairperson, Member secretary) are required to sign the confidentiality agreement and Conflict of Interest statement (Annexure 5, Annexure 6) at the start of their term. The confidentiality agreement protects the privacy and confidentiality of all parties whose information may be disclosed to the IHEC in the course of its work.

g. An investigator can be a member of the IHEC; however, the investigator as-member cannot participate in the review and approval process for any project in which he or she has presence as a PI, Co-PI or Co-I or potential conflict of interest.

8.1. Appointment Procedures

The IHEC will have the following office bearers who have the expertise and professional qualifications to review what comes in:

8.2. Chairperson

The Chairperson will be appointed by the Chairman, CFC & RI from amongst the members.

8.3. Criteria for selection of Chairperson

The Chairperson is selected based on their experience as members of ethics committee. The Chairperson should preferably be a medical professional. A person in order to be considered for the post of Chairperson should have the experience of serving in an ethics committee and should not be affiliated to CFC & RI Institutions.

8.4. Member-Secretary

He / She will be appointed by the Chairman, CFC & RI in consultation with the Chairperson, IHEC and will be affiliated to the CFC & RI.

8.4.1. Terms of Reference for Member-Secretary

Ensure that members and research investigators are functioning inconformity with the IHEC's SOP.

i. Liaisoning between the Chairperson, IHEC and Chairman, CFC & RI and updating them about the developments
ii. Liaisoning between the IHEC members and Chairman, CFC & RI.
iii. Communicating with Chairperson, members and Principal Investigators (PIs)
iv. Protection of safety, rights and confidentiality of the research participants.
v. Categorization of study proposals received
vi. Assigning categorized study proposals to primary reviewers
vii. Guiding the office staff in the day-to-day functioning of the IHEC Secretariat.
viii. Overseeing documentation and archiving of study documents (Preparation, maintenance and distribution of study files).
ix. Overseeing the maintenance of a database of all proposals received, reviewed and archived
x. Convening IHEC Expedited Committee Meeting as and when required (with the help of the IHEC Secretariat staff)
xi. Convening IHEC Full Board Review Meeting regularly (with the help of the IHEC Secretariat staff) \
xii. Preparation of agenda and minutes of the meetings (with the help of the IHEC Secretariat staff)
xiii. Communicating with IHEC members and PIs (with the help of IHEC Secretariat staff).
xiv. Monitor the review procedures
xv. Participate in the IHEC meeting regularly.
xvi. Maintain confidentiality of the documents and deliberations of the IHEC

meetings.

xvii. Declare conflict of interest, if any.

xviii. To provide information and documents related to training obtained in biomedical ethics and biomedical research to the IHEC Secretariat

xix. To be updated on relevant laws and regulations

xx. To participate in continuing education activities in biomedical ethics and biomedical research and encourage members to do so.

xxi. Arrangement of training for personnel and IHEC members

9. Members

All members shall be appointed by the Chairman, CFC&RI in consultation with the Chairperson and Member-Secretary of IHEC.

Standard Operating Procedures - Institutional Human Ethics Committee

Flow Chart

Activity		Responsibility
Appoint the SOP team	→	Chairman
List all relevant SOPs	→	Secretariat
Design a format and layout	→	Secretariat
Design a new / revised SOP	→	Secretariat
Approval for implementation	→	IHEC Members
Implement, distribute and file all SOPs	→	Secretariat
Review and request for a revision	→	Chairperson, Chairman
Review the new/revised SOP /Investigators of NIE	→	IHEC members / Secretariat
Manage and archive superseded SOP	→	Secretariat

10. Independent Consultants

The IHEC may call upon subject experts as independent consultants who may provide special review of selected research protocols, if needed. These experts may be specialists in ethical or legal aspects, specific diseases or methodologies, or represent specific communities; patient groups or special interest groups e.g. cancer patients, HIV/AIDS positive persons or ethnic minorities. They will be required to give their specialized views but should not take part in the decision-making process which will be made by the members of the IHEC. These consultants must sign the

confidentiality agreement (Annexure- 25) regarding meeting, deliberations, and related matters.

11. Secretariat

Secretariat is composed of Member-Secretary, IHEC and the administrative and supporting staff. The supporting staff consists of staff members of IHEC, CFC & RI appointed by the Chairman, CFC & RI.

11.1. The secretariat shall have the following functions:

a. Organizing an effective and efficient tracking procedure for each proposal received

b. Maintain a database of all proposals received, reviewed and archived.

c. Preparation, maintenance and distribution of study files

d. Organizing IHEC meetings regularly

e. Preparation of agenda and minutes of the meetings

f. Maintaining IHEC documentation and archive.

g. Communicating with IHEC members and PIs.

h. Arrangement of training for personnel and IHEC members.

i. Providing necessary administrative support for IHEC related activities to the Member-Secretary, IHEC.

11.2. Terms of Reference for the administrative officer/s/staff

a. Correspondence with the IHEC members and external experts

b. Correspondence with the investigators

c. Pre and post arrangements of IHEC meetings

d. Preparing agenda and minutes of the IHEC meetings

e. Answering queries of the investigators

f. Filing study related documents

g. Archiving and maintaining the study files

11.3. Duties of the attendant/s /Secretariat staff /s (as assigned by the Member-Secretary / Secretariat office in-charge)

a. Assisting the secretariat in arranging the IHEC meetings

b. Dispatching sets of study documents to IHEC members and externalexperts.

c. Receiving the study related documents from and dispatching the IHEClettersto the investigators.

d. Filing study related documents

e. Archiving and maintaining the study files

All staff of CFC & RI- IHEC secretariat will follow the rules and regulations as per CFC & RI norms.

12. SOP Team:

The Chairperson will constitute a SOP Committee consisting of the Member-Secretary and two-three more members of the IHEC / Independent Consultants/ Internal Investigators who have a thorough understanding of the ethical review process. The term of SOP Committee shall be as long as the member continues in the IHEC. If the term of a member of the SOP Committee as member of IHEC expires, that member shall automatically cease to be a member of the SOP Committee from that date.

13. Quorum Requirements:

Minimum of five members should be present to meet the quorum requirements.In case of clinical trials as per the ICMR- National Ethical Guidelines for Biomedical and Health Research involving Human Participants 2017, the following specialties should be represented in the meeting.

1. A minimum of five members should be present in the meeting.

2. The quorum should include medical, non-medical or technical or/andnon-technical members. *

3. Minimum one non-affiliated member should be part of the quorum.

4. Preferably the lay person should be part of the quorum.

5. The quorum for reviewing regulatory clinical trials should be in accordance with current CDSCO requirements.

6. No decision is valid without fulfillment of the quorum.

Without satisfying these conditions, any decision taken by the committee shall remain null and void.

No quorum should consist entirely of members of one profession or one sex. In absence of the Chairperson, any member who is independent of the institution will chair the meeting as acting Chairperson.

(*Medical members are clinicians with appropriate medical qualifications. Technical members are personswith qualifications related to a particular branch in which the study is conducted, for example social sciences.)

14. Conduct of the Meeting

The Chairperson will conduct all meetings of the IHEC. If for reasons beyond control, the Chairperson is not available, an alternate Chairperson will be elected by the members present from among themselves.

a. The Member secretary in consultation with the chairperson may convene the IHEC meeting once in every six months or as necessary. The Member Secretary is responsible for maintaining the records and communicating with all concerned. He/she will prepare the minutes of the meetings and get them approved by the Chairperson before communicating to the PI.

b. Additional review meetings can also be held with short notice as and when required. Meetings will be planned in accordance with the need of the workload.

c. All the IHEC meetings will be held regularly on scheduled dates that are announced and notified in advance.

d. All the proposals will be received at least three weeks before the meeting, checked for completeness as per check list initially by the office clerk (Annexure-9), subsequently by the member secretary (through a nominated person) using the evaluation form (Annexure-10).

e. Members will be given not less than 2 weeks' time in advance to review study proposals and the relevant documents.

f. Minutes of the IHEC meetings, all the proceedings and deliberation will be documented.

g. Signatures of the Chairperson and the Member secretary will be obtained on the minutes of the meeting document. The minutes will be circulated to all the guides / HODs in case of student proposals.

h. Applicant, sponsor or investigator may be invited to present the proposal or elaborate on specific issues.

i. There should be provision for allocating reasonable amount of funds for smooth functioning of the IHEC.

j. Members will be given appropriate remuneration for each sitting.

15. Categories of Risk

Type of Risk	Definition / Description
Less than minimal risk	Research on anonymous or non-identified data / samples, data available in the public domain, meta-analysis etc.,
Minimal risk	Research involving routine questioning or history taking, observing, physical examination, chest X-ray, obtaining body fluids without invasive intervention, such as hair, saliva or urine samples, etc.,
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.
More than minimal risk or High risk	Probability of harm or discomfort anticipated in the research is invasive and greater than minimal risk. Examples include research involving any interventional study using a drug, device or invasive procedure such as lumbar puncture, lung or liver biopsy, endoscopic procedure, intravenous sedation for diagnostic procedures, etc.

16. Application Procedures:

a. All proposals should be submitted in the prescribed application form.
b. All relevant documents should be enclosed with application form.
c. A soft copy of the proposal along with the application in prescribed format duly signed by the Principal Investigator (PI) and Co-investigators / Collaborators must be sent to the member secretary.
d. The date of meeting will be intimated to the researcher to be present for clarification.
e. The decision will be communicated in writing. If revision is to be made, the revised document should be submitted within a stipulated period of time as specified in the communication or before the next meeting.

16.1. Submission process:

16.1.1. Submission of Documents:

The PI can submit research proposal to the IHEC secretariat for review and approval under any of the 5 sections mentioned below within the specified time period mentioned below:

16.1.2. New proposals for Review:

Fifteen days prior to the upcoming IHEC meeting

16.1.3. Re-submission of Protocols with Corrections:

15 days from the date of receipt of IHEC decision letter

16.1.4. Protocol Amendment or any other Amendments:

Fifteen days prior to the IHEC meeting

16.2. Submission of SAE (On-Site):

For all clinical trials approved by DCGI the SAE will be submitted by the PI to

the licensing authority, the IHEC and the sponsor within 24 hours. The detailed report of SAEs, after due analysis, should be forwarded by the investigatorand sponsor to Chairman of the IHEC, Licensing Authority and the Head of theInstitution within fourteen calendar days of occurrence of the SAEs. If this SAE is death then the causality analysis will be forwarded to the expert committee of the licensing authority in addition to the above-mentioned authorities.

16.3.1. Submission of protocol deviations / violations:

Within 7 days of occurrence.

16.3.2. Continuing Review of Approved Protocols:

Fifteen days prior to the scheduled review/expiry date

16.3.3. Protocol Completion / Termination:

The study completion report should be submitted by the study PI in the prescribed formats within 30 days of completion / termination.

It is the responsibility of the IHEC members to review the study completion report and notify it or request for further information, if necessary.

16.3.4. Receiving and Verifying Contents of Submitted Protocols

Secretariat will check the protocol documents as per the checklist attached to the Application Form for Initial Review(Annexure-8) to ensure that all required forms and materials are submitted (see guidelines to prepare informed consent: Annexure -30)

i. Verification includes

a. Duly filled and signed Application Form for Initial Review(Annexure-8)

b. Study protocol

c. Other relevant documents

ii.Return the protocol documents to the applicants, if the documents are incomplete, clearly stating the missing items

17. Documentation:

For a thorough and complete review, all research proposals should be submitted with the following documents:

1. Name of the applicant with designation
2. Name of the Institute / Hospital / Field area where research will be conducted. Letter forwarded by the Head of the Institution / Head of the Department. (Should be there)
3. Protocol of the proposed research
4. List of Ethical issues in the study and plans to address these issues.
5. Proposal should be submitted with all relevant enclosures like proforma, case report forms, questionnaires, follow - up cards, etc.
6. Informed consent process, including patient information sheet and informed Consent form in local language(s).
7. For any drug / device trial, all relevant pre-clinical animal data and clinical trial data from other centres within the country / countries, if available.
8. Curriculum vitae of all the investigators with relevant publications in last five years.
9. Any regulatory clearances required.
10. Source of funding and financial requirements for the project.
11. Other financial issues including those related to insurance.
12. An agreement to report all Serious Adverse events (SAEs)
13. Statement of Conflict of interests, if any
14. An agreement to comply with all national and international guidelines
15. A statement describing any compensation for study participation (including expenses and access to medical care) to be given to research participants; a description of the arrangements for indemnity, if applicable (in study- related

injuries); a description of the arrangements for insurance coverage for research participants, if applicable;

16. All significant previous decisions (e.g., those leading to a negative decision or modified protocol) by other ECs or regulatory authorities for the proposed study (whether in the same location or elsewhere) and an indication of the modification(s) to the protocol made on that account. The reasons for negative decisions should be provided.

17. Plans for publication of results – positive or negative- while maintaining the privacy and confidentiality of the study participants.

18. Any other information relevant to the study

18. Responsibilities of Sponsor/Investigator

18.1. Responsibilities of Sponsor

(i) The clinical trial Sponsor is responsible for implementing and maintaining quality assurance systems to ensure that the clinical trial is conducted and data generated, documented and reported in compliance with the protocol, Good Clinical Practice (GCP-2012) Guidelines issued by the Central Drugs Standard Control Organization, New Drugs and Clinical Trials Rules (2019), Directorate General of Health Services guidelines, Government of India, ICMR ethical guidelines for biomedical research in human participants -2017, as well as with all applicable statutory provisions. Standard operating procedures should be documented to ensure compliance with GCP and applicable regulations.

(ii) Sponsors are required to submit a status report on the clinical trial to the Licensing Authority at the prescribed periodicity.

(iii) In case of studies prematurely discontinued for any reason including lack of commercial interest in pursuing the new drug application, a summary report should be submitted within 3 months. The summary report should provide a brief

description of the study, the number of patients exposed to the drug, dose and duration of exposure, details of Serious adverse drug reactions (Annexure-17), if any, and the reason for discontinuation of thestudy or non-pursuit of the new drug application;

(iv) Any report of serious adverse event /death occurring in clinical trial, after due analysis shall be forwarded by the sponsor to chairman of the ethics committee, DCGI and chairman of the expert committee constituted by the licensing authority as defined under New Drugs and Clinical Trials Rules (2019).

(v) In case of injury or death occurring to the clinical trial subject, the sponsor (whethera pharmaceutical company or an Institution) or his representative, whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial, shall make payment for medical management of the subject and also provide financialcompensation for the clinical trial related injury or death in the manner asprescribed in New Drugs and Clinical Trials Rules (2019).

(vi) The sponsor (whether a pharmaceutical company or an institution) or his representative, whosoever had obtained permission from the LicensingAuthority for conduct of the clinical trial, shall submit details ofcompensation provided or paid for clinical trial related injury or death, to the Licensing Authority as prescribed in New Drugs and Clinical Trials Rules (2019).

18.2. Responsibilities of the Investigator(s)

(i) The Investigator(s) shall be responsible for the conduct of the trial according to the protocol and the GCP Guidelines and for compliance as per the undertaking given in Appendix VII of New Drugs and Clinical Trials Rules (2019). Standard operating procedures are required to be documented by the investigators for the tasks performed by them. During and following a subject's participation in a trial, the investigator should ensure that adequate medical care is provided to the participant for any adverse events. Investigator(s) shall report

all serious and unexpected adverse events to the licensing authority as defined in New Drugs and Clinical Trials Rules (2019), the sponsor or his representative, whosoever had obtained permission form the licensing authority for conduct of the clinical trial, and the ethics committee that accorded approval to the study protocol, within the stipulated period of their occurrence as per New Drugs and Clinical Trials Rules (2019). The report of the serious adverse event of death, after due analysis shall be forwarded by the investigator to Chairman of the ethics committee and DCGI /Chairman of the Expert Committee constituted by the licensing authority under Appendix XII with a copy of the report to the licensing authority and the head of the institution where the trial has been conducted within the stipulated period of their occurrence as per New Drugs and Clinical Trials Rules (2019). The report of the serious adverse event/death, after due analysis shall be forwarded to the DCGI, Licensing Authority, Chairman of the Ethics Committee and the Head of the Institution where the trial has been conducted within thestipulated period of their occurrence as per New Drugs and Clinical Trials Rules (2019).

(ii) The investigator shall provide information to the clinical trial subject through informed consent process as provided in New Drugs and Clinical Trials Rules (2019) about the essential elements of the clinical trial and the subject's right to claim compensation in case of trial related injury or death. He/She shall also inform the subject or His/ Her nominee(s) of their rights to contact the sponsor or his representative whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial for the purpose of making claims in the case of trial related injury or death.

19. Record keeping and Archiving

a. Curriculum Vitae (CV) of all members of IHEC.

b. Copy of all study protocols with enclosed documents, progress reports, and SAEs.
c. Minutes of all meetings duly signed by the Chairperson.
d. Copy of all existing relevant national and international guidelines on research ethics and laws along with amendments.
e. Copy of all correspondence with members, researchers and other regulatory bodies.
f. Final report of the approved projects.
g. All the documents both hard copy and soft copy should be archived for prescribed period.

20. Follow up of research projects with respect to Serious Adverse Events:

i. IHEC will monitor the Serious Adverse Events related to the study orproduct / device in the follow up of the research proposal
ii. IHEC will review the exact nature of Serious Adverse Event and the time of reporting by the investigators and whether the Investigator followed the procedure regarding the medical and financial management of Serious Adverse Event as mentioned in the research protocol.
iii. The following events should be reported as Serious Adverse Events by the investigator.
iv. The death of a study subject, whether or not related to an investigational agent.
v. A life-threatening adverse drug event
vi. Inpatient hospitalization or prolongation of existing hospitalization for >24hours (excluding elective hospitalization for conditions unrelated to the study)

vii. A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions.

viii. A birth defect in an offspring of a study participant, regardless of the time after the study the congenital defect is diagnosed.

ix. Important Medical Event (IME) that (not resulting in death, be life threatening, or require hospitalization) may be considered an SAE when, based upon medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent these events listed in the definition.

x. Any Serious Adverse Event should be reported to the sponsor within 24hours and to the IHEC within 7 days (in the format given in New Drugs and Clinical Trials Rules (2019), Appendix XV). In case of death, it should be reported to the IHEC within 24 hours.

xi. All other Adverse Events that are not fatal or life threatening must be filed within 14 calendar days. The details will be evaluated and discussed indetail in the final report of the study.

xii. A decision of this follow up review will be issued and communicated to the applicant indicating modification / suspension / termination / continuation of the project.

21. Review procedures:

a. The meeting of the IHEC should be held at regular intervals based on the need and workload with prior intimation.

b. The proposals will be sent to members at least 2 weeks in advance.

c. Decisions will be taken by consensus after discussions, and whenever needed voting will be done.

d. Researchers will be invited to offer clarifications if need be.

e. Independent consultants/Experts will be invited to offer their opinion on specific research proposals if needed.
f. The decisions will be minuted and Chairperson's approval taken in writing.

22. Element of review

a. Scientific design and conduct of the study.
b. Approval of appropriate scientific review committees.
c. Examination of predictable risks / harms.
d. Examination of potential benefits.
e. Procedure for selection of subjects in methodology including inclusion / exclusion, withdrawal criteria and other issues like advertisement details.
f. Management of research related injuries, adverse events.
g. Compensation provisions.
h. Justification for placebo in control arm, if any.
i. Availability of products after the study, if applicable.
j. Patient information sheet and informed consent form in local language.
k. Protection of privacy and confidentiality.
l. Involvement of the community, wherever necessary.
m. Plans for data analysis and reporting
n. Adherence to all regulatory requirements and applicable guidelines
o. Competence of investigators, research and supporting staff
p. Facilities and infrastructure of study sites
q. Criteria for withdrawal of patients, suspending or terminating the study.

23. Expedited review

All revised proposals, unless specifically required to go to the main committee, will be examined in a meeting of identified members convened by the Chairperson to expedite decision making. Expedited review may also be taken up in cases of nationally relevant proposals requiring urgent review. The nature of the applications,

amendments, and other considerations that will be eligible for expedited review should be specified. To expedite review a sub-committee consisting of the member secretary, a non-scientific and a scientific member maybe constitutedto review the proposal and approved by the chairperson.

An expedited review may be conducted, only if the protocols involve minimal risk to the participants:

a. Revised proposal with minor modifications previously approved through full review by the IHEC.
b. Continuing review of approved proposals where there is no deviation from the original protocol approved by the IHEC.
c. Anonymous surveys and retrospective study of medical records.
d. Analysis of discarded pathological specimens / stored paraffin blocks without personal identifiers.
e. Proposals involving previously banked biological materials and/or tissues without any identifiers.

Research activities that involve only procedures listed in one or more of the following categories:

Clinical studies of drugs and medical devices only when –

i. Research is on already approved drugs except when,

a. Study of drug interaction
b. Conducting trial on vulnerable population OR
c. Adverse Event (AE) or unexpected Adverse Drug Reaction (ADR) of minor nature is reported

ii. Other documents which would be considered for expedited review are as follows but may not restrict to:

a. Minor deviations from originally approved research during the period of approval (usually of one-year duration)

c. Change in the name, address of sponsor
d. Change in contact details of PI and Member- Secretary, IHEC
e. Request for change in PI, Co-I, change in any member involved in the research.
f. Minor amendments in the protocol, CRF (Case Report Forms)
g. Minor corrections in budget other administrative changes in the IB (Investigator's Brochure), ICF (informed consent forms).

24. Full Board Review

All research presenting with more than minimal risk, research protocols which do not qualify for exemption or expedited review and projects that involve vulnerable population and special groups should be subjected to full board review by all the members.

25. Review of Research proposals involving vulnerable population

a. Vulnerable research participants are individuals who are socially, economically or politically disadvantaged and therefore susceptible tobeing exploited, whose willingness to volunteer in a research trial may beduly influenced by the expectation of (whether justified or not), benefits associatedwith participation, retaliatory response from higher authorityin case of refusal to participate, and whose consent may not be valid forvarious reasons. They include infants, children and adolescents, pregnantand lactating women, students and employees, mentally, challenged patients, critically ill patients, prisoners etc.

b. All the members will evaluate the possible risks to the study participants withproperjustifications,theexpectedbenefit and adequacy of documentation for ensuring privacy, confidentiality and justice issue.

c. Vulnerable group can become participants only if the study is designed to protect or advance the health of this population and for which the non-

vulnerable group would not be suitable participants.

d. In case of trials involving children, the assent of the child should be obtained from the age of seven to eighteen years unless there is no medically accepted alternative to the therapy (provided consent has been obtainedfrom parents / guardian)

e. Rights and welfare of people who are unable to give informed consent must be protected. Informed consent should be obtained from legally authorized representatives (LAR) in the presence of impartial witness with adequate explanation of risks and benefits.

26. Review of Protocol Deviation/Non-Compliance / Violation / Waiver:

1)IHEC secretariat is responsible for receiving deviations -Violations/waiver reports submitted by the PI and forwarding to Member-Secretary or the site monitoring team.

2) IHEC members review and act upon the reports.

3) The PI himself / herself may forward protocol deviation / non- compliance / violation / waiver reports to IHEC within 7 days of occurrence in the prescribed format (SOP – V 1.0/ ANX 13).

4) The Secretariat can detect protocol deviation / non-compliance / violation from:

- failure to comply with statutory requirements
- not responding to requests from IHEC within reasonable time limit
- not responding to communication made by IHEC

5) During site monitoring if conductof the project is not as per IHEC approved protocol study design / national / international regulations. The site monitoring team will inform the Secretariat in writing within 24 hours from the time of finding [one working day] violation. when scrutinizing annual / periodic reports / SAE reports

6)Communication received from the Investigator / trial site / sponsor /study monitor / CRO

7) Communication / complaint / information received by IHEC Secretariat from research participant who has been enrolled or any individual who has been approached for enrollment.

26.1. Categorization

Based on the risk involved the Member-Secretary will categorize the protocol violation / non-compliance / protocol deviation / waiver report/s for placing either in the expedited or full board review (SOP 04 – V 3.0). Reports on deviations involving major risk will be sent to the primary reviewer for comments.

26.2. Expedited review

Protocol violation / non-compliance / protocol deviation / waiver report/s categorized as expedited will be reviewed as per SOP Section 23.

26.3. Full Board Review

Full Board will review Protocol violation / non-compliance / protocol deviation / waiver report/sas per SOP Section 24.

26.4. Communicating the decision

i. Decision of the meeting on the proposals will be communicated by the Member Secretary/secretariat to the PI / Research Scholar within two weeks after the meeting at which the decision was taken in the specified ICMR format. All the approvals will be valid for one year or for the duration of the project whichever is less. Investigator has to get his or her project re- approved after one year, where required.

ii. The communication letters shall be collected by the PI from IHEC office.

26.5. Filing of the Documents

Copies of the notification letter, protocol deviation / violation / non-compliance / waiver reports and the IHEC decision letter are placed in the protocol file and an additional copy of the notification letter in the ‘‘non-compliance’ file.

26.6. Post-review activities

Compliance report to be submitted by the PI within the specified time period as decided by the IHEC. The IHEC Secretariat will keep track of the reports. Reminders will be sent if no reports are received.

In case of suspension, IHEC will revoke the suspension after receipt of satisfactory compliance report from the PI.

In case a PI fails to respond to the IHEC letter, it will be discussed at the next full board meeting and a decision will be taken for specific action.

A separate file that identifies investigators who are found to be non-compliant with national / international regulations or who fail to follow protocol approval stipulations or fail to respond to the IHEC request for information/action is maintained and reviewed by the IHEC periodically.

Protocol Deviation – explanation:

If the deviation meets any of the following criteria, it is considered a protocol violation. Example list is not exhaustive.

I. The deviation has harmed or posed a significant or substantive risk of harm to the research subject.

Examples:

- A research subject received the wrong treatment or incorrect dose.
- A research subject met withdrawal criteria during the study but was not withdrawn.
- A research subject received an excluded concomitant medication.

II. The deviation compromises the scientific integrity of the data collected for the study.

Examples:

- A research subject was enrolled but does not meet the protocol's eligibility criteria.

- Failure to treat research subjects per protocol procedures that specifically relate to primary efficacy outcomes. (if it involves patient safety it meets the first category above)
- Changing the protocol without prior IRB approval.
- Inadvertent loss of samples or data.

III. The deviation is a willful or knowing breach of human participant protection regulations, policies, or procedures on the part of the investigator(s).

Examples:

- Failure to obtain informed consent prior to initiation of study-related procedures
- Falsifying research or medical records.
- Performing tests or procedures beyond the individual's professional scope or privilege status (credentialing)

IV. The deviation involves a serious or continuing noncompliance with federal, state, local or institutional human participant protection regulations, policies, or procedures.

Examples:

- Working under an expired professional license or certification
- Failure to follow federal and/or local regulations, and intramural research or CC policies
- Repeated minor deviations.

V. The deviation is inconsistent with the NIH Human Research Protection Program's research, medical, and ethical principles.

Examples:

- A breach of confidentiality.
- Inadequate or improper informed consent procedure.

27. Decision Making

i. Decision is arrived at by consensus, if consensus is not possible, voting is

carried out.

ii. Opinions of absent members that are transmitted by mail or telephone or fax may be considered by the attending members during discussion but may not be counted as votes or quorum for formally convened full board meetings.

iii. Any committee member with a conflicting interest in a proposal will abstain from deliberations and in decision making process on that proposal, except to provide information as requested by the committee. Such abstentions will be recorded in the minutes.

iv. Any subject expert - Independent Consultant who is attending the meeting will take part in discussion and offer their expert comment – but will not take part in decision making.

28. Follow up procedures

a. Reports should be submitted annually for review.

b. Final report should be submitted at the end of study.

c. All SAEs and the interventions undertaken should be intimated.

d. Protocol deviation, if any, should be informed with adequate justifications.

e. Any amendment to the protocol should be resubmitted for renewed approval.

f. Any new information related to the study should be communicated.

g. Premature termination of study should be notified with reasons along with Summary of the data obtained so far.

h. Change of investigators / sites should be informed.

29. Updating IHEC Members

All relevant new guidelines should be brought to the attention of the members.

i. All IHEC members must be conversant with the ICMR guidelines for research involving human participants, New Drugs and Clinical Trials Rules (2009), the Declaration of Helsinki and ICH-GCP guidelines (1964).

ii. IHEC members will also be provided with a copy of the Standard Operating Procedure.

iii. IHEC members will be encouraged to attend national and international training programs/conferences/seminars in the field of research ethics to help in improving the quality of research protocols/ethics committee submissions and review.

iv. A record will be maintained of the training obtained by IHEC members and updated annually.

v. IHEC members will receive introductory training in ethical aspects of biomedical researches and functioning of IHEC and will be exposed to ongoing opportunities for enhancing their capacity for ethical review. All training programs will be organized by the IHEC.

30. Policy to monitor or prevent the conflict of interest along with standardoperating procedures:

(i) It has been recognized that the potential for conflict of interest will alwaysexist but has faith in the IHEC and its Chairperson to manage the conflict issues so that the ultimate outcome is the protection of human subjects.

(ii) When a member has a conflict of interest, the member should notify theChairpersonand may not participate in the HEC review or approval except to provide informationrequested by the Committee.

31. Annual report of the IHEC

Annual activity report (including details of study proposals received) should be prepared and submitted to the Chairman, CFC & RI and other relevant authorities.

32. Self-assessment

For continuous improvement of quality assurance of its services, the IHEC will undergo self-assessment once in 2 years or as and when required.

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33. List of Annexures

1. Invite Letter for IHEC Members-Annexure-1
2. Membership Consent Letter-Annexure-2
3. One-page CV for EC Members/Investigators-Annexure-2 (a)
4. Appointment order-Annexure-3
5. List of members of IHEC-CFC&RI - Annexure-4
6. Confidentiality agreement form for IHEC Members-Annexure-5
7. Conflict of Interest agreement form for IHEC Members-Annexure-6
8. Minutes of Meeting-Annexure-7
9. Application Form for Initial Review-Annexure-8
10. Initial check list to verify completeness of documents submitted Form-Annexure-9
11. Evaluationform for Verification of proposals submitted to IHEC-CFC&RI-Annexure-10
12. Application Form for Expedited Review-Annexure-11
13. Application Form for Exemption from Review-Annexure-12
14. Continuing Review / Annual report format-Annexure-13
15. Application/Notification form for Amendments- Annexure-14
16. Protocol Violation/ Deviation Reporting form (Reporting by case) - Annexure-15
17. Serious Adverse Event Reporting format (Biomedical Health Research)-Annexure-16
18. Premature Termination/ Suspension/ Discontinuation Report Format-Annexure-17
19. Application for Clinical Trials-Annexure-18
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21. Application Form for Human Genetics Testing Research (Clinical Trials) -Annexure-20
22. Application Form for Socio-Behavioural and Public Health Research- Annexure-21
23. Study Completion / Final Report-Annexure-22
24. Format for Curriculum Vitae for Investigators-Annexure-23
25. Certificate of Approval-Annexure-24
26. Confidentiality and Conflict of Interest Agreement Form for Independent Consultants-Annexure-25
27. Confidentiality Agreement Form for Observer Attendees to IHEC, CFC & RI Meetings-Annexure-26
28. Format for Communication to the Principal Investigator-Annexure-27
29. Six monthly progress Project-Annexure-28
30. Template for Participant Information Sheet (PIS) Participant Information Sheet-Annexure-29
31. Participant Informed Consent Form (PICF)-Annexure-30
32. Consent form (for participants less than 18 years of age) Parent/ Legally accepted representative (LAR)-Annexure-30 (a)
33. Undertaking by the Principal Investigator-Annexure-31
34. Intimation of start of the study-Annexure-32
35. Investigator’s Declaration-Annexure-33
36. Letter of Authorization-Annexure-34

34. Bibliography / References:

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