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AMALA INSTITUTE OF MEDICAL SCIENCES

INSTITUTIONAL ETHICS COMMITTEE

STANDARD OPERATING PROCEDURES

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(CDSCO)

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The Institutional Ethics Committee relating to Clinical Trials of Amala Institute of Medical Sciences, Kerala would be known as IEC, AMALA, in this document. It has been divided into different clauses and their sub clauses. It is recommended that these clauses should be referred as mentioned in this document. This Standard Operating Procedures are laid down in accordance with the regulations of New Drugs and Clinical Trials Rules, 2019, Ethical guidelines by ICMR, Declaration of Helsinki and Good Clinical Practical guidelines. This document may be amended either after 2 years or any specific requisite/regulatory requirement which might be considered relevant by the IEC.

1. DECLARATION:

The composition and working procedure of IEC, AMALA, is based on Operational Guidelines for IEC that review Biomedical Research (WHO, 2000), International Conference on Harmonization-Good Clinical Practices (ICH-GCP) Guidelines (1996), New Drugs and Clinical Trials Rules, 2019, Indian GCP guidelines (2016) and Ethical Guidelines for Biomedical Research on Human Participants by ICMR issued in 2017, 2018 and 2019.

2. ESTABLISHING AND CONSTITUTING IEC, AMALA:

Aims or the Purpose of IEC

The IEC, AMALA, has been constituted with an aim to provide public assurance of protection, by, among other things, reviewing and approving the clinical trial protocol, the suitability of the investigator(s), facilities and the methods and material to conduct clinical research at Amala Institute of Medical Sciences, Kerala under compliance of New Drugs and Clinical Trials Rules, 2019, National Ethical Guidelines for Biomedical Research on Human Participants by ICMR and its requirements.

3. OBJECTIVE:

Amala Institute of Medical Sciences, Kerala, herein referred to as "AMALA" is committed to the protection of the rights and welfare of human participants in biomedical and behavioral research conducted at AMALA. The objective of these SOPs for research involving human subjects is to maintain effective functioning of the IEC, AMALA and to ensure quality and technical excellence and consistent ethical review of all the submitted research proposals and the ongoing approved research projects involving human participants in accordance with the ICMR Ethical guidelines for biomedical research on human subjects.

4. AUTHORITY UNDER WHICH IEC, AMALA IS CONSTITUTED:

Amala Institute of Medical Sciences, Kerala has authorized the formation of IEC, AMALA as an independent body which functions independently at our site since 2006 as registered body under Drugs Controller General of India (DCGI), with respect to decision making and its working in order to provide public assurance of protection, by, among other things, reviewing and approving the clinical trial protocols, bioavailability and bioequivalence studies and Biomedical and Health Research projects, the suitability of the investigator(s), facilities and the methods and material to conduct clinical research at our site. In addition to this, the institute will provide all support to the ethics committee activities which includes provision of training, resources and infrastructure.

5. PREPARATION OF STANDARD OPERATING PROCEDURES (SOPS)

FOR IEC, AMALA:

5.1 Purpose:

The purpose of this Standard Operating Procedure (SOP) is to define the process for writing, reviewing, distributing and amending SOPs of IEC, AMALA. The SOPs provide clear, unambiguous instructions so that the related activities of the Committee are conducted in accordance with: New Drugs and Clinical Trials Rules (2019), National Ethical Guidelines for Biomedical Research on Human Participants by ICMR (2017), Indian GCP Guidelines (Access time 2003) http://cdsco.nic.in, WHO Operating Guidelines for Ethical Review Board that Review Biomedical Research (2000), The International Conference on Harmonization – Good Clinical Practices (ICH-GCP) Guidelines (1996), Declaration of Helsinki and the prevailing amendments from time to time and amendments from CDSCO office.

5.2 Responsibility:

5.2.1 IEC Secretary:

* Co-ordinate activities of writing, reviewing, distributing and amending SOPs

* Maintain on file all current SOPs and past SOPs

*Ensure that all the IEC members and involved staff have access to the SOPs

* Chairman/Member Secretary coordinates with the director for appointment of coordinating staff to assist IEC Functions.

*Member Secretary shall vote in IEC decisions but coordinating staff of IEC cannot vote in any decision-making procedure of the IEC.

5.2.2 SOP team (Member Secretary and one/more members):

*Assess the requests for SOP revision in consultation with the Chairman

* Propose new / modified SOPs as needed

*Select the format and coding system for SOPs

*Draft the SOP/modify in consultation with the IEC members and involved staff

* Review the draft SOP

* Submit the draft for approval to Chairman

5.2.3 Chairman of IEC:

*Chairman of IEC appoints the SOP team to formulate the SOPs consisting of Member

Secretary, one / more members of IEC and Coordinating staff

* Approve the SOPs

* Sign and date the approved SOPs

5.2.4 Coordinating staff of IEC:

* Maintain on file all current SOPs and the list of SOPs

* Maintain an up-to-date distribution list for each SOP distributed

* Maintain the SOPs with a receipt to all users

* Maintain file of all past SOPs of Institutional Ethics Committee

* Assist in the formulation of SOPs

* Assist Member Secretary with the needed clerical work

5.2.5 IEC members:

* Sign and date the acknowledgement form when they would receive approved SOP.

* Assist in all decision-making procedure of IEC

* Assist secretariat for any help in management

5.3 Identify the need for new or amending SOP:

Any member of the IEC who would like a revision or notices an inconsistency/ discrepancy /has any suggestions to improve the existing SOPs or requests to design an entirely new SOP can put forth his request to the Chairman. The Chairman will inform all the IEC members about this request in a regular full-Committee IEC meeting. If the IEC members agree to the request, the Member Secretary shall proceed with the revision process/ formulation process of the SOP. If the IEC members do not agree, the Chairman will inform the person/ IEC member who made the request for modification of the SOP in the same meeting. The SOPs will be updated regularly at the interval of 2 years or if there are major changes whichever is earlier.

5.4 Appoint the SOP Team:

The Chairman will identify appropriate members of the IEC who have a thorough understanding of the ethical review process to constitute the SOP writing team.

5.5 List of relevant SOPs:

(SOP writing team will carry out the subsequent steps)

* Write down step by step all the procedures of the IEC

*Organize, devise and name each process

5.6 New Standard Operating Procedures:

When the need for a new SOP has been identified and agreed on, a draft will be written by Member Secretary and the designated IEC members of SOP team, appointed by the Chairman.

5.7 Review by Consultation:

The draft SOP written by one or more members of the SOP team will be reviewed by the remaining members of the SOP team. After incorporating the suggestions put forth by the SOP team members, a copy of the revised draft SOP will be sent to the Member-Secretary, who will circulate it to all the IEC members to invite suggestions.

5.8 Preparation and submission of final draft:

* IEC members will review the revised draft SOP in IEC meeting.

* The suggestions agreed upon unanimously, by all the IEC members will be discussed and incorporated in the revised draft SOP and the final draft SOP will be formulated.

* The SOP team would stand automatically be dissolved once the IEC takes final decision regarding the SOP.

5.9 Approve a new/ revised SOP:

*The revised SOPs will be reviewed and approved in the same manner as a new SOP.

* The Chairman approves the SOP, after which SOP need to be made accessible to all stakeholders for reference. Member Secretary shall e-mail / share the approved SOP to all members.

5.10 Ensure implementation and file all SOPs:

*The approved SOPs will be implemented from the effective date.

* When the revised version is distributed, old version is retrieved from all members and destroyed for except for one copy; this copy of the earlier version will be placed in the file entitled 'Past SOPs of Institutional Ethics Committee'.

* One complete original set of current SOPs will be filed centrally in the SOP Master file, by the Member Secretary for review and request for a revision of existing SOPs and record the dates of review on the SOP Master file.

* Revision of approved SOPs shall occur at least once in 2 years.

5.11 Manage current and archive superseded SOPs:

*Member Secretary will manage current and archive old versions (superseded) of SOPs

* Superseded SOPs should be retained and clearly marked "superseded" and archived in the file entitled 'Past SOPs of Institutional Ethics Committee by the Member Secretary.

5.12 Glossary:

* Revision date: Date/year by which the SOP may be revised or reviewed.

* Recipients: Stakeholders who would receive a copy of SOP.

* SOP (Standard Operating Procedure): Detailed, written instructions, in a certain format, describing activities and actions undertaken by the IEC to achieve uniformity of the performance of a specific function. The aim of the SOPs and their accompanying checklists and forms is to simplify the functioning, whilst maintaining high standards of Good Clinical Practice.

*Institutional Ethics Committee (IEC): It is an independent body formally designated to review, approve and monitor clinical trials, bioavailability, bioequivalence, biomedical and behavioral research involving humans with the aim to protect the rights and welfare of the participants. It is an independent body whose responsibility is to ensure the protection of the rights, safety and well-being of human participants involved in a clinical trial and to provide public assurance of that protection.

5.13 Design a Format and layout:

The SOP would be given a number and a title that is self-explanatory and is easily understood.

A unique code number with the Institutional, Scientific format. Code as 'AMALA xx/Vy' will be assigned to SOP file by the Member Secretary wherein 'xx' represents the file number of SOP and 'Vy' represents version number of SOP e.g. V1 means Version 1. Each Annexure (AN) will be given unique code number with the format AN-V1/AMALA 01/V1. e.g. AN1– indicates AN is Annexure; n is Annexure no.1, V1 is Version 1, belonging to the. The SOP code will be on the cover page and also on bottom of each page along with the page number. The first page of SOP document will be signed and dated by the author/s (the IEC members who have reviewed the SOPs) and the IEC Chairman and subsequently the SOP will be implemented from that date.

6. CONSTITUTION OF THE IEC & ITS TERMS OF REFERENCES:

The IEC of the Amala Institute of Medical Sciences, Kerala (IEC, AMALA) is formed by the Director, Amala Institute of Medical Sciences in accordance with the guidelines laid down in the New Drugs and Clinical Trials Rules, 2019, National Ethical Guidelines for Biomedical Research on Human Participants by ICMR.

6.1. Appointment / relieving / acceptance of resignation of any member of the IEC, AMALA would be the prerogative of the Director on the recommendation of IEC, AMALA. The appointment of the IEC member will be confirmed only after they consent to abide by the Good Clinical Practice (GCP) guidelines and maintenance of confidentiality. The Director, Amala institute of medical sciences will appoint the coordinating staff for IEC. They will be supervised by the Member Secretary.

6.1.1. Ethics Committee composition

The IEC, AMALA will be multidisciplinary and multi-sectorial in composition and will have 7-15 members from medical, non-medical, scientific and non-scientific areas. At least 50% of members will be non-affiliated to this institute. It will have representation that is varied in terms of gender, age and social background. The members representing medical scientist and clinicians should have post graduate qualification & adequate experience in their respective fields.

6.1.2. Regular Members

*Chairman (from outside the institute)

*One Member Secretary (one of the members representing the institute as designated by the Director). One affiliated member may be designated as Alternate Member Secretary.

* One or more faculty members of Basic Medical Sciences

* One or more faculty members of Dept. of Pharmacology

* One or more clinicians

* One or more legal experts

* One or more independent social scientist/ representative of non-governmental agency or philosopher or ethicist or theologian

* One or more lay persons from community

* The committee should have at least one or more woman members

* The IEC may appoint alternate members who can take part in the IEC activities in absence of regular members to maintain the quorum. The IEC may invite member(s) of specific patient groups or other special interest groups for an IEC meeting (if required, based on the requirement of research area, e.g. HIV AIDS, genetic disorders, stem cell research etc.) for eliciting their views. Such individuals will have to sign confidentiality agreement and declare in writing, conflicts of interest, if any prior to attending the meeting. They will attend the meeting in the capacity of 'Observer' and will not have right to vote.

6.1.3. Hierarchy:

* The Chairman will be head of the committee.

* All the other IEC members will be regular committee members with equal ranking.

* The Member Secretary will be the guardian of all documents, record and funds in the possession of the committee.

6.1.4. Chairperson

a. The Head of Institution shall appoint a Chairperson who is from outside the institution.

b. The Chairperson will be responsible for conducting all committee meetings and will lead all discussions and deliberations pertinent to the review of research proposals.

c. The Chairperson will preside over all elections and administrative matters pertinent to the committee's functions.

d. In case of anticipated absence, the Chairperson will nominate a committee member as Acting Chairperson. The Acting Chairperson will have all the powers of the Chairperson for that meeting.

6.1.5. Member Secretary

a. Head of Institution shall appoint a Member Secretary who is affiliated to the institution.

b. In consultation with the Chairperson, the Member Secretary will be responsible for the following functions:

1. Receiving all research proposals.

2. Forwarding all materials for review by the committee members.

3. Preparation and dissemination of agenda for all committee meetings (at least 7 days prior to the meeting date).

4. Inviting special attendees from relevant therapeutic areas to the scheduled meetings, if needed.

5. Preparation and circulation of minutes (within 14 days of the meetings).

6. Retention and safekeeping of all records and documentation as described in VI.

7. Performance of other duties assigned by the Chairperson.

8. To maintain IEC record and to archive them.

9. To sign documents and communications related to IEC functioning.

10. To arrange for training of personnel and IEC members.

11. To organize the preparations, review, revision and distribution of SOPs and guidelines.

12. To provide necessary administrative support for IEC related activities to the Chairman.

13. To provide updates on relevant and contemporary issues to ethics in health research as well as relevant contemporary literature to the committee members.

14. To receive fees and issue official receipts.

15. To delegate various responsibilities to appropriate and authorized persons.

16. To ensure adherence of IEC functioning as per SOPs.

6.1.6. Tenure of Membership

a. The tenure of committee membership will be a continuous period of up to three (3) years.

b. Extension of membership may be done if needed as per the decision of the director.

c. There will be no limit to the number of times that membership can be extended.

6.1.7. Election of New Members

a. New members will be appointed under the following circumstances:

1. When a regular member completes his/her tenure.

2. If a regular member resigns or drops out before the tenure is completed.

3. If a regular member is found to be inappropriate by the committee.

b. A new member will be appointed for the same category as that of the member being replaced.

6.1.8. Membership requirements:

* The Director, AMALA is responsible for appointing new committee members.

*The Chairman, Member Secretary or any member can suggest names of potential members but the final decision will remain with the Director, AMALA.

* Members will be designated in their personal capacities, based on their interest, ethical and/or scientific knowledge and expertise, experience as well as their commitment and willingness to volunteer the necessary time and effort for IEC.

* Members must disclose their interest and involvement by providing Consent and the Appointment letters will be issued to members of IEC.

* New members will be identified according to the requirement i.e. as per the composition specified in clause 6.1.2.

* New / alternate members will be appointed if deemed necessary by Director, Amala

6.1.8.1 Chairperson/Vice Chairperson (optional)

* Non-affiliated

* Qualifications -A well-respected person from any background with prior experience of having served/ serving in an EC

6.1.8.2 Member Secretary/ Alternate Member Secretary (optional)

* Affiliated

* Qualifications - Should be a staff member of the institution

- Should have knowledge and experience in clinical research and ethics, be motivated and have good communication skills

- Should be able to devote adequate time to this activity which should be protected by the institution

6.1.8.3 Basic Medical Scientist(s)

* Affiliated/ non-affiliated

Qualifications - Non-medical or medical person with qualifications in basic medical sciences

* In case of EC reviewing clinical trials with drugs, the basic medical scientist should preferably be a pharmacologist

6.1.8.4 Clinician(s)

* Affiliated/ non-affiliated

* Qualifications - Should be individual/s with recognized medical qualification, expertise and training

6.1.8.5 Legal expert/s

* Affiliated/ non-affiliated

* Qualifications -Should have a basic degree in Law from a recognized university, with experience

- Desirable: Training in medical law.

6.1.8.6 Social scientist/ philosopher/ ethicist/theologian

* Affiliated/ non-affiliated

* Qualifications - Should be an individual with social behavioural science/ philosophy/ religious qualification and training and/or expertise and be sensitive to local cultural and moral values. Can be from an NGO involved in health-related activities

6.1.8.7 Lay person(s)

* Non-affiliated

*Qualifications - Literate person from the public or community

- Has not pursued a medical science/ health-related career in the last 5 years

- May be a representative of the community from which the participants are to be drawn

- Is aware of the local language, cultural and moral values of the community

- Desirable: involved in social and community welfare activities

6.1.9. Resignation:

* A member can resign by submitting a letter of resignation addressed to the Chairman and delivered to the Member Secretary and the same will be informed by the Secretary to the appointing authority for formal acceptance and to initiate necessary replacement/recruitment procedure for filling up the vacancy.

* The members if opts to step down due to any genuine cause may do so with prior notice and proper information to the appointing authority.

6.1.10. Disqualification:

* If Director AMALA, Chairman or Member Secretary receives a communication in writing, alleging misconduct by a member, enquiry will be done by the member secretary and the concerned member if found guilty will be disqualified after consultation with the Chairman and Director, Amala

* A member may be disqualified if fails to attend more than 3 regular consecutive IEC meetings without prior intimation.

6.2. Members list

A list of members of the IEC, AMALA, their appointment letters, biodata and consent forms would be maintained by Member Secretary of the IEC, AMALA. This and the copy of the working procedures would be made available to any investigator, for the purpose of filing of research projects, upon written request for the same to the Chairman/ member secretary.

6.3. Coordinating staff:

* To support the Member Secretary in executing functions of the IEC.

* Correspondence with the IEC members and investigators

* Arranging IEC meetings

* Receiving all research proposals

*Assisting in preparing agenda and minutes of the meetings

* Maintaining and archiving study documents

* To perform any other functions as instructed by Member Secretary/ Chairman

6.4. Responsibilities of IEC members:

* To attend IEC meetings and participate in discussions and deliberations for appropriate decisions.

* To review, discuss and consider research proposals submitted for evaluation.

* To monitor Serious Adverse Event reports and recommend appropriate action(s)

* To review the progress reports and monitor ongoing studies.

* To maintain confidentiality of the documents and deliberations of IEC meetings.

* To declare any conflict of interest, if any.

* To participate in continuing education activities in biomedical ethics and biomedical research.

* To provide information and documents related to training obtained in biomedical ethics and biomedical research to the IEC secretary.

* To carry out the work delegated by Chairman and Member Secretary

* To assist the Chairman and Member Secretary in carrying out IEC work as per SOP

6.5. However, following members should be held responsible for specific activities:

6.5.1. Clinician:

* To provide medical inputs on protocol: Informed consent forms and other aspects like standard of care, Placebo use, Sample size, dosing, Concomitant medications, prohibited medications, risk & benefit to patients, Age group, and Inclusion / exclusion criteria

* To take clinical judgment for the trial

6.5.2. Medical Scientist:

* To provide scientist aspects of the study: Investigator's brochure, safety of drug, Pharmacodynamics and pharmacokinetics of drug, lab procedures, study design, sample size, use of biological samples,

*To see: preclinical data and whether protocol adequately addresses issue of all this matter or not, Qualification of PI and GCP training certificate, Details of SAEs and reporting time limit from PI, all ethical issues and other procedures involved in the study.

6.5.3. Legal Expert:

* To review Clinical Trial Agreement (CTA): Parties involved, scope of agreement, responsibilities of parties and payment details

*To review whether provision for reporting of incidence of SAE included or not, and arrangement for compensation as per NDCTR 2019.

* To see whether any clause is violating the norm, confidentiality, dispute resolution, updated with regulatory requirements, insurance policy, validity, countries for which the policy provides cover and liability limit - per person and total.

*Indemnity: it should cover the liability of investigator and sponsor and could be part of CTA or separate document to see informed consent document

6.5.4. Social Scientist / NGO representative / Philosopher / Ethicist:

* To see community perspective, informed consent process, compensation, design of trial - whether it is uncomfortable to subjects, number of blood samples, post-trial access to involved community, confidentiality, vulnerable population and recruitment process.

6.5.5. Layperson:

* To see informed consent process, trial procedures, post-trial access, compensation, confidentiality, think from the subject's perspective, ensure non exploitation of subject, and whether the subject diary is simple or not.

7. QUORUM REQUIREMENTS:

The requisite quorum of at least five members consisting one Medical scientist (preferably a pharmacologist), Clinician, Legal expert, Social scientist or representative of a nongovernmental voluntary agency or a Philosopher or an Ethicist or a Theologian and one Layperson from the community including the Chairman and member Secretary are must for discussion on any research proposal. At least one of the members must be non-affiliated. For clinical trial, the five members of quorum must be from medical scientist (preferably a pharmacologist), Clinician, Legal expert, Social scientist or representative of a nongovernmental voluntary agency or a Philosopher or an Ethicist or a Theologian or a similar person and one Layperson from the community as per New Drugs and Clinical Trials Rules, 2019.

8. RESPONSIBILITIES OF THE ETHICS COMMITTEE:

8.1. The IEC, AMALA is to designed to ensure that the research projects carried out or supported by AMALA are sound in scientific design, have statistical validity and are carried according to the standard guidelines as prescribed by Good Clinical Practice (GCP), Indian council of Medical Research (ICMR) guidelines and New Drugs and Clinical Trials Rules, 2019.

The responsibilities of IEC, AMALA are:

*To protect the safety, dignity, rights and wellbeing of the potential research participants.

* To include solely those patients who have given informed consent for participation in the research.

*To ensure that universal ethical values and international scientific standards are expressed in terms of local community values and customs.

* To ensure equitable recruitment of subjects in the study.

* To ensure that the research is conducted under the supervision of the medical persons or scientists with required experience and expertise.

* To assist in the development and the education of a research community responsive to local health care requirements.

8.2. The IEC, AMALA would review all new research projects and if approval is given, it would be for the duration as mentioned in the study protocol. Interim reports will have to submit as advised in the approval letter. After completion of the duration, the progress of the project would be reviewed and further extension may be provided if requested. Status of any project can be retrieved by tracking the record document. The IEC, AMALA would maintain a list of all projects submitted, approved, disapproved and outcome of each project with confidentiality.

8.3. The IEC, AMALA should ensure those patients' rights are not compromised and look into any payments proposed to be made in the study to the patients towards reimbursement of incidental expenses.

9. POLICY FOR UPDATING/TRAINING OF IEC MEMBERS:

9.1. All relevant information on ethics will be brought to the attention of the members of IEC,

AMALA by the Member Secretary.

9.2. All IEC members shall be required to undergo refresher course in Good clinical practice (GCP) once in three years or earlier in case of indication for the same.

9.3. The Chairman, Member Secretary and members will be encouraged by the appointing authority to attend national and international training programs/ conferences/ workshops/ seminars/ courses at least once in three years in the field of research ethics (over and above his own discipline) to help in improving the quality of review of research protocols/ethics committee submissions and other related activities.

10. SELECTION AND RESPONSIBILITIES OF SUBJECT EXPERT:

10.1. Purpose:

For obtaining the expertise of a professional as a subject expert either affiliated or non-affiliated, to the Institutional Ethics Committee.

10.2. Responsibility:

Upon the advice or recommendation of the secretary or any IEC member, it is the responsibility of the IEC to nominate the name of one or more special subject experts and be endorsed by the Chairman for the given project.

10.3. Recommendation:

The IEC will designate subject experts from the different specialties and the Chairman / Member Secretary on behalf of the IEC will invite subject expert selected by the IEC in writing to assist in the review of the project and provide his/ her independent opinion. Depending upon the complexity of the issue(s) the Chairman/ Member Secretary on behalf of the IEC will invite one or more experts.

10.4. Selection:

The final approval from the IEC Chairman to refer the project to the specified subject expert will be taken by the Secretary

10.5. Co-ordination with subject expert:

Subject experts will participate after they agree to the confidentiality clause and abide by the rules and regulations of IEC, whose opinion would be valuable but they would not be involved in the decision making process of the Ethics committee. The expert would be requested to provide an opinion in writing within 30 working days, depending upon the gravity and seriousness of the matter. The following would be designated as Subject expert during the meetings of the IEC, AMALA.

* Investigator or Co-investigator/ Study coordinator of the project under review.

* Any expert in the field of study as and when invited by the IEC, AMALA.

The Member Secretary will provide explanations/ clarifications (telephonically or in writing) to the subject experts if any doubts or questions are raised. The Chairman / Legal expert / IEC members can provide any further explanations. If deemed necessary, subject expert may be reimbursed for expenses on travel, time spent, documents referred to in library/ internet, incidental expenses, etc.

11. TERMS OF REFERENCE – ACCEPTING PROPOSALS FOR REVIEW

IEC AMALA will accept, review and approve, proposals for clinical, basic, translational and public health research projects (Intra and Extra mural), and clinical trials (investigator initiated and sponsor initiated) in which at least one investigator is a regular employee of AIMS, Thrissur, for scientific and ethical content.

11.1. POLICY FOR ACCEPTING PROPOSALS FROM OUTSIDE AMALA

Under certain circumstances, IEC AMALA would extend its services to review and approve proposals submitted from institutions outside AIMS, Thrissur. The following requirements must be fulfilled by institutions that use the services of IEC AMALA.

• The concerned institution should enter into an MoU with Amala institute of medical sciences for utilizing the services or the user institution should provide a 'No Objection certificate' and agree to be overseen by IEC AMALA.

• The institution should grant IEC AMALA access to all research records including the source documents and research participants for continuing review of the implemented project, including site visits.

• The user institution should grant permission to IEC AMALA to undertake site monitoring and all the rights and responsibilities related to ethical review of the projects submitted by the user institutions.

11.2. SUBMISSION PROCESS OF RESEARCH PROPOSALS:

All research proposals are to be submitted to the Member Secretary of the IEC, AMALA, in the prescribed Application format along with check list in the prescribed format and detailed study protocol at least three

weeks in advance, especially for all clinical trials. However, in special situations, the submission may be done up to 7 days of IEC meeting with the special permission of the director, Amala. Covering letter addressed to the Chairman / Member Secretary, IEC, AMALA should also be attached.

The protocol would include the following:

i. Title of the Protocol

ii. Name and contact details of Principal Investigator

iii. Name and contact details of Sponsor

iv. Summary / Synopsis

v. Clear research objectives and rationale for undertaking the investigation in human subjects in the light of existing knowledge.

vi. Recent curriculum vitae of the investigators indicating qualification and experience.

vii. Subject recruitment procedures or proposed methods / advertisement / notices

viii. Inclusion and exclusion criteria for entry of subjects in the study.

ix. Precise description of methodology of the proposed research, including intended dosages of drugs, planned duration of treatment and details of invasive procedures if any.

x. A description of plans to withdraw or withhold standard therapies in the course of research.

xi. The details of statistical analysis of the study.

xii. Procedure for seeking and obtaining informed consent with sample of patient information sheet and informed consent forms in English and vernacular languages and the validity of the translation and back translation (certificate).

xiii. Safety of proposed intervention and any drug or vaccine to be tested, including results of relevant laboratory and animal research. *

xiv. For research carrying more than minimal risk, an account of plans to provide medical therapy for such risk or injury or toxicity due to over-dosage should be included.

xv. Case Record Form / Proforma / Questionnaire

xvi. Proposed compensation for participation and reimbursement of incidental expenses/ serious adverse events occurring during the study participation. *

xvii. Plans for storage and maintenance of all data collected during the trial.

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

xix. A statement on probable ethical issues and steps taken to tackle the same.

xx. Activity plan / Timeline

xxi. Amendments to protocol (if any)

xxii. Protocol signature page

xxiii. All other relevant documents related to the study protocol including regulatory clearances and insurance documents as applicable. *

xxiv. Investigator's agreement with the sponsor / Clinical Trial Agreement (CTA) / Agreement

to comply with national and international GCP protocols for clinical trials. *

xxv. GCP training certificate (3 yrs.) of Principle investigator and study team members

xxvi. Details of Funding agency / Sponsors and fund allocation for the proposed work. *

xxvii. Insurance policy of the study. *

xxviii. Investigator's Brochure. *

xxix. Undertaking by the Investigator*

xxx. Memorandum of Understanding (MOU) between collaborative institutions

xxxi. CTRI registration*

xxxii. DCGI/CDSCO Approval letter. *

xxxiii. FDA marketing/manufacturing license for herbal drugs*

xxxiv. Health Ministry Screening Committee (HMSC) approval*

xxxv. Bhabha Atomic Research Centre (BARC) approval*

xxxvi. Genetic Engineering Advisory Committee (GEAC) approval*

xxxvii. Ethics Committee clearance of other centers (if applicable)

xxxviii. Any additional document(s), as required by IEC

Note: One or more copies of the research proposals for clinical trial as instructed by the secretary and checklist filled in by PI along with soft copy sent by email need to be submitted. The hard copy will be kept for the records of the IEC, AMALA. IEC may constraint the need for hard copy based submission of research projects to practice eco- friendly paperless system of operation. (*as applicable for Clinical trials).

12. CONSENT REVIEW PROCESS:

AMALA INSTITUTE OF MEDICAL SCIENCES THRISSUR

The principal investigator must be obtained subject's consent in writing using Informed Consent Form (ICF). Patient information sheet and Informed consent form should be approved before initiation of study and furnished to central licensing authority. Any changes in Informed Consent Document (ICD) should be approved before implementation and submitted to Central Licensing Authority (CLA). As per the new requirements, Table 3 of Third Schedule in New Drugs and Clinical Trials Rules, 2019 the ICD should clearly state that the subject is entitled to free medical management as long as required in case of injury, and financial compensation in case of clinical trial related injury or death. The investigator will have to clearly inform the subject about his right to claim compensation in case of trial related injury or death and to contact the sponsor / representative directly for any claim related queries. The contact details of sponsor representative should be provided in the ICD. In order to aid the calculation of compensation amount, the ICD now should have further details about the subject like qualification, occupation, annual income, address and contact details of the nominee and his/her relation with the subject. A copy of ICD should be provided to subject and same should be mentioned in the ICD document. IEC, AMALA periodically review the following (by the way of performing random inspection visits).

12.1. The investigator shall provide information about the study verbally as well as using a patient information sheet, in a language that is nontechnical and understandable by the subject.

12.2. The PI shall describe procedures for obtaining informed consent including the procedure of Audio Video recording if needed from the research participant prior to enrolling into a research study, especially vulnerable subjects.

12.3. If the subject is unable to give consent (unconscious or minor or suffering from severe mental illness or disability), the same should be obtained from a legally acceptable representative. A Legally Acceptable Representative (LAR) is who is able to give consent for or authorize and intervention in the patient as provided by law of India.

12.4. If the LAR is unable to read or write, an impartial witness should be included in the consent process who will sign in the consent on behalf of his / her.

12.5. If subject is from pediatrics age group, the subjects are legally unable to provide written informed consent and are dependent on their parent or legal guardian to assume responsibility for their participation in clinical studies. In such case: -

12.5.1. Written informed consent should be obtained from the parent or legal guardian. However, all pediatric participants should be informed to the fullest extent possible about the study in a language and in terms that they are able to understand.

12.5.2. Where appropriate, pediatric participants (age between 7 to 18 years) should additionally assent to enroll in the study. Mature minors and adolescents should personally sign and date a separately designed written assent form.

12.5.3. Although a participant's wish to withdraw from a study must be respected, there may be circumstances in therapeutic studies for serious or life-threatening diseases in which, in the opinion of the Investigator and parent or legal guardian, the welfare of the pediatric patient would be jeopardized by his or

her failing to participate in the study. In this situation, continued parental or legal guardian consent should be sufficient to allow participation in the study.

12.6. Assurance that the research participants shall receive information that becomes available during the research relevant to their participation including their rights, safety and wellbeing is documented.

12.7. The provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project.

12.8. Any payments proposed to be made to subjects/ patients have to be documented and notified to IEC and included on the ICD (Informed Consent Document)/ ICF (Informed Consent Form).

12.9. Audio Visual (AV) Recording of Informed Consent process shall follow as following:

12.9.1. According to ICMR guidelines, when a participant is willing to participate but not willing to sign or give a thumb impression or cannot do so, then verbal/oral consent may be taken on approval by the EC, in the presence of an impartial witness who should sign and date the consent document. This process can be documented through audio or video recording of the participant, the PI and the impartial witness, all of whom should be seen in the frame. However, verbal/oral consent should only be taken in exceptional circumstances and for specific, justifiable reasons with the approval of the IEC. It should not be practiced routinely.

12.9.2. In case of vulnerable subjects in clinical trials of New Chemical Entity (NCE) or New Molecular Entity (NME) including procedure of providing information to the subject and his understanding on such consent, should be maintained by investigator for record: In case of clinical trial of anti-HIV and anti-leprosy drugs, only audio recording of the informed consent process of individual subject including the procedure of providing information to the subject and his understanding on such consent should be maintained by the investigator for record.

13. PROCESS OF CONDUCTION OF IEC, AMALA MEETINGS:

13.1. The committee would meet once in every 3 months or whenever it is necessary. If needed where the situation is justified the meeting may be called more than once in 3months.

13.2. The meetings would be called by the Member Secretary and the notice for the meetings would be sent usually 7 working days prior to the scheduled date.

13.3. The member-secretary will record the minutes of the meeting and circulate the same to the members within a month of the meeting.

13.4. The meeting may take place in physical presence of the members at designated venue or via online mode.

14. PROTOCOL REVIEW PROCEDURE:

14.1. The IEC, AMALA should review every research proposal involving human subjects (as per the checklist). It would ensure that a scientific evaluation has been completed before ethics review is taken up.

14.2. The ethics review of a new project would be done through formal meetings and would not resort to decisions on them through circulation of proposals. The protocols may initially be reviewed by subcommittee when necessary and comments would be put up in the formal meeting. However, decision regarding approval will be taken during formal meeting in presence of required quorum of the committee. The following decisions may be provisionally taken by the Member Secretary in communication with the Chairman, without a formal meeting, subject to the approval of the IEC AMALA at the next scheduled meeting:

a) Extension of the study beyond the approved period.

b) Amendment to the study related document not involving the study design*.

c) Restarting a previously discontinued research project.

d) All notifications related to adverse events.

e) Decision to exempt a study from review

14.3. Reviewing of Academic Research proposals submitted by Post graduate and undergraduate students: A separate Ethics committee/ subcommittee with identified members may be constituted by the Chairman, IEC, AMALA for reviewing the proposals of academic research submitted by Postgraduate students as part of their thesis work & proposals by UG students.

14.4. The IEC will not allow the use of trainees/employees working within the organization to be used as trial participants unless students and staff have the same rights as any other potential subject to participate in the research project, irrespective of the degree of risk, provided all of the following conditions exist.

14.5. The research must not bestow upon participating Institutional subjects any competitive academic or occupational advantage over other Institutional students or staff who does not volunteer and the researchers must not impose any academic or occupational penalty on those Institutional trainees or staff who does not volunteer.

14.6. Institutional students and staff must not be systematically treated differently from non- Institutional subjects as part of the project. Due to the potential for perceived or real coercion to participate, Institutional students and staff who desire to participate in the research (especially those under the direct supervision of the PI or listed research collaborators) must be reviewed by the Head of the Institution.

14.7. Where the protocol indicates that the prior consent of the trial subject or the subject's legally acceptable representative is not possible, PI may submit a request for waiver of consent. The IEC will determine whether the proposed protocol and/or other document (s) adequately addresses the relevant ethical concerns and meet applicable regulatory requirements for such trials (i.e., in emergency situations). The waiver of consent may be granted and this shall be communicated to the investigator in writing while approving the protocol.

14.8. It will also take note of the adverse events of the ongoing projects from the concerned investigators time to time and if considered may take up on site monitoring with the help of the suitable sub-committee

(formed with the formal permission from the Director, AMALA) who will submit report to the IEC for reviewing. It will also report the same to DCGI within the specified time.

14.9. The committee will also take up the issue of compensation following standard guidelines in case of any adverse events deemed to be caused by the direct association of the concerned clinical trial (guidelines for determining quantum of financial compensation to be paid in a case of clinical trial related injury or death; as per scope and provisions made in the New Drugs and Clinical Trials Rules, 2019 and ICMR guidelines).

14.10. The following types of research are considered to involve more than minimal risk and require ethical approval:

* Research involving those who lack normal physical / mental capacity.

*All research involving those who lack normal capacity, or those who during the research project has become lacking in capacity.

* Research involving sensitive topics - for example participant's sexual behavior, their illegal or political behavior, their experience of violence, their abuse or exploitation, their mental health, or their gender or ethnic status.

* Research involving groups where permission of a guardian is normally required for initial access to members. This includes research involving guardians such as adult professionals (e.g. those working with children or the elderly), or research in where access to research participants is not possible without the permission of another adult, such as another family member (e.g. the parent or husband of the participant)

* Research involving access to records of personal or confidential information, including genetic or other biological information, concerning identifiable individuals.

* Research which could induce psychological stress, anxiety or humiliation or cause more than minimal pain.

* Research involving intrusive interventions or data collection methods - for example, the administration of substances, vigorous physical exercise, or techniques such as hypnotism. In particular, where participants are persuaded to reveal information which they would not otherwise disclose in the course of everyday life. The Committee would evaluate the possible risks to the subjects, the expected benefits and adequacy of documentation for ensuring privacy, confidentiality and justice issues.

14.11. Research involving potentially vulnerable groups:

It describes the requirements concerning review of research that involves groups that could be potentially vulnerable to coercion in regard to autonomy and present conditions that may affect risk/benefit determinations or bearing unequal burden in research. IEC members are responsible for receiving, verifying, and reviewing the research protocols pertaining to vulnerable populations using the Risk benefit assessment tool. Such protocols should be reviewed keeping in mind the following points when it concerns research that involves groups that could be potentially vulnerable to coercion:

14.11.6. IEC members will complete checklist during review of research with vulnerable populations and present recommendations at the convened meeting.

14.12. Protocol deviation/ non-compliance/ violation:

IEC will be responsible to review deviation / non-compliance/ violation. The member secretary / Chairman will categorize the protocol deviation as minor and major or may designate members (one/more) to review and take a decision depending on the seriousness of the deviation/non-compliance/violation. For this purpose, a separate committee: Clinical Trial and Research Monitoring Committee (CTRMC) will be established when needed which will report to the Chairman or Member Secretary of IEC. The decision will be taken by IEC AMALA to ensure that the safety and rights of the research participants are safeguarded. Following the procedures mentioned in protocol in accordance with statutory provisions, National /International ethical guidelines and procedures mandated by IEC, protocol deviation/non-compliance/violation will be detected accordingly.

14.12.1. Protocol deviation/s: Any change, divergence or departure from the study design or procedures of protocol which does not have a major impact on the subject's rights, safety or well-being or completeness, accuracy, study outcome and reliability of study data and has not been approved by IEC will be considered minor deviation. On the content of a deviation, the protocol has approved by IEC that may affect the subject's rights, safety or wellbeing and/or the completeness accuracy, study outcome and reliability of study data will be considered major deviation. The PI should submit the protocol deviation report as per the format.

14.12.2. Protocol violation/s: A protocol violation is a deviation from the IEC approved protocol that may affect the subject's rights, safety, or wellbeing and/or the completeness, accuracy, study outcome and reliability of the study data will be considered a protocol violation. The PI should submit the protocol violation report as per the format.

* Review of Protocol Amendments:

In any occasion of amendments to the already approved protocol by the IEC, the said amendment is reviewed by the IEC in the next meeting following submission. The content of amendment is critically reviewed with justification in ethics point of view following Good Clinical Practice (GCP) guidelines. The consensus approval from the committee members regarding this is recorded and communicated to the Principal Investigator.

15. POLICY FOR RESOLUTION OF CONFLICT:

The IEC, AMALA would refer to the GCP guidelines, ICMR guidelines and New Drugs and Clinical Trials Rules, 2019 and their modifications in case of any conflict as mentioned below for which the following format will be used to take undertaking from the concerned member of IEC. No members having a conflict of interest will be involved in the oversight of the clinical trial or bioavailability or bioequivalence or biomedical or any health research study being reviewed by his/her and it is responsibility of each member to withdraw voluntarily, by expressing to the Chairman in writing that there is no conflict of interest with a sign. The details in respect of the conflict of interest of the members will be recorded in the minutes of, the meetings.

* Measure to protect autonomy

* Risk/benefit determinations with respect to the vulnerability

* Bearing unequal burden in research

Member of the IEC who would be reviewing such protocols should be well versed with the potential harm or risk of such population participating in the study. For example, children and young people, those with a learning disability or cognitive impairment, or individuals in a dependent or unequal relationship. Committee will review the safety and the rights of justice issues involving vulnerable population if applicable for any particular study involving such populations. Vulnerable Subjects will be defined as per the standard guidelines by ICMR (http://www.icmr.nic.in/guidelines/ICMR_Ethical_Guidelines_2017.pdf] A vulnerable category of subjects are those who are relatively (or absolutely) incapable of protecting their own interests which includes children, prisoners, pregnant women, handicapped or mentally disabled persons, refugees, displaced persons and economically or educationally disadvantaged persons, who are likely to be vulnerable to coercion or undue influence. When a trial is to be carried out in the vulnerable populations like the paediatric, geriatric population, pregnant women, etc., the consent of the trial subject and subject's Legally Acceptable Representative (LAR) is to be mandatorily taken and the IEC will determine that the proposed protocol and/or other document(s) adequately address the relevant ethical concerns and meet applicable regulatory requirements for such trials. Where required assent of the participant will also be taken and this will be ensured during review and approval of the ICF.

14.11.1. Responsibility

It is the responsibility of the Secretary of IEC to maintain up-to-date tools for review of research pertaining to vulnerable groups based on new and evolving applicable regulations and guidelines.

14.11.2. IEC Chairperson/ Member Secretary is responsible for ensuring that IEC members are, well versed in new and evolving regulations and guidelines pertaining to vulnerable populations, for selecting primary reviewers with appropriate expertise to conduct the reviews of such research, and for securing appropriate consulting expertise as needed for selected reviews.

14.11.3. IEC member is responsible for conducting appropriate review of research planned for vulnerable populations, including an assessment of potential for coercion, in consultation with any appropriate experts and resources as described in this SOP

14.11.4. Secretary of the Institute Ethics Committee will

*Maintain on file the update checklist (1-5) which conforms to applicable regulations and guidelines.

*Document review of risk assessment in IEC minutes for the protocols involving vulnerable population.

*Confirm that the complete informed consent and assent documents as relevant.

14.11.5. Chairperson / Member Secretary will select appropriate primary reviewer(s).

14.11.6. IEC members will complete checklist during review of research with vulnerable populations and present recommendations at the convened meeting.

14.12. Protocol deviation/ non-compliance/ violation:

IEC will be responsible to review deviation / non-compliance/ violation. The member secretary / Chairman will categorize the protocol deviation as minor and major or may designate members (one/more) to review and take a decision depending on the seriousness of the deviation/non-compliance/violation. For this purpose, a separate committee: Clinical Trial and Research Monitoring Committee (CTRMC) will be established when needed which will report to the Chairman or Member Secretary of IEC. The decision will be taken by IEC AMALA to ensure that the safety and rights of the research participants are safeguarded. Following the procedures mentioned in protocol in accordance with statutory provisions, National /International ethical guidelines and procedures mandated by IEC, protocol deviation/non-compliance/violation will be detected accordingly.

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16. DECISION MAKING PROCESS:

* Only those IEC, AMALA members who are independent of the investigator and the sponsor of the proposal and with no conflict of interest, would vote/provide opinion on the proposal. If a member is also an investigator for a proposal, he would not be involved in the decision-making process when the said proposal is being discussed and would not chair the session. Such a member must voluntarily withdraw from the meeting while the IEC is deciding on an application which evokes such a conflict of interest, which should be indicated in writing in the above-mentioned format for undertaking and should be recorded so in the minutes.

* The study team member (Investigator / Co-investigator / Study coordinator's) nonparticipation in the decision-making process would be recorded in the minutes and also in the opinion letter issued for the project.

* The decision of the IEC, AMALA would be by consensus after the quorum requirements are fulfilled to approve / reject /suggest modifications for a repeat review/ exempt from review. If any experts are invited, they would not participate in decision making on a proposal. The decision of the IEC, AMALA would be one of the following ways:

* Approved: The study is approved in its present form. When committee approves the study, the certificate will be issued within a period of 15 days.

* Approved with modifications: This is a conditional approval. The revisions are required. If revisions are found satisfactory, approval will be granted.

* Resubmit: Extensive revisions are necessary. Principal Investigator has to comply with the changes suggested by IEC during the meeting. The revised project will then be reviewed in the next meeting.

* Not approved: The study is not approved in its current form. The required modifications will be suggested during the meeting with reasons. If the investigator wishes to appeal to the decision, he/she may do so by contacting the IEC Secretary. The IEC may decide to accept or deny the appeal. If the appeal is denied, the IEC decision is final, and the study may not be approved or resumed.

* Defer: The decision cannot be arrived at present and therefore postpone to next meeting. Grounds for this: lack of quorum, lack of expertise etc.

16.1. Communicating the decision:

The IEC, AMALA would issue an opinion letter to communicate the decision taken on any project following prescribed format of approval letter as per recommendation of New Drugs and Clinical Trials Rules, 2019. This opinion letter would be issued by the Member Secretary to convey the decision of the IEC, AMALA to the Principal Investigator and must include the following information mentioned with turnaround time of 15 days:

* The name of the Project (Same as the Project title).

* List of documents reviewed by the IEC, AMALA including the revised version of documents if any.

Betsy

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