KASTURBA MEDICAL COLLEGE
and
KASTURBA HOSPITAL
INSTITUTIONAL ETHICS COMMITTEE

STANDARD OPERATING PROCEDURES

Version 10

11th February 2020

CONTROL OF THE DOCUMENT

- The holder of the copy of this document is responsible for maintaining it in good and safe condition and as readily identifiable and retrievable.
- The holder of the copy of this document shall maintain it in current status by inserting latest amendments as and when the amended versions are received.
- The Secretary is responsible for issuing the amended copies to the copyholders, the copyholder should acknowledge the same and he/she should return the obsolete copies to the Institutional Ethics Committee Secretariat.
- The amendment sheet, to be updated (as and when amendments received) and referred for details of amendments issued.
- The Standard Operating Procedures is reviewed at least once during the term of the committee or within a period of two years from the last revision (whichever is earlier) and is updated as relevant to the Institutional Ethics Committee guidelines and procedures.
- The document with original signatures of the above on the title page is considered as 'Master Document' and two copies considered as 'Controlled Copy' will be held by the Dean, Kasturba Medical College, Manipal and Medical Superintendent, Kasturba Hospital, Manipal. An uncontrolled copy will be displayed on the webpage of the Institutional Ethics Committee (www.khinfoedu, Knowledge Base, Ethics Committee)

Prepared	Reviewed	Approved

Approval Sheet

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Date: 11.02.2020

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Kasturba Medical College & Kasturba Hospital, Manipal
Institutional Ethics Committee
Standard Operating Procedures

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1. Objective of the SOP

The objective of this Standard Operating Procedures (SOP) is to contribute to the effective functioning of the Kasturba Medical College (KMC) and Kasturba Hospital (KH) Institutional Ethics Committee (IEC) so that a quality and consistent ethical review mechanism for health and biomedical research is in place for all proposals dealt by the Committee as prescribed by the National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR, New Drugs and Clinical Trial Rules 2019 and International Conference on Harmonization - Good Clinical Practice

2. SOP on SOP - Writing, Reviewing & Amending the SOP

The procedure and instructions for writing, reviewing and amending the existing SOP to conduct activities of the IEC in accordance with the 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR, Medical Devices Rules, 2017, the New Drugs and Clinical Trial Rules 2019), and ICH - GCP (International Conference on Harmonization - Good Clinical Practice) and Indian GCP is described.

2.1 Any member of the IEC can request for revision of SOP if she / he notices an inconsistency / discrepancy / has any suggestions on how to improve the existing SOP or finds the need to design an entirely new SOP. A person who is not a member of the IEC can make a request through an IEC member.

2.2 It is the responsibility of the Chairperson of the IEC to appoint the SOP team to formulate the SOP. The SOP team will be formed as and when required, to amend the existing SOP. The SOP team

would be selected from the existing IEC members.

2.3 The SOP shall be reviewed and revised at least once during the term of the committee or within a period of two years from the last revision, whichever is earlier.

2.4 The SOP team will prepare the draft SOP. The draft SOP will be reviewed and approved by the IEC members at the full board meeting. Once approved at the IEC full board, it will be notified by the Member Secretary for immediate implementation. The SOP team would stand automatically dissolved once the IEC full board approves the SOP.

2.5 Any Full Committee Meeting approved changes to the SOP shall be filed as Amendments to the Current SOP giving a specified Amendment number (in the format xx / Meeting Date / Year) and an appropriate SOP item number (in the format x.xx.xx.xx). When 5 Amendments accrue, it will be considered as a Revision. Any major change to the SOP will be a Version change. When the Version change of SOP is being done, all Amendments and Revisions shall be incorporated into the new Version.

2.6 The SOP shall have a summary of Amendments and Revisions made to the earlier Version, filed at the beginning of the document.

2.7 The approved SOP will be implemented from the issue date. The SOP will be identified by a Version number, Revision number, Issue number and Issue date. When a revised version of the SOP is implemented (from the issue date), the old version will no longer be effective. A copy of the old version will be archived in the IEC Secretariat.

2.8 One Master Document (complete, original set with signatures affixed) of current SOP will be maintained by the IEC Secretariat in the SOP Master File. Another controlled copy will be made available to the Institutional Head of KMC (Dean) and Institutional Head of KH (Medical Superintendent). An uncontrolled copy of the current SOP will be available in the IEC office for use during the regular full board IEC meeting and reference. An uncontrolled copy of the SOP in PDF format will also be uploaded and displayed on the www.khinfo.edu intranet webpage.

3. Authority under which the IEC is constituted

The Institutional Head of KMC (Dean) constitutes the IEC. The members will be appointed on the basis of their competencies and integrity and could be drawn from a private or public domain of disciplines. The Institutional Head of KMC (Dean) shall also designate a Chairperson and Member Secretary for the IEC.

3.1 The Institutional Head of KMC (Dean) shall assign office space for the Secretariat and human resources including a Secretary for the efficient functioning of the IEC. Any additional human resource requirement shall be appointed after justification of the need from the Appointing Authority.

3.2 The Institutional Head of KMC (Dean) shall provide the IEC with any infrastructural requirements including stationery, gadgets (computers, printers and hard disks), furniture including storage cabinets, network access and appropriate software for its optimal functioning.

3.3 The Institutional Head of KMC (Dean) shall provide approved remuneration for Secretariat staff and internal / external members

3.4 The project processing fees (for printing / photocopying for regulatory compliance) paid by the research team shall be deposited with the institution and the Institutional Head of KMC (Dean) shall provide for the operational costs of the IEC. A statement of accounts, at the end of the financial year, is provided as per Institution guidelines and policies

3.5 The IEC is an autonomous body and shall have an MoU with the institute/institutes. The signatory of the MoU will be the Chairperson (representative of the IEC) and the Head of the Institute/institutes.

3.6 The IEC is an autonomous body and the appointing authority or any other administrative office shall not direct nor influence the functioning and review process undertaken by the IEC, except as an appellate authority to redress the complaints of researchers

3.7 The Institutional Head of KMC (Dean) shall be the appellate authority to whom researchers or their administrative superiors may forward complaints to, for redressal

3.8 The IEC shall function in compliance with current regulatory and statutory provisions laid out in the New Drugs and Clinical Trial Rules 2019, Good Clinical Practice Guidelines and 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR

3.9 Communication with appointing authority
The Member Secretary shall present the quality indicators of the IEC at quarterly intervals at the meeting convened by the appointing authority or his representative. The Member Secretary can raise any concerns relating to the functioning of the IEC during the above meetings or directly

represent the same to the Dean of KMC as and when required. The Member Secretary shall communicate the following to the Dean in writing

- Any revision of SOP
- Registration and renewal of registration of IEC Accreditation and renewal of accreditation of IEC
- An administrative action for defaulters / non compliance recommended by the full board of the IEC
- Compensation to participants of research projects
- All communications will be recorded in the minutes of the next Full Committee Meeting.

3.10 Communication with regulatory authority

The Member Secretary shall communicate with the regulatory authority as and when need arises. The following shall be communicated through email or print copies.

- Renewal of registration of IEC
- Any change in composition of IEC Any change / revision of SOP
- Reports of SAE and Compensation
- Accreditation procedures of an appropriate agency
- Any clarifications regarding regulatory nature of projects which border between academic and regulatory trial

If the communications are by email, print versions shall be archived with the other hard copy versions.

4. Terms of Reference

4.1 Responsibility and Scope of IEC

The responsibility of the IEC is to ensure that all the cardinal principles of research ethics viz. Autonomy, Beneficence, Non-maleficence and Justice are addressed in planning, conduct and reporting of the proposed research. For this purpose, the IEC will look into aspects of informed consent process, risk benefit ratio and distributive justice in the proposals before start of the study.

The Institutional Ethics committee will ensure that the clinical trials are conducted in compliance with the study protocol, 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR, Good Clinical Practice Guidelines, statutory provisions of the New Drugs and Clinical Trial Rules 2019 as well as all current statutory requirements

The scope of IEC shall include review, approval and monitoring of :

4.1.1 The IEC will review, approve and monitor all non regulatory research proposals involving human participants conducted at Kasturba Hospital (KH), Manipal, Karnataka and its affiliated hospitals, including but not restricted to biomedical and health research (whether clinical, basic science, policy, implementation, epidemiological, behavioural, public health research), social and behavioural science research for health involving human participants, their biological material and data with a view to safeguard the dignity, rights, safety and well being of all actual and potential research participants. The IEC will also review, approve and monitor regulatory device trials involving human participants and ensure its compliance with the New Drugs and Clinical Trail Rules 2019.

4.1.2 The IEC shall also review, approve and monitor all studies conducted amongst students or staff of any institution under Manipal Academy of Higher Education.

4.1.3 The IEC will also review, approve and monitor research projects being conducted by the staff / students of KMC & KH or other institutes of the Manipal Academy of Higher Education in centers other than Kasturba Hospital, Manipal and its associate hospitals – provided such centers do not have their own Ethics Committees.

4.1.4 The IEC shall also review, approve and monitor all community based studies if any of the team of investigators is a student or staff of any institution under Manipal Academy of Higher Education.

4.1.5 The IEC shall also review and approve all in-vitro studies conducted in any institution under Manipal Academy of Higher Education involving collected or archived samples of human tissues or fluids.

4.1.6 The IEC shall also review, approve and monitor projects from other institutes in the country

which are not affiliated to Manipal Academy of Higher Education, provided such institutes do not have their own ethics committee and if any of the Coinvestigator is a student or faculty of Manipal Academy of Higher Education

4.1.7 The IEC shall also review, approve and monitor projects by investigators elsewhere, if the participants are being recruited or data is being collected in one of the Manipal Academy of Higher Education institutes.

4.1.8 The IEC shall be guided by the statement of general principles in 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR namely the principle of essentiality, voluntariness, non-exploitation, social responsibility, ensuring privacy and confidentiality, risk minimization, professional competence, maximization of benefit, institutional arrangements, transparency and accountability totality of responsibility and environmental protection

4.1.9 The IEC shall be guided by the statement of general ethical issues in 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR namely benefit-risk assessment, informed consent process, privacy and confidentiality, distributive justice, payment for participation, compensation for research-related harm, ancillary care, conflict of interest, selection of vulnerable and special groups as research participants, community engagement, post research access and benefit sharing

4.1.10 The IEC shall be guided by the statement of responsible conduct of research in 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR namely values of research, the protection of human participants, animal experimentation, conflict of interest issues, data acquisition, management, sharing and ownership, reviewing and reporting research, responsible authorship and publication, research misconduct and policies for handling misconduct, registration with Clinical Trials Registry–India and collaborative research

4.1.11 When an ethical dilemma occurs in clinical practice at Kasturba Hospital, Manipal the involved parties (physicians, nurses, other paramedical staff, patients, their relatives, caregivers and administrators) may approach the KMC and KH IEC for opinion and guidance. The IEC shall offer all assistance to them in making the best decision and attempting to resolve ethical issues

4.1.12 The IEC may consult the "Guidelines for end-of-life and palliative care in Indian intensive care units: ISCCM consensus Ethical Position Statement" 2012, "End-of-life care policy: An integrated care plan for the dying" 2014 and "Definition of terms used in limitation of treatment and providing palliative care at end of life" 2018 by ICMR to guide decision making for care of the terminally ill to the extent that does not conflict with "The Medical Treatment of Terminally Ill patients (protection of patients and medical practitioners) Bill" as and when legislated

4.1.13 The IEC will periodically, update and revise SOPs for effective functioning of IEC as and when necessary.

4.1.14 The IEC will also be involved in training members of the committee and non members through continuing education in bioethics, both clinical and research ethics.

4.1.15 The IEC shall register itself under the CDSCO as part of regulatory requirement for reviewing projects which come under the purview of the New Drugs and Clinical Trial Rules 2019 and the Medical Devices Rules 2017. The IEC shall also register under the ICMR – Department of Health Research for reviewing projects which are non-regulatory and come under the purview of Biomedical and Health Research. The IEC shall also register from time to time as per the regulatory and ICMR guidelines as and when updated.

4.2 Composition of IEC

The IEC shall be multidisciplinary and multi sectoral in composition. The members of the IEC will be a diverse group composed of medical and non medical, scientific and non - scientific persons including lay public persons to reflect different viewpoints and in compliance with the New Drugs and Clinical Trial Rules 2019 / CDSCO statutory regulations. Those members who do not belong to constituent colleges of Manipal Academy of Higher Education will be compensated for their journey and work for the IEC in an appropriate monetary form by the appointing authority (Dean of KMC).

4.2.1 The number of persons in the ethics committee shall be between 7 and 15 members.

4.2.2 The IEC will have as its members, individuals from other institutions or communities. An adequate representation of age, gender and community will be maintained - in order to safeguard the interests and welfare of all sections of the society. All the IEC members will be expected to be aware of local social and cultural norms.

4.2.3 The appointing authority (Dean of KMC, Manipal) shall appoint the Chairperson of the IEC, who shall not be a permanent employee of any constituent college of Manipal Academy of Higher Education. The Member Secretary of the Committee will be appointed by the Dean, Kasturba Medical College, Manipal.

4.2.4 The composition of the IEC will be according to the following guidelines :

- 1 Clinical pharmacologist
- 1 - 3 Basic medical scientists from various institutions including KMC, MCODS, MCOPS, MCHP, MMMC, MCON etc
- 1 - 3 Clinicians from various institutions including KMC, TMA Pai Rotary Hospital Karkala, TMA Pai Hospital Udupi or outside MAHE etc
- 1 Legal expert or retired judge
- 1 Social scientist / representative of non-governmental voluntary agencies /persons from other institutions such as MIT, MIM, MCPH, TAPMI etc.
- 1 Philosopher / ethicist / theologian /social activist / epidemiologist (s), sociologist

(s), statistician (s)

- 1 Lay person from the community

The composition shall ensure that at least 50% of the members are non – affiliated and at least one female member in the committee be designated as a woman representative.

4.2.5 The Deputy Chairperson of the Committee will be elected from among the members of the IEC. The Deputy Chairperson will act in the capacity of the Chairperson when the latter is absent.

4.2.6 The Deputy Member Secretary of the Committee will be elected from among the members of the IEC. The Deputy Member Secretary will act in the capacity of the Member Secretary when the latter is absent.

4.2.7 If any of the IEC members desires he / she can apply in writing to the Chairperson of IEC, to select an alternative member to perform the duties of the original member in the latter's absence. This will be placed on record. However, the IEC will have to be informed at least 2 weeks before the next IEC meeting, by the original member that he / she will be unavailable so that the alternate member is informed and acquainted of the agenda of the meeting. At any IEC meeting only one of the two (original member or alternate member) will have voting right. In the normal course, it is expected that the original member will attend to the major part of the IEC work and the alternate member will only be a standby arrangement to help in the smooth functioning of the IEC.

4.3. Membership requirements

4.3.1 The duration of appointment is initially for a period of 2 years. A member may be reappointed for further terms at the discretion of the appointing authority

4.3.2 At the end of 2 years, as the case may be, the committee will be reconstituted and at least 30% of the members will be replaced and new members will be appointed by the authority**.**

4.3.3 A member can be replaced in the event of death, long term non availability, being absent for more than three IEC meetings without giving prior notice / sufficient reasons to the chairperson, or for any action not commensurate with the responsibilities and duties of a member

4.3.4 A member can tender resignation from the committee with proper reasons to do so. Such a resignation will be accepted if the appointing authority is satisfied. An alternative new member may be appointed in such an event

4.3.5 The Appointing Authority (Dean) shall provide a relieving order to the superannuated member. A member who leaves the committee because of superannuation does not need to submit a resignation letter. The superannuation of the member/ members will be recorded in the next full committee meeting minutes.

4.3.6 The appointing authority (Dean) may designate alternate members with their specific roles in the committee. The alternate members will be appointed for the term of the committee and all rules, roles and responsibilities of the members will also apply to the alternate member. Superannuated members may be re-appointed to the committee in the role of an alternate member

4.3.7 All members shall maintain absolute confidentiality of all discussions during the meeting. All members shall sign a confidentiality agreement at the beginning of their term

4.3.8 The member should agree to his / her name, gender, profession, and affiliation to be publicized

4.3.9 Addressing conflict of interest

4.3.9.1 Members are required to sign the conflict of interest and financial disclosure agreement at the start of their term. All IEC members shall disclose in writing to the IEC all conflicts of interest for themselves

4.3.9.2 A member of the IEC may also be one of the investigators in a project submitted for review to the IEC. However, the member-as-investigator cannot participate in the review and approval process for any project in which he or she is present as a PI or CoI or has any other potential conflict of interest except to provide information requested by the IEC

4.3.9.3 Non-financial conflict of interest that require disclosure include but are not limited to :

- Participation in the research project as PI or Co-Investigator
- Co-author in a publication of the research project's results
- Other relationships which may influence judgment of the IEC member in reviewing the research project :

i) has family relation to a researcher whose project is under consideration
ii) is a direct supervisor / mentor or trainee of the researcher(s)
iii) has a prominent role in a directly competing research team or product
iv) has a close personal relationship with a researcher or for other reasons feels unable to render a fair and unbiased review

4.3.9.4 If any IEC member has a conflict of interest, he/she will notify the same to the Member Secretary and will withdraw (leave the room) during the period when the particular project is taken up in the meeting. The Member shall not participate in the IEC discussion or vote on that particular project

4.3.9.5 The recusal of the IEC member for conflict of interest shall be recorded in the meeting minutes

4.3.9.6 In case the member secretary of the IEC has a conflict of interest, the discussion and decision making process for that study shall be convened by the Deputy Member Secretary

4.3.10 IEC members have a need for initial and continued education regarding the science and

ethics of biomedical research. Members must apprise themselves of the ICMR guidelines, New Drugs and Clinical Trial Rules 2019, ICH - GCP for clinical trials in India and KH and KMC IEC SOP. IEC members will receive introductory training material and will be exposed to ongoing opportunities for enhancing their capacity for ethical review. The IEC shall conduct at least one update/ training program for the members to ensure the same.

4.3.11 All relevant new guidelines should be brought to the attention of the members by the Member Secretary

4.3.12 Members should be encouraged to attend national and international training programs in research ethics for maintaining quality in ethical practices and be aware of the latest development in this area. Such activities may be sponsored by the appointing authority

4.4. Quorum requirements

A minimum of five (05) members is required to compose a quorum. When reviewing a regulatory clinical trial the quorum will be in compliance with and as specified in the New Drugs and Clinical Trial Rules 2019 /current CDSCO requirements.

When reviewing non regulatory studies

- A minimum of five members present in the meeting room
- The quorum should include both medical, non medical or technical or/and non-technical members. Medical members are clinicians with appropriate medical qualifications. Technical members are persons with qualifications related to a particular branch in which the study is conducted, for example social sciences.
- Minimum one non-affiliated member should be part of the quorum.
- Preferably the lay person should be part of the quorum
- At least one of the members should be a woman.

No decision is valid without fulfillment of the quorum.

All decisions will be taken during the meetings and not by circulation of project proposals. However, in exceptional cases, if a member is unable to attend a meeting, he / she, after obtaining permission from the Chairperson, may submit his / her report on the agenda to the Chairperson before the IEC meeting, to be considered in absentia. This should however be done as an exception and not as a routine. If such a provision is utilized, it should be documented in the minutes and that member will not be considered as contributing to the quorum.

5. Organization

The Chairperson is responsible for conduct of all meetings of the IEC. If the Chairperson is not available, due to unavoidable circumstances, the Deputy Chairperson will conduct the meeting. The Member Secretary is responsible for organizing the meetings, maintaining the records and communicating with all concerned. He / She will prepare the minutes of the meetings and get it approved by the Chairperson before communicating to the researchers. The Member Secretary will be helped in his / her work by clerical support (Secretary), computers, physical facilities etc. supplied by the appointing authority.

The Chairperson shall constitute a monitoring subcommittee consisting of not less than 2 existing IEC members with a leader designated as Convener amongst them to carry out the following:

Adverse and serious adverse event (SAE) monitoring
Site monitoring
Annual status reports of all ongoing studies
Completion reports of all studies

6. Application procedures

6.1 All proposals should be submitted in the prescribed application format. Consequent to the revision of SOP all submissions will henceforth be only as soft copies through IEC Interface

6.2 The application and documents in the prescribed format, duly signed by the Principal Investigator (PI) and Co-investigators / Collaborators should be forwarded to the ethics committee, through the Head of the Department / Institution where the PI normally works.

6.3 All relevant documents should be forwarded with the appropriate application form. There are separate forms for application according to the type of the proposal - Clinical trials, prospective interventional, prospective, observational, retrospective studies, in- vitro studies, and case reports (see http://172.16.7.105 / Knowledge Base / Ethics committee). The principal investigator or researcher will be able to specify their designation in the form itself (i.e. undergraduate, post graduate, faculty, PhD candidate etc.

6.4 A nominal application fee, as decided by the appointing authority (Dean of KMC, Manipal), shall be paid by the Principal Investigator. The payment will be made to the Student's Finance Section, First Floor, Manipal Academy of Higher Education Building. The original fee paid receipt is to be scanned and uploaded with e submission. The IEC may over a period of time consider adding an online payment facility in the portal itself.

6.5 The principal investigator shall submit a soft copy (e-submission) of the entire project by uploading the project using the dedicated e-submission portal – IEC Interface. The instructions for such e-submission shall be openly displayed in the KH intranet webpage of http://172.16.7.105 / Knowledge Base / Ethics committee.

6.6 The IEC Secretariat, on receipt of the completed application, will prescreen the submission for any procedural deficiencies. If there is any procedural deficiency, the Principal Investigator will be informed of the deficiencies by a reply through IEC Interface. The PI shall resubmit the entire project ensuring that all procedural deficiencies noted are rectified

6.7 The last day for project submissions (after pre screening approval - to ensure that there are no procedural deficiencies) will be two weeks prior to the next IEC meeting (last Tuesday of the preceding month) to enable appropriate review by the IEC members. Late submissions will be deferred (and considered only in the next meeting)

6.8 The IEC Secretariat shall assign a unique number to the project. The IEC number will be intimated to the PI along with details of the IEC review meeting no later than 7 days before the scheduled full board meeting of the IEC. The IEC project number is to be used for all communications with the IEC

6.9 Investigators from outside KMC & KH desirous of carrying out research work under IEC will be

required to pay a fee to the KMC & KH as stipulated by the appointing authority.

6.10 Submission of Documents : One soft copy of the research project should be submitted with the following information

6.10.1 Name of the applicant with designation

6.10.2 Name of the Institute / Hospital / Field and area where research will be conducted

6.10.3 The departmental / institutional scientific committee should have approved the research prior to forwarding to the KMC & KH IEC

6.10.4 Approval of the Head of the Department/ Departmental Scientific committee / Head of the Institution where the PI normally works. A certificate to such effect should be enclosed or should be verified by the HOD that such a review process occurred before application to the ethics committee. The date of such a review shall be clearly stated in the letter to the chairperson.

6.10.5 A statement signed by all the investigators that the proposed study has not yet commenced. In case of retrospective studies, it is expected that data collection should not have commenced until after IEC approval has been obtained

6.10.6 A proposal rejected by another IEC of the Manipal Academy of Higher Education is not normally accepted for review by KMC & KH IEC, unless supported by a no objection certificate and details of previous submission

6.10.7 IEC Protocol submission form is to be filled in all aspects

6.10.8 Protocol of the proposed research

6.10.9 Ethical issues in the study and the plans to address these issues

6.10.10 All documents to be used in the study, such as proforma, case report forms, questionnaires, follow-up cards, rating scales, laboratory standardization certificates etc.

6.10.11 In case a module or a tool is to be developed as part of the study – the broad categories/ outline based on which the same will be developed should be submitted

6.10.12 Informed consent process, including Participant Information Sheet and Informed Consent form in the language(s) to be used in the study. (It is expected that the consenting subject will be given one Participant Information Sheet and a copy of the signed Informed Consent form, the other being retained by the Investigator

6.10.13 All submissions to the IEC have to be in typed versions (including translations and letters). No hand written material will be accepted by the IEC

6.10.14 For any drug / device trial, all relevant pre-clinical animal data and clinical trial data from other centres within the country / or other countries, if available

6.10.15 Curriculum vitae of all the investigators with a list of their relevant publications (numbers only) in the prescribed format.

6.10.16 For all Clinical trial (academic and regulatory), GCP training certificate of at least 1 investigator should be enclosed at the time of submission and all investigators before submission of the pilot/annual report.

6.10.17 Information regarding any regulatory clearance required from other agencies

6.10.18 Source of funding and financial requirements for the project. In case the source is yet to be finalized, the tentative source needs to be mentioned.

6.10.19 Other financial issues including those related to insurance and indemnification

6.10.20 An agreement to report any Serious Adverse Events (SAEs) to the IEC within 24hrs of actual occurrence or study team learning of the occurrence

6.10.21 Statement of conflicts of interest, if any

6.10.22 Declaration to comply with the relevant national and international guidelines

6.10.23 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.

6.10.24 A Memorandum of Understanding (MoU) for collaborative work being carried out with other institutes, multi-centric studies and International collaboration. For all projects involving collaborative work with faculty from Kasturba Medical college and Kasturba Hospital and/or recruitment from the said hospital, the investigators shall submit the permission letter in the format Approved by Dean, KMC

6.10.25 All significant previous decisions (e.g., those leading to a negative decision or a 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 also be provided

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

6.10.27 Any other information relevant to the study

6.11 When an investigator seeks KMC &KH IEC clearance for retrospective studies involving patients/their medical records he / she should submit the following

6.11.1 A written undertaking that the data reflects clinical features, treatments and outcomes which have arisen from following routine standards of care of patients and not an experiment of any sort outside such routine standard of care

6.11.2 A letter from the Medical Superintendent/Chief Operating Officer of the hospital sanctioning the use of such subject / patient information records

6.11.3 Hospital number of the subjects whose data is being accessed

6.11.4 When the subjects/patients concerned in the study have undergone care or intervention from more than one care giver/doctor for the problem under study, the investigator approaching the KMC &KH IEC must submit a letter from the primary care giver / other caregiver(s) stating their no-objection to use of the data for the study

6.11.5 The investigator must give an undertaking to the KMC &KH IEC that adequate care has been taken by him/her to anonymise the records to protect subject/patient confidentiality

6.11.6 Such above clarifications must be provided before collection of data along with a study design protocol and other information as in a routine submission to KMC &KH IEC for clearance.

6.12 Investigation team/ Research team shall be adequately qualified for carrying out the proposed research to ensure adequate quality of care provided during research. The applicant shall ensure that the following research team requirements are met while proposing to conduct research.

6.12.1 The Investigating team shall have a minimum of two members if the study involves any human population to ensure the safety of the participants and communications to the concerned in case of any unanticipated problems to one of the investigators.

6.12.2 Single person research shall be permitted only for certain in vitro and retrospective studies where risk to human participants is less than minimal.

6.12.3 All Interventional (treatment – pharmacological, device and non-pharmacological) studies which involve patient population mandatorily requires the presence of a Clinician and/or the intervention expert in the team based on the type of health condition and the nature of intervention.

6.12.4 For all interventional (treatment – pharmacological, device and non-pharmacological) studies, the intervention shall be delivered only by the trained/ qualified person only and the team shall comprise of at least one such investigator.

6.12.5 For all student projects (Undergraduate, Post graduate, Mphil, PhD etc.), the presence of a Qualified Guide is mandated and such additional investigators whose expertise may be required.

6.12.6 For all Collaborative research, each investigators shall declare their role in the study team in the MOU and/or Declaration form.

6.13 PhD candidates shall abide by the following additional considerations while applying for IEC clearance for their PhD research.

6.13.1 The PhD candidate shall submit the proposals to the Ethics committee only if the Guide is from constituent institutes of MAHE, Manipal or if the data collection is happening from the Kasturba Hospital or associated hospitals, centres of MAHE in the region.

6.13.2 The PhD candidate shall be termed as the Primary Student Researcher/ PhD Scholar and the Guide holds the Status of Principal Investigator.

6.13.3 However if the PhD candidate is already a teaching faculty in the institute, then he/she can be considered as Principal Investigator if the research domain comes under the expertise of the faculty. The Guide will be considered as Co-PI in such a scenario.

6.13.4 PhD candidates shall submit the Protocol to the Ethics committee for review only after the IRC and University DAC committee have given their approval.

6.13.5 For those PhD projects which require a pilot study to be conducted, and the design is different compared to the main study, the candidate is expected to seek a separate approval for the Pilot study with an appropriate modified title. Such candidates shall specifically state in the covering letter that the said study is a Pilot/ Preliminary work for assessing feasibility/ to finalize the design for the main Project and submit the IRC approval of the main project. The ethics committee submission for the main

PhD project shall occur once the project is finalized and the DAC has approved the main study.

6.13.6 PhD projects, where the need of pilot is just a smaller sample size of the main Project and purpose is to assess the safety/ defining the dose or frequency of intervention or assessment, the whole project may be submitted as a single submission.

6.13.7 PhD projects, where the project is streamlined with multiple phases and the initial phases are used to systematically arrive at a final tool or intervention, may also be submitted as a full project. However, the candidate should in such case, have a broad outline for the intervention planned or the tool to be developed. The candidate shall submit to the ethics committee, all the relevant PIS and IC appropriate for each of the phases at the time of application itself. The finalized tool/ intervention module may be submitted at a later date once developed as part of the progress report/ interim report.

6.13.8 If a PhD project is called for Full board review, then it is mandated that the Guide or Co-Guide is present for the discussion during the full board meeting. Failing which the project will be postponed for the next full board meeting.

6.13.9 If a PhD Project is called for monitoring, it is recommended that the Guide is also present during the meeting to ensure a single step process of decision making and communication of action.

6.13.10 All Comments to PhD projects will be sent as an Email to the Guide, provided they have submitted their manipal.edu email id.

6.14 Projects submitted by postgraduates, where the conduct of research is part fulfillment of their academic requirement shall be adequately scrutinized for feasibility during the time frame available for research. (Applicable for MD/ MS/ MCh/ DM/ Mphil/ Masters Program)

6.14.1 The Post graduate student shall submit Proposals to the IEC only with a teaching faculty as a Guide present in the investigating team.

6.14.2 The Post graduate shall be termed as the Primary Student Researcher and the Guide holds the Status of Principal Investigator.

6.14.3 The Post graduate student shall get approval of the Department Scientific Committee and/or Institutional Review Committee as applicable before submission to the Ethics Committee.

6.14.4 The Post graduate holds the primary responsibility of submission and follow up on the approvals and timely reporting of the project while the Guide holds the overall onus of the project and supervision of the research conduct by the Post graduate.

6.14.5 The Post graduate student shall submit all reports/ amendments/ other documents duly countersigned by the Guide to ensure that the Guide is able to monitor progress and changes occurring in the projects and provide appropriate guidance during submissions.

6.14.6 If a post graduate student project is called for the Full Board Review, then it is mandated that the Guide or Co-guide are present for the discussion during the full board meeting failing which the project will be postponed for the next full board

meeting.

6.14.7 If a Post graduate Student Project is called for monitoring, it is recommended that the Guide is also present during the process to ensure a single step process of decision making and communication of action.

6.14.8 All Comments to Post graduate projects will be sent as an Email to the Guide, provided they have submitted their manipal.edu email id.

6.15 Undergraduate projects which include projects taken as part of ICMR STS projects as well as non – ICMR related projects shall ensure that the research is kept simple and doable with the level of understanding at the undergraduate level. Research during internship will also be considered as an undergraduate project for the purposes of ethics of research.

6.15.1 The Undergraduate student shall submit Proposals to the IEC only with a teaching faculty as a Guide present in the investigating team.

6.15.2 The undergraduate student shall be termed as the Primary Student Researcher and the Guide holds the Status of Principal Investigator.

6.15.3 The Undergraduate student shall get approval of the Student Research Forum (SRF) in case of ICMR/ grant sponsored projects (to ensure that the research is found to be scientifically sound for application of the grant) before submission to the Ethics Committee.

6.15.4 The Guide or the guide's department as the policy may be in the department, may vouch for the scientific validity of the study allotted to the Undergraduate where it is not coming under the purview of ICMR or other grant projects.

6.15.5 While the undergraduate student may be responsible for the submission of documents to the Ethics committee and do the data collection as per his/her capacity, the Guide shall be primarily responsible for the research conduct and integrity of the research.

6.15.6 Undergraduate projects which are interdepartmental in nature, shall get the necessary permission from the department where the recruitment actually occurs or whose records are accessed.

6.16 Data collection in soft copy form or e-form is an acceptable form of data recording and storing recognized by the ICMR guidelines and is in keeping with the times of technology. The use of digital forms also appears as a viable solution for the space constraints specifically in research that have large recruitments or have huge number of data sheets and evaluation points. All such data collection research shall ensure that the following guidelines are adhered to while submitting the proposals or doing the data recording.

6.16.1 Data collection is preferred to be in a hard copy/ paper format to ensure adequate, timely and appropriate documentation.

6.16.2 The Ethics committee recognizing the need may permit projects that have clearly expressed the use of digital forms of data collection at time of submission of the proposal to the IEC. The investigators should in such case, have in its Protocol under

the procedure section, a sub heading on digital entry and storing of data and describe clearly the process to address the following concerns

6.16.3 Concerns to be addressed For digital data entry and storage.

a. Mention the software or portal that will be used to enter the data
b. Process in place to ensure that the data entry date and modification date is tracked.
c. All such forms shall be saved as a non-editable PDF on the same day as the data collection to ensure that the data is entered on real time basis.
d. The place where the data collection happens has no objections to use of electronic gadgets or such recording devices or has the necessary network access to upload data on real time basis.
e. The gadget used is exclusive for use of the research or that there is sufficient encryption and password protection in place to prevent data breach, data loss or data corruption.
f. The investigator also has a back up system in place which is equally encrypted and password protected to ensure safety of the data. The frequency at which the back up will be done should also be defined in the section on data entry and storage.
g. In case of cloud based back up system, the investigator should ensure that the facility has adequate privacy settings to prevent data access by service providers.

NOTE: Email based service providers may not have adequate sophistication for data privacy without payment for the services.

6.16.4 Any sharing of the data to person's outside the study team (in case study is part of multi-centric study), should be clearly stated and the methods used to ensure confidentiality should be detailed.

6.17 The investigators / Researchers, participants or any interested party may address or contact the Chairperson / Member Secretary for any further information at the meeting time slots advertised on the IEC webpage every week or at the below address, by prior appointment

The Chairperson / The Member Secretary
IEC Secretariat, KMC & KH Institutional Ethics Committee
Room 22, Ground floor
KMC Faculty Rooms Complex (adjacent to KMC Administrative Block)
Kasturba Medical College, Manipal - 576 104
Phone : +91 820 29 33522 E-mail : iec.kmc@manipal.edu
Intranet webpage : www.khinfo.edu (Knowledge base - Ethics Committee)

7. Review process

The purpose of this procedure is to elaborate administrative process and provide instructions for the IEC meeting agenda, review, approval, minutes, and communicating the decision to the Principal

Investigator (PI). It comprises conduct the IEC meeting and communicating decisions with the PI.

7.1 It is the responsibility of the Member Secretary, IEC and IEC staff to prepare and conduct the IEC meeting

7.2 Before full board IEC meeting

7.2.1 The Member Secretary prepares the agenda for IEC meeting

7.2.2 Review and passing of minutes from previous month

7.2.3 Schedule studies on the agenda on first come first serve basis. No limit is placed on the number of items on the agenda.

7.2.4 Primary and secondary reviewers will be assigned as necessary taking into account conflicts of interests of members. If a conflict of interest is identified, the study is assigned to another member who does not have a conflict of interest. It is the responsibility of the IEC member to identify any conflict of interest in a research project that will be reviewed at a convened IEC meeting and notify the IEC office of the conflict prior to the meeting.

7.2.5 It is general practice that IEC Chairperson and Member Secretary are not assigned primary reviewer responsibilities except in circumstances when their expertise is the most appropriate.

7.2.6 All projects to be reviewed by the IEC are to be forwarded to the IEC only by the PI of the project. All communications of the IEC will be only with the PI of the project who has the access to the project page on the Interface. Only if the PI is not available (on leave / outside the country / left the institute) will the IEC opt to communicate with the other investigators. All the Co-investigators shall get an SMS update indicating the name of the PI. The co-investigators shall then clarify from the PI the communication made by the Ethics committee. In case of Monitoring or SAE, All investigators shall be additionally communicated through Email.

7.2.7 The office of the IEC, after receiving a proposal, will pre screen each proposal and communicate with the PI through IEC Interface or telephonically to ensure that all incomplete submissions and deficiencies are corrected before acceptance of the proposal for review. Preliminary communication, following prescreening approval, is sent to all the investigators informing them of the decision to review the project in the next full board meeting.

7.2.8 The Member Secretary shall assign the responsibilities of prescreening of projects submitted by e-submission to the members of IEC. The members of IEC during prescreening shall check for adequateness of document submission, compliance with rules and regulations, adequate representation of information including duration of study, availing permission, and information of study participants, etc.

7.2.9 It is the responsibility of the Member Secretary to screen, identify and categorize research studies and documents depending on the risk involved in the research study. Categorization of projects shall be in reference to 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR into three types, viz.

Exempt from review : Proposals with less than minimal risk where there are no linked identifiers

Expedited review : Proposals that pose minimal risk or minor increase over minimal risk (low risk) may undergo expedited review

Full committee review : All research proposals presenting more than minimal risk (high risk) that are not covered under exempt or expedited review should be subjected to full committee review

7.2.10 A researcher cannot decide that her/his proposal falls in the exempted, expedited or full review category. All research proposals must be submitted to the EC. The decision on the type of review required rests with the IEC and will be decided on a case-to-case basis. Researchers can approach the EC with appropriate justification for the proposal to be considered as exempt, expedited or if waiver of consent is requested.

7.2.11 If the IEC Secretariat receives a project eligible for exempt category, the Member Secretary shall assign a Member to review the project as a whole. The assigned Member shall communicate the decision to permit exempt status by e-mail/ Interface. The exempt status approval certificate shall be granted forthwith, however all exempt category projects will be ratified at the next full committee meeting

7.2.12 Approval granted through expedited review and the decisions of the Monitoring Subcommittee shall be ratified at the next full committee meeting.

7.2.13 The office of the IEC will ensure that project documents are distributed to the IEC members / uploaded to the webpage or printed copies are dispatched by courier (to external members) at least 7 days in advance of the scheduled meeting

7.2.14 The individual members will notify the Member Secretary or Secretariat if they have not received their project packages.

7.2.15 The IEC secretariat will inform the Principal Investigators of the Full Committee Review through IEC Interface, the Scheduled meeting date and time. The Principal investigators of the Expedited and exempt category projects will receive the communication of the meeting date (for ratification) but without a time slot.

7.3 At the IEC meeting

7.3.1 Day: The meeting will be held on **s**econd Tuesday of the month (unless otherwise notified). If the second Tuesday is a holiday, the IEC meeting will be scheduled for the following Tuesday. Additional meetings may be held as and when the proposals are received for review, and cannot be accommodated in the regular meeting or when such proposal need to be disposed off as an emergency. The decision for calling additional meetings rests with the Chairperson.

7.3.2 Time : 2.00 PM (unless otherwise notified)

7.3.3 Venue : Research Cell, Ground Floor, KMC Faculty Rooms Complex, Adjacent to KMC Administrative Building, Kasturba Medical College, Manipal.

7.3.4 All original files of studies on the agenda will be made available for projection in the meeting room, for ready reference during the meeting

7.3.5 Copies of SOPs, ICMR guidelines, ICH-GCP, New Drugs and Clinical Trials Rules 2019, CIOMS guidelines and any other relevant reference document are kept available for ready reference

7.3.6 The meeting will be re-scheduled or cancelled if it becomes apparent that meeting requirements (quorum, sufficient expertise) will not be met. If an individual project cannot be taken up due to lack of expertise, the same will be conveyed to the Principal Investigator and an alternate time schedule informed.

7.3.7 There is no fixed number of projects to be reviewed by the IEC. The number of research projects reviewed may vary as per the submission and approval by pre-screening.

7.4 Conduct of the IEC meeting

The IEC members will meet in the IEC meeting room at the scheduled time.

The Member Secretary shall begin the meeting and ensure the following

7.4.1 Ensure that the quorum is fulfilled.

7.4.2 Request to declare conflict of interest either verbally or written on any project for discussion. The members with a conflict of interest must excuse themselves from deliberation and voting on that research project. This will be recorded in the minutes.

7.4.3 The Member Secretary should present the agenda for the current meeting

7.4.4 The Member Secretary should present minutes of IEC as well as major issues / policies discussed in the previous meeting.

7.4.8 Though all Members will have access to all projects being reviewed by the committee, and can review and comment on any project even if they are not primary / secondary reviewers, each member shall fulfill the specific roles in the review process as elucidated in the ICMR Guidelines 2017. For regulatory studies, a print version of comments in the form of a checklist, will be required to be completed by the specified member based on the below mentioned specific role as reviewer

Basic Medical Scientist(s)	• Scientific and ethical review with special emphasis on the intervention, benefit-risk analysis, research design, methodology and statistics, continuing review process, SAE, protocol deviation, progress and completion report • For clinical trials, pharmacologist to review the drug safety & pharmacodynamics
Clinician(s)	• Scientific review of protocols including review of the intervention, benefit-risk analysis, research design, methodology, sample size, site of study and statistics • Ongoing review of the protocol (SAE, protocol deviation or violation, progress and completion report) • Review medical care, facility and appropriateness of the principal investigator, provision for medical care, management and compensation • Thorough review of protocol, investigators brochure (if applicable) and all other protocol details and submitted documents
Legal expert/s	• Ethical review of the proposal, ICD along with translations, MoU, Clinical Trial Agreement (CTA), regulatory approval, insurance document, other site approvals, researcher's undertaking, protocol specific other permissions, such as, stem cell committee for stem cell research, HMSC for international collaboration, compliance with guidelines etc. • Interpret and inform EC members about new regulations if any
Social scientist / philosopher/ Ethicist / theologian	• Ethical review of the proposal, ICD along with the translations. • Assess impact on community involvement, socio–cultural context, religious or philosophical context, if any • Serve as a patient/participant/ societal / community representative and bring in ethical and societal concerns
Lay person(s)	• Ethical review of the proposal, ICD along with translation(s) • Evaluate benefits and risks from the participant's perspective and opine whether benefits justify the risks • Serve as a patient/participant/ community representative and bring in ethical and societal concerns • Assess on societal aspects if any

7.4.5 Amendment /Continuing review application /SAEs / Documents will ordinarily be reviewed by Member Secretary or a previously assigned lead discussant of the respective sub committee

7.4.6 In case the Member Secretary of the IEC is the Principal Investigator for project under discussion, the IEC member nominated as Deputy Member Secretary will perform the function of the Secretary only for that study. The Member Secretary should declare his conflict of interest and leave the meeting room.

7.4.7 The IEC members shall indicate their observations and comment for each project, under two headings, viz.

Procedural issues (missing documents / information, unclear methodology / recruitment process, inconsistencies in the protocol etc.)

Ethical issues (vulnerability, consenting process, confidentiality, risk benefit analysis,

equitable distribution, justice etc.)

7.4.9 All procedural and ethical issues of the protocols requiring full board review shall be clarified from the PI during the meeting and a decision shall be arrived at after discussion of the same.

7.4.10 In case the lead discussant cannot attend the meeting, the Member Secretary or any other IEC member may brief the IEC about the research study and also discuss the written comments /duly filled study assessment form, if provided by the lead discussant

7.4.11 During the initial or continuing review of the research, material provided to IEC members will be considered confidential and the IEC members will assure the confidentiality of the information provided to them.

7.4.12 Audio or video recording of the proceedings is not permitted.

7.4.13 In the normal course, the PI / guide would be present at the meeting to offer clarifications, if necessary. Prior permission may be sought for the absence of the PI / guide and substitution with his / her representative. For all Student projects called for Full committee meeting, the presence of a Guide/Co-guide is mandatory.

7.4.14 Only the investigators are expected to attend the meeting and if any other person interested in the study wants to be present at the IEC meeting, prior written permission from the Chairperson / Member Secretary shall be obtained.

7.4.15 The Member Secretary minutes the proceedings of the IEC meeting

7.5 Elements of review : The IEC during the full board meeting may seek clarifications from the PI on any aspect of the project including but not restricted to

- Scientific design and conduct of the study.
- Approval of appropriate scientific review committees if existing. Examination of predictable risks / harms.
- Examination of potential benefits.
- Procedure for selection of subjects in methodology such as inclusion, exclusion and withdrawal criteria and other issues like advertisement details.
- Management of research related injuries, adverse events. Compensation provisions.
- Justification for placebo in control arm, if any. Availability of products after the study, if applicable.
- Patient information sheet and informed consent form in local languages.
- Protection of privacy and confidentiality. Involvement of the community, wherever necessary. Plans for data analysis and reporting.
- Adherence to all regulatory requirements and applicable guidelines. Competence of investigators, research and supporting staff.
- Facilities and infrastructure of study sites.
- Criteria for withdrawal of patients, and suspension or termination of the study.

7.6 Decision Making Process

The purpose of this procedure is to elaborate on the steps involved in the decision making process of the IEC for the projects reviewed as well as for any post approval deliberations.

7.6.1 Decisions will only be made at meetings where a quorum is present

7.6.2 An IEC member will withdraw from the meeting for the discussion and decision procedure concerning the study where conflict of interest exists

7.6.3 If any IEC member has her/his own proposal for IEC review he/she will not participate in the IEC discussion or vote on that particular project

7.6.4 Decisions will be arrived at through consensus/unanimous or majority opinion amongst the voting members of IEC. The decision-making is thus concerned with the process of deliberating and finalizing a decision. Only when a consensus is not possible, the IEC members will vote.

7.6.5 Voting procedure:

- This may be in the form of voice vote, show of hands, or by secret ballot, as determined by the Chairperson, IEC.
- All members including the Chairperson are entitled to one vote. However, in case of a tie, the Chairperson will have the casting vote
- If voting is resorted to, the number of members voting for, against, and abstaining will be recorded. The recusal of the IEC member for conflict of interest is recorded in the IEC meeting minutes. The concurrence/voting of the members will be recorded in the minutes as - Agreed / Disagreed / Abstained

7.6.6 Representative of the patient groups or community may be invited during deliberations to offer their viewpoint. Subject expert(s) may be invited to offer their views, but expert(s) will not participate in the decision making process. However, his / her opinion will be recorded.

7.6.7 Subject experts may be invited by the Chairperson of IEC, to offer their views on a specific issue or a proposal being reviewed. These experts may be specialists in ethical or legal aspects, specific diseases, technologies or methodologies. The IEC may adopt system for pre-meeting peer review by subject experts and obtain clarifications from the researchers prior to the meeting.

7.6.8 If expertise with a specific population (like Neonatology, Genetics and Artificial Reproductive Technology) is needed but not available from the IEC members, an expert opinion is sought or a consultant is invited to the meeting or join via video / tele conference to discuss the issues involved. His/her opinion is minuted.

7.6.9 If expertise is needed but not available from the IEC members regarding Alternate Medicine (including Yoga, Ayurveda, Unani, Siddha, Homeopathy and naturopathy), an expert opinion is sought as in 7.6.8 above.

7.6.10 The IEC shall ensure that the expert invited to give an opinion will have the requisite experience, but not less than two years of practice in that field of expertise. A copy of the CV of the invited expert specifying his expertise shall be archived by the IEC

7.6.11 The comments of the subject experts / an independent consultant may be presented by the Member Secretary, if the subject expert is not attending the meeting. The

invited expert may also be permitted to communicate with the Full Committee by online video conferencing.

7.6.12 The invited expert will be required to sign a Conflict of Interest and Confidentiality agreement before being assigned any review.

7.6.13 The invited expert shall be paid a review fee and if required to attend the meeting, An additional sitting fee as approved by the Dean / Appointing authority

7.6.14 When specific patient subpopulations (based on disease, social status or other variable) are the subject of investigation, their own representative may also be invited as a subject expert.

7.6.15 In all the above circumstances where a subject expert is invited by the IEC, the subject expert will not participate in the decision making and will not have a voting right in IEC.

7.6.16 When projects with vulnerable patient subpopulations (as defined in the ICMR Guidelines 2017) is submitted to the IEC for review, the IEC shall specify what measures are being taken by the PI/research team and the IEC to address the vulnerability.

7.7 Decisions regarding recruitment

7.7.1 The IEC approval certificate shall specify the time period for which the study is approved (date to date) during which recruitment and study procedures / process can be taken up by the investigator.

7.7.2 The IEC shall inform the PI of any pending (applied but not received) permission / approval letters from administrative / regulatory bodies. These are to be submitted before commencement of recruitment.

7.7.3 The IEC shall intimate the PI to prospectively register select studies in the Clinical Trial Registry of India (CTRI).

7.7.4 All clinical research involving human participants including any intervention such as drugs, surgical procedures, devices, biomedical, educational or behavioural research, public health intervention studies, observational studies, implementation research and preclinical studies of experimental therapeutics and preventives or AYUSH studies may be registered prospectively with the CTRI.

7.7.5 The IEC approval certificate shall state that PI will commence recruitment of participants only after such registration. The IEC on its part will document the CTRI acknowledgment and registration numbers in the consolidated comments form.

7.7.6 The IEC shall also recommend GCP training for investigators involved in Regulatory clinical trials as well as academic clinical trials and interventional studies.

7.7.7 For changes in the recruitment process (change in sample size, recruitment place and/or recruitment period, inclusion / exclusion criteria etc), the PI shall seek an amendment and obtain approval prospectively.

7.7.8 In case of any noncompliance in recruitment process, the PI will be asked to exclude the participants from the study analysis. The IEC shall record the same in the minutes of the monitoring meeting

7.7.9 The Ethics Committee shall mandate Health Ministry's screening committee (HMSC)

clearance for all studies with International Collaboration as per the recommendation of the ICMR Guidelines for Biomedical Research.

7.7.10 Any self funded, Scholarship/Fellowship awarded to the candidate/scholars to work in India for pursuing higher education/research may not require HMSC clearance but shall require to abide by and follow the requirements of the host institutes and/or concerned department by circulation. These are considered as an educational activity as part of their career development. The IEC, if felt necessary as the case may refer the projects for HMSC consideration.

7.8 Addressing risk, scientific validity and ethical concerns during decision making process and periodic approvals

7.8.1 The IEC's Protocol Submission form, protocol and PIS specifically mandates the investigator to indicate the type and degree of risk involved to the participants. The risk categorization shall be in reference to 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR.

7.8.2 For all projects, the risks will be indicated in one of the 4 broad categories (for an individual project only one (the higher category if there are multiple phases / components) category will be applied

Less than minimal risk : Probability of harm or discomfort anticipated in the research is nil or not expected.

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

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 research on vulnerable population, delaying or withholding a proven intervention or standard of care, use of minimally invasive procedures and trying a new diagnostic technique in pregnant and breastfeeding women. 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.

7.8.3 Risk associated with devices will be indicated in 4 broad categories

A - Low : Thermometers/ bandages /tongue depressors

B - Low moderate : Hypodermic needles /suction equipment

C - Moderate high : Lung ventilator /bone fixation plate

D - High : Heart valves/implantable defibrillator

7.8.4 For all projects, the benefits will be indicated in 3 broad categories (for an individual project any or all three (direct benefit to participant, indirect benefit to participant and benefit to society) benefit categories may be indicated

7.8.5 Benefit-risk assessment involving diagnostic agents additionally includes the assessment of benefits, such as technical performance, diagnostic performance, impact on diagnostic thinking and impact on patient management/outcome, and the risks related to the agent itself, such as immunogenicity, allergic reactions, but also risks related to incorrect handling of test procedures or incorrect diagnosis induced by its use.

7.8.6 The Protocol submission format also ensures that the investigator gives justification for conduct of the study, declares ethical concerns and provides a review of literature which will aid the reviewer in the decision making process.

7.8.7 The IEC ensures that the research proposals are approved by the Institutional Research Committee / Departmental Scientific Committee before submission to IEC for review.

7.8.8 The office of the IEC, after receiving a proposal, will prescreen each proposal and communicate with the PI by e-mail or telephonically to ensure that all incomplete submissions and deficiencies are corrected before acceptance of the proposal for review.

7.9 Types of decisions

7.9.1 Approved : The study is approved in its present form, with or without suggestions or comments

7.9.2 Revision with minor modifications : In cases of revision with minor modifications clear suggestions and reasons for revision will be specified. When modifications are submitted; these will be reviewed either by the Member Secretary, by the respective lead discussant or expedited review. If revisions are found satisfactory, approval will be granted.

7.9.3 Revision with major modifications for resubmission : Extensive revisions are necessary. Principal Investigator has to comply with the changes suggested by IEC and respond to the queries. The revised project will then be reviewed in the next full committee for reconsideration for approval.

7.9.4 Not approved (or termination/revoking of permission if applicable) : The study is not approved in its current form. A negative decision on an application will be supported by clearly stated reasons. If an investigator disagrees with the IEC decision to disapprove or terminate a study, the Investigator may submit a written appeal within 14 days of being notified of the decision. The appeal should address the specific concerns of the IEC and a justification for the appeal with relevant review of literature and references. The appeal will be reviewed by the full committee. The PI will be invited to the convened meeting to provide clarification or additional information to

the IEC.

The IEC may decide to accept or deny the appeal. This will be done by voting and a record of division of votes will be recorded in the minutes. The Principal Investigator will be notified in writing of the decision. If denied, the IEC will not consider any further deliberations of the proposed project in the existing format.

7.9.5 Defer : The decision cannot be arrived at present and therefore postponed to the next meeting. Grounds for this include lack of quorum, lack of expertise etc. The Principal Investigator will be informed in writing regarding the next schedule.

7.10 After the IEC meeting

7.10.1 The Member Secretary will document and compile the proceedings of IEC meeting in a concise and easy-to-read style and will check spelling, grammar and context of the written minutes.

7.10.2 The minutes of the meeting will be finalized within 15 working days. The basis for requiring changes in or disapproving research; and a written summary of the discussion of controversial issues and their resolution must be recorded.

7.10.3 The comments of the IEC will be intimated to the PI through IEC Interface. The communication of the comments shall only be done after endorsement by the Chairperson and the Member Secretary.

7.10.4 It is the responsibility of the PI to contact the Secretariat if he / she has not received the e-mail communicating the decision, and enquire about the status of the review. The PI should then comply with additional requirements / clarifications at the earliest.

7.10.5 The minutes of the IEC meeting will be endorsed by the Chairperson and Member Secretary who shall sign the minutes as soon as finalized. The minutes will be ratified in the next Full Committee Meeting and then filed in the IEC minutes file. The IEC minutes file will be used by the IEC secretariat for administrative purposes.

7.10.6 The active comments form shall be maintained as a soft copy on the iec.kmc@manipal.edu drive and dynamically updated and compiled. The IEC shall aim at having all the active comments in the IEC Interface in the long run.

7.10.7 All pending corrections and amendments will be closed if not addressed within 100 days of the IEC meeting and be deemed lapsed. If the lapsed project has not been reverted with the due penalty fee equivalent to the processing fee by 180 days of the IEC meeting, the project will be considered as withdrawn.

7.11 Communicating Decision

The purpose of this procedure is to specify the mode and process of communicating the decisions to the principal investigators and the regulatory bodies as per the rules and regulations

7.11.1 The Member Secretary as part of the communication of the review decision shall intimate the PI through IEC Interface the modifications / corrections / comments recommended by the IEC. However, it is the responsibility of the PI, after the scheduled IEC full board meeting, to enquire with the Member Secretary the comments and modifications suggested by the IEC if the expected communication

has not been received even after 15 working days following the IEC meeting.

7.11.2 The PI shall submit all revisions in due time, preferably within a period of 14 working days of the IEC meeting at which the decision was made.

7.11.3 If the PI does not submit the required corrections within 60 days, a reminder alert maybe sent by the IEC Secretariat to the PIs IEC Interface. If the PI does not comply with the suggestions of the IEC within a period of 100 days from the IEC meeting at which the decision was made, the proposal shall be deemed to have lapsed and will not accept any corrections unless reverted.

7.11.4 A penal fee, equal to the original application fee shall be payable by the PI to revert a lapsed project. The decision to revert a lapsed study after a period of 100 days shall rest with the IEC, but shall not exceed 180 days from the Full Committee Meeting date for the project. At end of 180 days, if the investigator has not reverted the project and submitted the modifications, the project shall be deemed permanently withdrawn.

7.11.5 Validity of approval will be for the complete duration of the study. This approval is subject to at least an annual review and the endorsement in the IEC project approval certificate. Failure to submit annual status report by the due date will result in the expiration of approval. More frequent review may be asked for specific proposals with higher risk perception, at the discretion of the IEC.

7.11.6 After approval of the project by the IEC, the PI is issued a project approval certificate in the prescribed format. Annual endorsement (as indicated in the IEC project approval certificate) is the responsibility of the PI.

7.11.7 The IEC may decide to reverse its positive decision on a study if it receives information (through either Amendment, Monitoring, annual status report, report of Serious Adverse Events or new review of literature) that may adversely affect the risk/ benefit ratio

7.11.8 All decision and approval letters will be dated and signed by the Member Secretary of the IEC. In case the Member Secretary IEC is an Investigator, the decision letters will be duly signed by Deputy Member Secretary IEC.

7.12 Continued approval for projects with duration more than one year

7.12.1 When approval is sought for a project period of more than one year, the IEC shall approve and issue a certificate for the requested time period, with the certificate having provision for annual endorsements of continued approval. The PI is responsible for timely (**BEFORE** the due date indicated in the IEC approval certificate) e-submission of the Interim Annual Report Form along with the scanned copy of the IEC approval certificate. The IEC Secretariat will subsequently endorse the same in the original IEC certificate.

7.12.2 When approval is sought for a project that has a pilot study for determining the sample size, time frame or an intervention to be designed or checked for safety, the IEC shall issue a certificate for the project, with the certificate having provisions for endorsement of continued approval after the pilot study. The PI is responsible for timely submission of the pilot study report (as indicated in the IEC approval

certificate) and subsequent endorsement in the IEC certificate. If the IEC considers that the pilot study justifies termination of project, the same will be communicated to the PI.

7.12.3 Upon submission of interim report / pilot report / annual report by the investigator, the IEC shall evaluate the submitted report. If required, the IEC shall reassess the project and its progress for continuation of approval status. If there is any concern regarding the project, clarifications may be sought from the PI and / or may be referred to the full board. The PI may be intimated to withhold the project until the IEC communicates its decision on continued approval.

8. Exempt from review

This procedure will guide the Member Secretary to determine whether the study qualifies for exemption from review and do not require the approval of the IEC. The decision should be taken by the Member Secretary in consultation with the Chairperson and should be minuted in the forthcoming IEC meeting.

8.1 Proposals which **involve less than minimal risk** fall under this category.

Minimal risk would be defined as one which may be anticipated as harm or discomfort not greater than that encountered during routine daily life activities of the general population or during the performance of routine physical or psychological examination or tests.

Proposals with less than minimal risk where there are no linked identifiers may be considered as having potential for exemption from review

8.1.1 Research conducted on data available in the public domain for systematic reviews or meta-analysis

8.1.2 Observation of public behaviour when information is recorded without any linked identifiers and disclosure would not harm the interests of the observed person

8.1.3 Quality control and quality assurance audits in the institution

8.1.4 Comparison of instructional techniques, curricula, or classroom management methods

8.1.5 Consumer acceptance studies related to taste and food quality

8.1.6 Public health programmes by Govt agencies such as programme evaluation where the sole purpose of the exercise is refinement and improvement of the programme or monitoring (where there are no individual identifiers).

8.1.7 Research proposals which do not involve living human participants.

8.1.8 Research proposals which involve data derived from humans without any possibility of access to identifiable personal data

8.1.9 Research on microbes cultured in the laboratory or commercially available

8.1.10 Research on commercially available immortalized cell lines

8.1.11 Analysis of data freely available in the public domain

8.1.12 Studies involving anonymized extracted teeth

8.2 If the IEC Secretariat receives a project eligible for exempt category, the Member Secretary shall assign a Member to review the project as a whole. The assigned Member shall communicate the decision to permit exempt status by e-mail. The IEC Secretariat will communicate the decision to the PI, at the earliest, certainly within 7 working days of assigning a project IEC number / prescreening approval. The exempt status approval certificate shall be granted forthwith, however all exempt category projects will be ratified at the next full committee meeting

9. Expedited review

This procedure will guide the Member Secretary to determine whether the study qualifies for expedited review by the IEC.

9.1 The proposals which involve no more than minimal risk to research participants may be subjected to expedited review.

9.2 The IEC shall consider the following situations as having potential for expedited review :

9.2.1 Research involving non-identifiable specimen and human tissue from sources like blood banks, tissue banks and left-over clinical samples

9.2.2 Research involving clinical documentation materials that are non- identifiable (data, documents, records) that have been collected for non-research (clinical) purposes

9.2.3 Modification or amendment to an approved protocol. Study related documents which would be considered for expedited review:

i. Minor deviations from originally approved protocol
ii. Inclusion or deletion of name/s of co-investigator/s
iii. Request for change in PI or hand over of trials or projects
iv. Minor amendments in the protocol, CRF, eCRF or correction of typographical errors
v. Minor corrections in budget
vi. Other administrative revisions like change in the name, address of sponsor, change in contact details of PI and IEC.

9.2.4 Revised proposals previously approved through expedited review, full review or continuing review of approved proposals

9.2.5 Minor deviations from originally approved research during the period of approval causing minimal or less than minimal risk.

9.2.6 Progress/annual reports where there is no additional risk, for example activity limited to data analysis. Expedited review of SAEs / unexpected AEs will be conducted by the Monitoring Subcommittee

9.2.7 For multicentre research where a designated main EC among the participating sites has reviewed and approved the study, a local EC may conduct only an expedited review for site specific requirements in addition to the full committee common review

9.2.8 Research during emergencies and disasters when a full committee review of the research is not possible

9.3 The PI submits study protocol with necessary documents attached as mentioned in SOP for IEC in the covering letter. Upon receipt Member Secretary, IEC makes a preliminary determination that the application / research proposal / documents meet the criteria for expedited review. All the necessary documents will be provided to the designated reviewer/s.

9.4 The IEC shall endeavor to complete the expedited review process for the above category of projects within a period of 14 working days from the date of assigning a project IEC number.

9.5 Expedited review does not imply faster review. It does not mean that the proposal will be circulated and decision taken by only the designated reviewer(s).

9.6 Research during humanitarian emergencies, epidemics and disasters can be reviewed through an expedited review/scheduled/unscheduled full committee meetings and this may be decided by the Member Secretary on a case-to-case basis depending on the urgency and need. In exceptional situations, preliminary research procedures including but not restricted to data/sample collection that are likely to rapidly deteriorate or perish may be allowed while the review process is underway. If an expedited review is done, full ethical review should follow as soon as possible.

9.7 A natural disaster of cyclical frequency is an expected phenomenon. Researchers and sponsors could make arrangements about research questions to be addressed in the design, collection of samples and data, and sharing mechanisms much in advance of a future humanitarian emergency.

9.8 The EC could review proposals prior to the occurrence of the emergency and determine who could be an acceptable LAR in the absence of intended LARs (authorized /acceptable) in such situations.

9.9 The different roles of researchers, caregivers and volunteer workers must always be clarified, and potential Conflict of Interest declared. If research involves incompetent individuals (such as minors), then the LAR should give consent. Additional protections might be required in special cases, for example children with untraceable or deceased relatives. In these situations, the consent should be obtained from an individual who is not part of the research team who should be designated by the institution/agency conducting research. When the relatives are traced reconsent should be obtained

10. Full Committee Meeting

This procedure will guide the Member Secretary to determine whether the study qualifies for full committee review by the IEC.

10.1 The proposals which involve more than minimal risk to research participants may be subjected to full committee review.

10.2 The IEC shall consider the following situations as having potential for full committee review :

10.2.1 Research involving vulnerable populations, even if the risk is minimal

10.2.2 Research with minor increase over minimal risk

10.2.3 Studies involving deception of participants

10.2.4 research proposals that have received exemption from review, or have undergone expedited review/undergone subcommittee review should be ratified by the full committee, which has the right to reverse/or modify any decision taken by the subcommittee or expedited committee

10.2.5 Amendments of proposals/related documents (including but not limited to informed consent documents, investigator's brochure, advertisements, recruitment methods, etc.) involving an altered risk

10.2.6 Major deviations and violations in the protocol

10.2.7 Any new information that emerges during the course of the research for deciding whether or not to terminate the study in view of the altered benefit–risk assessment

10.2.8 Research during emergencies and disasters either through an expedited review / scheduled or unscheduled full committee meetings. This may be decided by Member Secretary depending on the urgency and need

10.2.9 Prior approval of research on predictable emergencies or disasters before the actual crisis occurs for implementation later when the actual emergency or disaster occurs.

10.3 The Member secretary shall ensure that sufficient time is allotted for discussion during the meeting based on the nature of the project and the risks involved.

11. Regulatory Clinical trials and Academic Clinical Trials

A clinical trial is any research/study that prospectively assigns human participants or groups of humans to one or more health-related intervention(s) to evaluate the effects on health outcomes. The intervention could be drugs, vaccines, biosimilars, biologics, phytopharmaceuticals, radiopharmaceuticals, diagnostic agents, public health interventions, socio-behavioural interventions, technologies, devices, surgical techniques or interventions involving traditional systems of medicine, etc.

As per the New Drugs and Clinical Trial Rules 2019, "clinical trial" in relation to a new drug or investigational new drug means any systematic study of such new drug or investigational new drug in human subjects to generate data for discovering or verifying its,- (i) clinical or; (ii) pharmacological including pharmacodynamics, pharmacokinetics or; (iii) adverse effects, with the objective of determining the safety, efficacy or tolerance of such new drug or investigational new drug

11.1 SOP on Medical Devices

A medical device is defined as a medical tool which does not achieve its primary intended action in or on the human body by pharmacological, immunological, or metabolic means but which may be assisted in its intended function by such means. It may be an instrument, apparatus, appliance, implant, material or other article, whether used alone or in combination, including a software or an accessory, intended by its manufacturer to be used specially for human beings or animals for one or more of the specific purposes of:
(i) detection, diagnosis, prevention, monitoring;
(ii) treatment or alleviation of any physiological condition or state of health, or illness;
(iii) replacement or modification or support of the anatomy or congenital deformity;
(iv) supporting or sustaining life;
(v) disinfection of medical devices; or
(vi) control of conception.

Medicated devices: These are devices that contain pharmacologically active substances which are treated as drugs.

Medical devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intra-ocular lenses, orthopedic pins and other orthopedic accessories. Their purpose varies from being used primarily for specific affected parts of the body to being used as adjunct to primary therapies

11.1.1 The ethics committee shall ensure that Clinical trials on devices should be conducted in accordance with the ethical principles in New clinical trial and Drugs Act 2019, Indian GCP as well as applicable regulations for medical and medicated devices, that is, GSR 78 (E) dated 31.1.2017 or as per amendments/modifications issued from time-to-time.

11.1.2 For all in vivo devices safety data of the medical device in animals should be obtained and likely risks posed by the device should be considered in the same way as for a new drug under the New Drugs and Clinical Trial Rules 2019.

11.1.3 The ethics committee shall look at the safety aspect of the device and if required seek opinion from external expert from the specified field. Apart from safety considerations the EC shall ensure that

a) Devices should be provided free of cost or, if expensive in case of post marketing surveillance or academic trials (for standard of care), at feasible reduced rates.
b) Avoid therapeutic misconceptions.
c) Any AE/SAE should be reported within timelines as per the schedule for a new drug.
d) That the user/ operator of the device is adequately trained/ skilled for the purpose. To ensure that the user error as the cause of AE/SAE can be minimized.
e) In case of internal devices, the Participant information sheet should clearly explain the fact that it may not be possible to remove the device, even if they withdraw from the study. The participant, however, should be allowed to opt out of continuing in the trial without prejudice to her/his ongoing treatment.
f) If feasible, post-trial obligations should be emphasized with the sponsor.
g) The duration of follow-up should be long enough to detect late onset adverse reactions, especially when the device is implanted within the body.
h) Devices could be used internally or externally for diagnosis, treatment, mitigation or prevention of disease or disorder.

11.1.4 Depending upon risks involved, devices (other than in vitro diagnostic devices) are classified as given in the table below.

Class	Level of risk	Device examples
A	Low	Thermometers/ bandages / tongue depressors
B	Low – Moderate	Hypodermic needles /suction equipment
C	Moderate – High	Lung ventilator /bone fixation plate
D	High	Heart valves/implantable defibrillator

11.1.5 In-vitro devices: Devices used for in vitro diagnosis could be a reagent, calibrator, control material, kit, instrument, apparatus, equipment, system, or specimen receptacle, whether used alone or in combination with any other such devices, that is intended by its manufacturer to be used in vitro for examination of any specimen, including any blood or tissue donation derived from the human body solely or principally for the purpose of providing information.

- The information could be related to:
  (i) a physiological or pathological state;
  (ii) congenital deformity;
  (iii) determining the safety and compatibility of any blood or tissue donation with a potential recipient thereof; or

(iv) monitoring of therapeutic measures.

11.1.6 Diagnostics devices can be notified and non-notified. Notified are in vitro diagnostic devices for testing HIV, HBsAg, HCV and blood grouping. Non-notified are those for testing malaria, TB, dengue, chikungunya, typhoid, syphilis, cancer markers, etc.

11.1.7 List of Documents to be submitted for the DEVICE studies

a. Ethics Committee submission form
b. Ethics Committee review fee receipt
c. Scientific committee/ research committee/ Governing body approval
d. Project Protocol (with Title, aims and objectives, study type, justification for the study/ brief introduction, recruitment sites, sample size, study period, methodology, inclusion/exclusion criteria, Tools being used, time lines, Risks and benefits, outcome measures, safety check/risk reduction measures, withdrawal, early termination criteria, any monitoring/audit processes in place for quality assurance, ethical concerns anticipated and ways to address the same.
e. Budget and financial statement including break up of the budget to carry out the project
f. Investigator's brochure for recruiting subjects
g. Clinical Research Form, Questionnaires with permission or purchase document (in vernacular languages as well if self-rated instruments involved)
h. Participant information Sheet and Informed consent for the device trial (including in vernacular languages)
i. Additional ICF for any Audio visual recording involved.
j. Sponsor information and undertaking
k. MOU with Sites/investigators and Clinical Trial Agreement
l. CDSCO Device registration – This is now done online through Sugam portal as per the Medical Devices Act 2017.
m. Validation Report if any, Studies using similar technology if available to be submitted.
n. New Device information (technology, components, materials used, operation method, potential risks and effects)
o. HMSC approval (after Ethics Committee approval – in case of data/material transfer outside India)
p. Trial Insurance copy – including payout limits, premium paid, Terms and Conditions.
q. CV of Investigators
r. GCP training certificate of investigators
s. Any Additional documents as requested by the Ethics committee where the submission is occurring.
t. Checklist of the documents

11.1.8 Academic Device trials: academic device trials are those trails which are academician or investigator initiated trail where the purpose of study is to explore the possibilities of use of device for a new indication, modification of an existing device to suit local patient needs and where the intent is not for marketing purposes.

11.1.9 Device Validation studies submitted by investigator and done in collaboration with industry and/or in collaboration with BIRAC and such other govt. funding agencies shall submit a letter from the industry stating that the said study findings will only be used for device development and not for marketing purposes.

11.1.10 The IEC takes cognizance of the fact that all devices will be considered as notified from April 2020 and recommend for CDSCO registration unless specified by the CDSCO as non-notified. The investigator shall get an NOC from the CDSCO to stake the claim of the same in case of lack of clarity.

11.2 Investigator Initiated Studies and Academic Clinical Trials

The academic (non regulatory) clinical trial as per 227 (E) means a clinical trial of a drug already approved for a certain claim and initiated by any investigator, academic or research institution for a new indication or new route of administration or new dose or new dosage form, where the results of such a trial are intended to be used only for academic or research purposes and not for seeking approval of the Central Licencing Authority or regulatory authority of any country for marketing or commercial purpose. These studies may not currently require regulatory approval. The IEC has to approve such studies after due consideration of benefits and risks and all other ethical aspects and the licensing authority has to be informed as per the prescribed procedures.

All clinical trials must be conducted in accordance with the Indian GCP guidelines, the Declaration of Helsinki (2013 or later versions as applicable), National Guidelines for Biomedical and Health Research Involving Human Participants (2017), the New Drugs and Clinical Trial Rules 2019 and other relevant regulations and guidelines, wherever applicable.

11.2.1 The investigator should make an assessment to determine if a clinical trial is under the regulatory ambit and if so, to ensure that all requirements as specified by CDSCO must also be followed. Applicable regulatory approvals must be taken (if required). In addition to EC approval, a Phase IV clinical trial on drugs with a market authorization of less than 4 years requires regulatory approval (CDSCO).

11.2.2 At least one member of the research team must have the qualifications and adequate research experience in the subject on which the academic clinical trial is planned and has a GCP training certificate.

11.2.3 All clinical trials must be registered with the Clinical Trial Registry -India (CTRI)

11.2.4 SAEs must be reported for all trials (regulatory and non regulatory) and if applicable timelines as specified by regulators to be followed (within 24 hours to the sponsor, EC and regulator, if applicable, followed by a due analysis report in 14 days). If a SAE occurs in a blinded study, and it is imperative, in the interest of managing the event to know what the patient was receiving, unblinding mechanisms should be available to the researcher

11.2.5 Free medical management of AEs and SAEs, irrespective of relatedness to the clinical trial,

should be given for as long as required or till such time as it is established that the injury is not related to the clinical trial (regulatory and non regulatory), whichever is earlier

11.2.6 In addition, compensation must be given if the SAE is proven to be related to the trial. Institutional mechanisms must be established to allow for insurance coverage of trial related or unrelated illnesses (ancillary care) and compensation wherever deemed necessary by the IEC.

11.2.7 Ancillary care may be provided to clinical trial participants for non-study/trial related illnesses arising during the period of the trial. This could be in the form of medical care or reference to facilities, as may be appropriate.

11.2.8 The review and approval of phase I, Phase II, bioavailability/bioequivalence studies, phytopharmaceutical drugs, vaccine trials, placebo controlled studies, biologicals and biosimilars, medical devices, clinical trials of products using any new technology, synthetic biology, stem cell research, research with surgical procedures as an intervention, community trials (public health interventions), clinical trials of interventions in HIV/AIDS, clinical trials on traditional systems of medicine, radioactive materials and X-rays and trials of diagnostic agents shall be in reference to 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR.

11.2.9 The review and approval of studies with participants who are pregnant or become pregnant while enrolled in a clinical trial and clinical trials on contraceptives shall be in reference to 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR.

11.2.10 The review and approval of studies with participants who are terminally ill with advanced cancer shall be in reference to 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR.

11.2.11 The review and approval of genetic studies shall be in reference to 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR.

11.2.12 In Investigator Initiated Studies and Academic Clinical Trials without any external / pharma sponsorship.

11.2.12.1 The investigator has the dual responsibility of being an investigator as well as the sponsor.

11.2.12.2 Financial arrangements must be made by the institution/investigator for the conduct of the study as well as to pay for free management of research-related injury and compensation, if applicable. Funds should be made available or appropriate mechanisms be established.

11.2.12.3 The institution must have or introduce policies that establish mechanisms to ensure quality of the data generated and safety of the intervention, such as monitoring

11.2.12.4 For student conducting clinical trials as part of their academic thesis, the guide and the academic institution should take up the responsibilities of the sponsor.

11.3 Clinical Trials on Nutraceuticals and ASU products

All Clinical Trials (academic) involving the ASU (Ayurveda, Siddha ad Unani) system shall be conducted as per the Guidelines specified under the ministry of AYUSH. For research on Ayurveda products, the General guidelines for clinical evaluation of ayurvedic interventions - 2018 given by the Central Council For Research In Ayurvedic Sciences, Ministry of AYUSH, Government of India, New Delhi.

11.3.1 For trials which are using medicinal plants or its extracts, the documented evidence of usefulness of the said medicinal plants should be found in standard text books of the said discipline (Ayurveda, Siddha and Unani). For research on traditional medicines or indigenous medicines, the said product must be prepared or extracted in the same way as the traditional method if no reference of such medicines are available in the standard text books.

11.3.2 If intervention involves using the approved medicinal plants in a form different from what is referred to in the standard texts, then appropriate safety aspects are addressed. The manufacturing methods, lab testing for concentration, effects related to the excipients and additional chemicals used should also be noted.

11.3.3 For food products and nutraceuticals related research which may or may not have medicinal plants, the preparation method, the kitchen practice standards and shelf life of the product needs to be certified.

11.3.4 Any food products or AYUSH medicinal preparations which are already available in the market and being experimented as part of research should have a certificate of clearance by the FSSAI or AYUSH as appropriate.

11.3.5 Any intervention involving medicinal plants that are listed under the Schedule E1 category of plants as per AYUSH, should get a regulatory clearance before the intervention.

11.3.6 Phytopharmaceuticals are fraction of extracts made from medicinal plants with 4 or more active ingredients and will be considered as regulatory in nature. All Pharma Sponsored/ regulatory clinical trials on patented and propriety medicines shall be referred to the MAHE Ethics committee for review.

12. Research involving vulnerable populations

This describes procedures to review research protocol involving vulnerable populations. Vulnerable persons are those individuals who are relatively or absolutely incapable of protecting their own interests because of personal disability; environmental burdens; social injustice; lack of power,

understanding or ability to communicate or are in a situation that prevents them from doing so.

12.1 The IEC shall consider vulnerable persons as those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests.

12.2 The IEC shall make efforts to ensure that individuals or communities invited for research be selected in such a way that the burdens and benefits of the research are equally distributed.

12.3 Vulnerable groups :

12.3.1 Research on genetics should not lead to racial inequalities

12.3.2 Persons who are economically or socially disadvantaged should not be used to benefit those who are better off than them

12.3.3 Rights and welfare of persons or populations with mental illness or behavioral disorders, cognitive impairment, or the differently abled (mentally and physically) who are incapable of giving informed consent must be protected. Appropriate proxy consent from the legal guardian should be taken after the person is well informed about the study, need for participation, risks and benefits involved and the privacy and confidentiality procedures. The entire consent process should be properly documented.

12.3.4 Adequate justification is required for the involvement of participants such as prisoners, students, subordinates, employees, service personnel etc. who have reduced autonomy as research participants, since the consent provided may be under duress or various other compelling reasons.

12.3.5 Individuals whose willingness to volunteer in a research study may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate may also be considered vulnerable. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention.

12.3.6 Vulnerable populations include

- Economically and socially disadvantaged (unemployed individuals, orphans, abandoned individuals, persons below the poverty line, ethnic minorities, sexual minorities – lesbian/gay/bisexual/transgender and Queer (LGBTQ), etc.)
- Unduly influenced either by the expectation of benefits or fear of retaliation in case of refusal to participate which may lead them to give consent
- Children (up to 18 years)
- Women in special situations (pregnant or lactating women, or those who have poor decision-making powers/poor access to healthcare)
- Tribals and marginalized communities
- Refugees, migrants, homeless, persons or populations in conflict zones, riot areas or disaster situations
- Afflicted with mental illness and cognitively impaired individuals, differently abled – mentally and physically disabled
- Terminally ill or are in search of new interventions having exhausted all therapies Suffering from stigmatizing or rare diseases
- Have diminished autonomy due to dependency or being under a hierarchical system (students, employees, subordinates, defence services personnel, healthcare workers, institutionalized individuals, under trials and prisoners)

12.4 The following is required when children are enrolled in research:

12.4.1 Children will not be involved in research that can be carried out equally well with adults.

12.4.2 The purpose of the research is to obtain knowledge relevant to health needs of children. For clinical evaluation of a new drug the study in children should always be carried out after the phase III clinical trials in adults.

12.4.3 For studies prior to phase III the drug has a therapeutic value in a primary disease of the children.

12.4.4 The settings of the research provide the child and parent adequate medical and psychological support.

12.4.5 Interventions intended to provide direct diagnostic, therapeutic, or preventive benefit for the individual child participants must be justified in relation to potential risks involved in the study and potential benefits to society.

12.4.6 The study must take into consideration the circumstances of the children to be enrolled in the study including their age, health status, and other factors and potential benefits to other children with the same disease or condition, or to society as a whole.

12.4.7 The risk presented by interventions not intended to benefit the individual child participant is low when compared to the importance of the knowledge that is to be gained.

12.4.8 Interventions that are intended to provide therapeutic benefit are likely to be at least as advantageous to the individual child participant as any available alternative interventions.

12.4.9 A parent or legal guardian of the child has given proxy consent. For children between 7 and 12 years of age, verbal/oral assent must be obtained in presence of the parents/LAR and should be recorded. For children between 12 and 18 years, written assent must be obtained and signed by the parents/LAR.

12.4.10 The assent of the child should be obtained if the child is above 7 years and below 18 years old, to the extent of the child's capabilities such as in the case of mature minors or adolescents, unless there is no medically acceptable alternative to the therapy provided or tested, and consent has been obtained from at least one parent or guardian.

12.4.11 If the consent of parents/legal guardian will affect the validity of the study, waiver of consent (from the relevant adult) should be taken and recorded with the approval of the EC (for eg. in behavioral studies in IV drug users where parental consent may not be possible)

12.5 If research involves adults unable to consent, the ethics committee must consider additional safeguards to protect their rights and welfare : When conducting nontherapeutic research(i.e. a trial in which there is no anticipated direct clinical benefit to the participant), consent must be obtained directly from the participant and such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Participants in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

12.6 As a general rule, pregnant or nursing women should not be participants of any clinical trial

12.6.1 Pregnant or nursing women should not be participants except such trials as are designed to protect or advance the health of pregnant or nursing women or foetuses or nursing infants, and for which women who are not pregnant or nursing would not be suitable participants.

12.6.2 Pregnant or nursing women should in no circumstances be the participant of any research unless the research carries no more than minimal risk to the foetus or nursing infant and the object of the research is to obtain new knowledge about the foetus, pregnancy and lactation.

12.6.3 The justification for participation of pregnant women in clinical trials would be that they should not be deprived arbitrarily of the opportunity to benefit from investigations, drugs, vaccines or other agents that promise therapeutic or preventive benefits. Example of such trials are, to test the efficacy and safety of a drug for reducing perinatal transmission of HIV infection from mother to child, trials for detecting foetal abnormalities and for conditions associated with or aggravated by pregnancy etc.

12.6.4 Women should not be encouraged to discontinue nursing for the sake of participation in research and in case she decides to do so, harm of cessation of breastfeeding to the nursing child should be properly assessed except in those studies where breast feeding is harmful to the infant. Compensation in terms of supplying supplementary food such as milk formula should be considered in such

instances.

12.6.5 Research related to termination of pregnancy : Pregnant women who desire to undergo Medical Termination of Pregnancy (MTP) could be made participants for such research as per The Medical Termination of Pregnancy Act, GOI, 1971.

12.6.6 Research related to pre-natal diagnostic techniques: In pregnant women such research should be limited to detect the foetal abnormalities or genetic disorders as per the Prenatal Diagnostic Techniques (Regulation and Prevention of Misuse) Act, GOI, 1994 and not for sex determination of the foetus.

12.6.7 In clinical trials/intervention studies, if women in reproductive age are recruited they need to be informed of potential risk to foetus if they become pregnant. They should be informed about effective contraceptive methods as well as options available in case of failure of contraception.

12.6.8 A woman participating in clinical trial/intervention study who becomes pregnant during study must not be automatically removed from the study when there is no evidence showing potential harm to the foetus. The matter must be carefully reviewed and she must be offered the option to withdraw or continue. In case the woman opts for continued participation, adequate monitoring and support should be provided by the sponsors/researchers.

12.6.9 Where research is planned on sensitive topics (such as domestic violence, genetic disorders, rape etc.), confidentiality should be strictly maintained and privacy protected. In risk mitigation strategies, appropriate support systems such as counseling centers, police protection, etc. would be recommended.

12.7 For research among tribal populations : Research to be conducted only if it is of specific therapeutic, diagnostic and preventive nature with appropriate benefits to the tribal population. Due approval to be taken from competent administrative authorities, and whenever possible, it is desirable to seek help of government functionaries/local bodies or registered NGOS who work closely with the tribal groups and have their confidence. Benefit sharing to be ensured with the tribal group for any research done using tribal knowledge that may have potential for commercialization.

12.8 In any research involving individuals with mental illness or cognitively impaired/affected individuals, interventions should be of short duration, least restrictive a possible and involved only when necessary in accordance with relevant laws. If there is risk of people causing hard to themselves or others, the issues should be addressed during informed consent process and confidentiality may be breached (for reporting to family members, police, or other authorities) upon expression of such thoughts of harm to self or others.

12.9 Research on individuals with diminished autonomy due to dependency on being under a hierarchical system (students, employees, subordinates, defence services personal, healthcare workers, institutionalized individuals, under trials, prisoners) should be done as specifically pertinent to the research questions and not as a matter of convenience. They should be allowed to deny consent and/or later withdraw from study without any negative repercussions on her/his care.

12.10 Research on sexual minorities and sex workers to take into account issues of privacy, confidentiality, possibility of stigma, discrimination and exploitation resulting in increased vulnerability. A representative of the sexual minority group (LGBT community) may be invited as special invitee/member to participate in IEC meeting if there is a research proposal involving these participants.

12.11 Research on patients who are terminally ill to take into account that therapeutic misconceptions are high for those who are in search of new interventions have exhausted all available therapies. Benefit-risk assessment to be performed considering perceptions of benefits and risks by the potential participant. Post-trail access to the medication, especially if it is beneficial to the participant, will be carefully reviewed.

12.12 Review process for projects with vulnerable population as participants

12.12.1 Research involving vulnerable populations is not eligible for expedited review or exemption from review and will be subjected to full board Initial review.

12.12.2 The IEC evaluates whether additional safeguards have been included in the study to protect the rights and welfare of vulnerable participants.

12.12.3 If expertise is not available within the IEC members, expert opinion may be sought / expert may be invited to the full board meeting for their opinion.

12.12.4 Additional study submissions, amendment and continuing review applications involving vulnerable populations (except prisoners, which should be reviewed by the full board) may be reviewed by the convened board or by expedited review, as decided during initial review

12.12.5 The IEC may advise risk minimization strategies wherever possible

12.12.6 The IEC may ask for more frequent review and monitoring of studies on vulnerable populations, including site visits.

12.12.7 The IEC can suggest setting up of a community advisory board to act as an interface between the researchers and the community for certain studies involving vulnerable populations

13. Informed Consent

The researcher must obtain voluntary written informed consent from the prospective participant for any biomedical and health research involving human participants. This requirement is based on the principle that competent individuals are entitled to choose freely whether or not to participate or continue to participate in the research. Informed voluntary consent protects the individual's freedom of choice and respects the individual's autonomy

13.1 Informed consent is a continuous process involving three main components - providing relevant information to potential participants, ensuring competence of the individual, ensuring the information is easily comprehended by the participants and assuring voluntariness of participation

13.2 Informed consent is always to be in the written form. However, verbal/oral consent may be taken in exceptional circumstances and for specific, justifiable reasons with the approval of the IEC. It should not to be practiced routinely.

13.3 The ICD has two parts – patient/participant information sheet (PIS) and the informed consent (IC) form

13.4 The researcher must provide all potential research participants with detailed information and discuss her/his queries about the research in the language she/he is able to understand. The language should not only be scientifically accurate and simple, but should also be sensitive to the social and cultural context of the participant

13.5 Adequate time should be given to the participant to read the consent form, if necessary discuss it with family and friends, and seek clarification of her/his doubts from the researchers/research team before deciding to enroll in the research. Model formats of the PIS (made available in English, Kannada and Malayalam) should be appropriately modified for the individual project. The researcher should only use the IEC approved version of the PIS

13.6 Model formats of the IC (made available in English, Kannada and Malayalam) should be appropriately modified for the individual project The researcher should only use the IEC approved version of the IC form, including its local language translations

13.7 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 IEC, 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

13.8 If the participant cannot sign then a thumb impression must be obtained and the reason for the same documented.

13.9 The researcher who administers the consent must also sign and date the consent form

13.10 The process of consent for an illiterate participant/LAR should be witnessed by an impartial literate witness who is not a relative of the participant and is in no way connected to the conduct of research (such as other patients in the ward who are not in the study, staff from the social service department and counselors). The witness should be a literate person who can read the participant information sheet and consent form and understand the language of the participant, should be present throughout the consent process as witness.

13.11 An audio-video recording of the informed consent process in case of vulnerable subjects in clinical trials of New Chemical Entity or New Molecular Entity including procedure of providing information to the subject and his understanding on such consent, shall be maintained by the investigator for record. A separate consent for the audio video recording should be obtained first before undertaking the audio visual recording.

13.12 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 shall be maintained by the investigator for record.

13.13 Online consent may be obtained, for example, in research involving sensitive data such as unsafe sex, high risk behaviour, use of contraceptives (condoms, oral pills), or emergency contraceptive pills among unmarried females

13.14 Electronic media can be used to provide information (text, graphics, audio, video, podcasts or interactive websites) as in the written informed consent document, which can be administered and documented using electronic informed consent (including electronic / digital signatures) systems. The electronic consent must contain all elements of informed consent in a language understandable by the participant. When electronic informed consent is contemplated, screenshots of the same should be provided to the IEC along with other documents with the original project submission

13.15 After consent is obtained, the participant should be given a copy of the PIS and signed IC form or use two IC forms with one for the researcher and one to be given to the participant.

13.16 Waiver of consent

The following criteria must be met for a research projects that it can qualify for granting a waiver of both written and verbal consent.

13.16.1 Retrospective review of patient case records where it is impractical to get consent subject to the research presenting no more than minimal risk.

13.16.2 When it is impractical to conduct research since confidentiality of personally identifiable information has to be maintained throughout research as may be required by the sensitivity of the research objective.

13.16.3 When there is a possible legal, social or economic risk to the participant entailed in signing the consent form as they might be identified as such by signing the consent form, the requirement for obtaining consent can be waived of by the IEC.

13.16.4 Research on publicly available information, documents, records, work performances, reviews, quality assurance studies, archival materials or third party interviews, service programs for benefit of public having a bearing on public health programs, and consumer acceptance studies.

13.16.5 Research on anonymised biological samples from deceased individuals, left over samples after clinical investigation, cell lines or cell free derivatives like viral isolates, DNA or RNA from recognized institutions or qualified investigators, samples or data from repositories or registries and data, documents, records, or specimens that have been collected for non research (clinical) purposes.

13.16.6 Certain types of public health studies / surveillance programmes / programme evaluation studies

13.16.7 In emergency situations when no surrogate consents can be taken. When consent of person / patient / responsible relative or custodian / team of designated doctors for such an event is not possible, the IEC can allow waiver of consent for recruiting participant in a research study. However, informed consent should be administered whenever participant regains consciousness / capacity to consent or to relative / legal guardian when available later.

13.17 Telephonic interviews

In case of telephonic interviews, waiver of written informed consent may be requested but this does not mean that verbal consent cannot be utilized.

The telephonic interview shall be a two step process. The first call shall confirm the participant's identity and obtain oral consent for conducting an interview with a specific request for a future time and date for administering the interview. A script for verbal consent, which provides all of the elements of consent in a more informal style, should be available. In addition, each subject should be provided the option of obtaining an information sheet that describes the study and gives contact names and numbers.

The second call shall administer the interview schedule (questions to be asked) and will usually conform to a simple 5 minute call and that no questions are asked that compromise a person's confidentiality or position.

Investigators should keep a log of those who were approached about the study, and offered verbal consent and the date with time of both (or more) calls.

13. 18 Re-consent

Re-consent is required in the following situations when :

13.18.1 New information pertaining to the study becomes available which has implications for participant or which changes the benefit and risk ratio

13.18.2 A research participant who is unconscious regains consciousness or who had suffered loss of insight regains mental competence and is able to understand the implications of the research

13.18.3 A child becomes an adult during the course of the study

13.18.4 Research requires a long-term follow-up or requires extension

13.18.5 There is a change in treatment modality, procedures, site visits, data collection methods or tenure of participation which may impact the participant's decision to continue in the research

13.18.6 There is possibility of disclosure of identity through data presentation or photographs (this should be camouflaged adequately) in an upcoming publication

13.18.7 The partner/spouse may also be required to give additional re-consent in some of the above cases

13.19 Assent and parental / LAR consent when children are participants in research :

Adolescents may have the capacity to give consent like adults. However, as they have not attained the legal age to provide consent, it is termed as assent and the consent of the parents/LAR should be obtained. If the latter will affect the validity of the study, waiver of consent from the relevant adult should be taken and recorded with the approval of the IEC, for example, in behavioural studies in IV drug users where parental consent may not be possible.

Content of the assent form has to be in accordance with the developmental level and maturity of the children to be enrolled and explained while considering the differences in individual understanding. The language of the assent form must be consistent with the cognitive, social and emotional status of the child. It must be simple and appropriate to the age of the child

Waiver of informed consent from the parent / LAR may be sought from the IEC when students in professional courses (first year students may not have attained 18 years of age) are enrolled in studies involving minimal risk and minor increase over minimal risk (low risk)

13.19.1 There is no need to document assent for children below 7 years of age

13.19.2 For children between 7 and 12 years, verbal/oral assent must be obtained in the presence of the parents/LAR and should be recorded

13.19.3 For children between 12 and 18 years, written assent must be obtained. This assent form also has to be signed by the parents/LAR.

13.19.4 Generally, consent from one parent/LAR may be considered sufficient for research involving no more than minimal risk and/or that offers direct benefit to the child. Consent from both parents may have to be obtained when the research involves more than minimal risk and/or offers no benefit to the child. The IEC should determine if consent of one or both parents would be required before a child could

be enrolled. Only one parent's consent is acceptable if only one parent has legal responsibility for the care and custody of the child, irrespective of the risk involved.

13.19.5 Whenever relevant, the protocol should include a parent/LAR information sheet that contains information about specific aspects relevant to the child such as effects on growth and development, psychological well-being and school attendance, in addition to all components described in the participant information sheet

13.19.6 When the research involves sensitive issues related to neglect and abuse of a child, the IEC may waive the requirement of obtaining parental/LAR consent and prescribe an appropriate mechanism to safeguard the interests of the child

13.19.7 Cognitively impaired children or children with developmental disorders form one of the most vulnerable populations. In fact, their parents are also vulnerable and there is a high likelihood of therapeutic misconception. The potential benefits and risks must be carefully explained to parents so as to make them understand the proposed research

13.19.8 Research involving institutionalized children would require assent of the child, consent of parents/LAR, permission of the relevant institutional authorities (for example, for research in a school setting: the child, parents, teacher, principal or management may be involved).

13.20 Waiver of assent: All the conditions that are applicable to waiver of informed consent in adults also apply for waiver of assent in children. If the available intervention is anticipated to definitely benefit the child but would be available only if the child participates in the study, waiver of assent could be allowed. However, this situation should be accepted only in exceptional cases where all forms of assent/consent have failed. In such cases, approval of the IEC should be obtained.

13.21 Permission of the gatekeepers, that is, the head/leader of the group or culturally appropriate authorities, may be obtained in writing or audio/video recorded on behalf of the group and should be witnessed.

13.22 When permission is obtained from an organization that represents the community, the quorum required for such a committee must be met. For example, in a village panchayat the number of members ordinarily required to conduct a meeting must be present while giving consent. Individual consent is important and required even if the community gives permission.

14. Research on biological material and datasets

Biological materials or biospecimens or samples include biological fluids, such as blood, dried blood spots, body fluids, urine, tissues, organs, cord blood, oocytes, sperm, semen or embryos. These may be stored or prospectively collected.

A repository or biobank is an organized collection of resources that can be accessed to retrieve human biological material and data for research purposes. The bio resources would therefore be protocol-based prospective collection of biospecimens, left-over samples after clinical investigations or research proposals, biopsy materials, surgical or autopsy specimens/tissues, embryos or foetuses, cell lines, or waste materials like abandoned organs/tissues. The biological materials could be kept for research, assisted reproductive technology (ART) purposes or for forensic purposes and be commercial or non commercial

A dataset is an organized collection of data and information maintained in physical and/or electronic/digital form that can be used for biomedical and health research

Besides data related to biospecimens as in biobanks, there are other repositories like disease registries, health surveys, disease surveillance, census data and even personal health records in health-care institutions which can be used for subsequent research

14.1 As a general principle, research must be conducted on least identifiable data (anonymized preferable to anonymous or unidentified, which is preferable to identifiable data)

14.2 Informed consent for biobanking may be with multiple options in a multi-layered consent document as the aims of scientific study are not defined clearly at the time of collection and when there are no specific end points and there is a time lag between the collection of the sample and its use in research

14.3 The consent format shall be in reference to 2017 National Ethical Guidelines for Biomedical and Health Research involving Human Participants of ICMR and includes blanket or broad consent, tiered consent (with opt out option, data benefit sharing and return of results), specific consent and dynamic consent

14.4 The participant shall own the biological sample and data collected from her/him and therefore, could withdraw both the biological material donated to the biobank and the related data unless the latter is required for outcome measurement and is so mentioned in the initial informed consent document. Complete anonymization would practically make the original donor lose the right of ownership. A participant may withdraw from one component of the study, like continued follow-up/data collection when withdrawal may be referred to as partial

14.5 The informed consent document should emphasize the aspect about benefit sharing

14.5.1 The document should describe whether donors, their families, or communities would receive any financial or non-financial benefits by having access to the products, tests, or discoveries resulting from the research

14.5.2 The benefits accrued should be returned to the communities from where the donors were drawn in community-based studies

14.5.3 To the maximum extent possible, benefits should be indirect or in kind

14.6 Re-consent should be done when secondary or extended uses of stored samples/dataset is being contemplated and in paediatric donors when they reach 18 years

14.7 The IEC will examine circumstances under which the biological material or the data were originally collected and informed consent obtained, but a secondary or extended uses of stored samples is contemplated. The decision about anonymization/informed consent waiver or re-consent will be made on a case-by-case basis

14.8 Results of the study should be communicated back to the providers of samples/ data

14.8.1 If the findings are in an aggregate form, the participant will not be able to receive any feedback on individual data

14.8.2 Wherever applicable, research findings in aggregate form (which does not reveal individual results) must be discussed with the community, especially when research involves populations who are more vulnerable, such as tribal populations, ethnic groups and people living with certain diseases.

14.8.3 An appropriate mechanism to deal with informational harm, when participants are provided feedback that is not actionable or when such information is unrelated, should be in place

14.8.4 At the time of sample collection, donors should be extended the choice of receiving the results of the research whether they are beneficial or not. Participants shall be given the option of receiving an aggregate report of all the results of the study which could become a shared benefit for the community

14.8.5 Participants may also choose not to be contacted about their results.

14.9 Biobanks/institutes are the custodians or trustees of the samples and data and current and future use would be done after IEC approval. Researchers have no claim for either ownership or custodianship

14.10 A Material Transfer Agreement should be executed if the bio specimens are likely to be shipped from the host institution to collaborating institutions within the country or abroad. The IEC should be informed of the intention to transfer material. Mandatory regulatory clearances (Directorate General of Foreign Trade (DGFT) notification) with appropriate MoU are required if bio specimens are to be sent overseas

14.11 Biobanks can use the stored material/data for doing research themselves or they can outsource or supply such material/data to other researchers or institutions on a nonprofit basis

14.12 If there is no written consent by the deceased person (relating to biological material/data in forensic departments) permitting use of organs or tissues, the family can be approached for consent for use of left-over organs or tissues.

14.12.1 The quantity of tissue taken should ideally be minimal, particularly if it is seen externally on the body in order to preserve the dignity of the dead and be culturally acceptable by the next of kin or closest relative or friend

14.12.2 The informed consent document should state what tissue/organ will be retained, who will be the custodian, duration of storage of sample, what type of research would be conducted and method for disposal of the remains

14.12.3. No consent would be required if sample or data is anonymized

14.12.4 If the deceased has no claimant then forensic officials will be authorized to give permission for use of material/data from its sources and be responsible for use of unclaimed cadavers

14.12.5 Genetic research or revelation of any other stigmatizing factors like HIV, etc. in the deceased may have implications for family members. In such instances, all ethical requirements as in the case of live participants should be followed

14.13 Databases maintained in electronic/digital formats, linked by internet or other networks, using cloud computing technologies and those associated with big data initiatives, pose additional risks to privacy and confidentiality than what is described under biobanks or traditional paper-based data repositories. Hence the following measures must be adopted to respect and protect privacy and confidentiality of individuals

14.13.1 Ensure physical safety and security of the involved devices and computer servers

14.13.2 Take data security measures such as password protection

14.13.3 Provide differential and role-based controlled access to data elements for members of the research team

14.13.4 Ensure use of data encryption when data is transferred from one location/device to another

14.13.5 Ensure benefit sharing with owners and related legal issues

14.13.6 If data is outsourced or sold, data privacy, data accuracy, data security, and possibility of legal liability should be addessed

14.13.7 Auditing shall be done to detect misuse

14.14 While using anonymized (de-identified) samples/data, researchers should seek the approval of the IEC for waiver of consent from donors

14.15 When biospecimen or data has be collected for appropriate research from critically ill patients who may not have given prior consent for research, a delayed consent may be administered in the post-medical procedure period from the participant or LAR when it is practical

15. Amendments

Prepared	Reviewed	Approved

The purpose of this procedure is to describe how protocol amendments or any other amendments/letters are reviewed by the KMC & KH IEC.

Amendment: Any change in protocol and documents from that of previously IEC approved protocol/document. This applies to amended study protocols/ documents and letters that are submitted for IEC approval. Amendments made to protocols or any other amendments related to the study may not be implemented until reviewed and approved by the IEC

15.1 It is the responsibility of the IEC secretariat to manage protocol amendments / documents and letters.

15.2 Receipt of the Amendment Package

15.2.1. The amendment /documents forwarded by the PI is received by the secretariat. The amendment / documents should be accompanied by Amendment Reporting Form

15.2.2. The PI shall ensure that the changes or modifications in the amended version are underlined or highlighted.

15.2.3. The PI shall also forward a scanned copy of the original IEC project approval certificate

The Secretariat will check for completeness of the submission and inform the Principal Investigator by e-mail / telephonically to submit the required documents at the earliest, if any of the documents are missing/ incomplete.

15.3 The Member Secretary, IEC, classifies the amendments into minor or major.

15.4 Minor amendments include those that do not increase the risk or decrease the potential benefit to subjects and minor changes in previously approved research during the period covered by the original approval. Minor amendments may be reviewed by the expedited review process.

Minor notifications may be noted by the Member Secretary and not tabled in IEC meeting. This may include but may not be restricted to:

Renewed insurance policy

DCGI approvals, permission letters for Government authorities, schools

Administrative notes

Documents of administrative nature

15.5 The major amendments are reported on the agenda of the subsequent scheduled IEC meeting. If the amendments and other documents which need full board review, they will be processed as per the process described for full board review

15.6 If the IEC approves the amendments, the decision is communicated to the PI. If the IEC recommends or suggests modifications to any of the documents, or the amendments, the secretariat sends a written communication to the investigator about the specific changes asking him or her to make the necessary changes and resubmit the documents to IEC by email. All amendments

and modification associated documents are filed in the corresponding research protocol file.

15.7 All investigators have to update the Amendments made in the CTRI portal if the project has been registered under CTRI.

16. Serious Adverse Events

This describes the process on the submission, reporting, review of serious adverse events and unexpected events for any active study approved by the IEC. It applies to the Monitoring subcommittee / IEC review of serious adverse events and unexpected events reports, both onsite and offsite, including follow up reports submitted by investigators.

Onsite : Event occurring at KH

Offsite : Event occurring at other centers/sites

Adverse Event (AE) : Any untoward medical occurrence in a patient or clinical investigation participant administered an investigational product and which does not necessarily have a causal relationship with this treatment. The adverse event can therefore be any unfavorable or unintended sign or experience associated with the use of the investigational product, whether or not related to the product.

Serious Adverse Event (SAE) : Any untoward medical occurrence (due to the participation in the concerned trial) that at any dose that results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability / incapacity, congenital anomaly/birth defect

16.1 Investigators, IEC members and Monitoring Subcommittee members must follow the procedure notified in the Gazette of India notification GSR 227(E) dated March 19, 2019 called the New Drug and Clinical Trial Rules 2019 and the Medical Device Rules 2017. These rules prescribes procedures for reporting of SAEs and the provision of compensation in case of injury or death during clinical trial.

16.2 The primary responsibility of the Monitoring subcommittee (MSC) of IEC is to review and address SAE's and unexpected events involving risks to research participants. In addition, the committee is authorized to offer mediation under appropriate circumstances.

16.3 IEC should also make sure that researchers are made aware of the policies and procedures concerning reporting and continuing review requirements. The IEC Secretariat is responsible for receiving the complete SAE / unexpected events reports and directing them to Monitoring Subcommittee for detailed review. Following this the convener of the Monitoring Subcommittee will present the report in subsequent full board meeting of the IEC.

Notifying the IEC / MSC does not relieve the PI from his / her responsibility to notify the sponsor and regulatory authorities.

16.4 Responsibility of Principal Investigator

16.4.1 To ensure adequate care in case of AE to the subjects

16.4.2 Report all serious & unexpected AEs to sponsor, IEC & Licensing Authority (DCGI) within 24 hrs. If there is failure to report within time, submit reason along with the report. The SAE (death or others) report after analysis, should be submitted within 14 days to chairman of the IEC, Head of the institution and the Licensing Authority (DCGI).

16.4.3 Serious Adverse Event should be graded as per Common Terminology Criteria for Adverse Events, Version 4.02, of U.S. Department of Health and Human Services, National Institutes of Health and National Cancer Institute

16.4.4 One original and two photo copies and a soft copy of the SAE should be submitted by the PI to the IEC Secretariat. If the IEC Secretariat is closed due to holidays, the Member Secretary shall be contacted for alternate arrangements.

16.4.5 The IEC Secretariat will verify that the reports are complete, signed and dated by the PI / Co I and are checked for dates and typo errors in the SAE event description, SAE event term and CTCAE grading

16.4.6 In case the IEC Secretariat notes that the report is incomplete, the report will be reverted back to PI

16.4.7 In case of death reporting, the hard copy is reviewed by Monitoring Subcommittee & IEC Secretary or else the soft copy is sent to convener monitoring subcommittee and IEC Secretary for comments within 24 hrs of SAE reporting.

16.4.8 The SAE reported for death will be stamped “Death” on the right corner of the 1st page of SAE form for easy / immediate identification.

16.4.9 The Member Secretary will review the SAE report, write comments and forward it to the Monitoring Subcommittee, immediately. If the outcome of any SAE reported is ‘death’, he will review the SAE report and forward it, either the hard copy or via email (particularly if it is a holiday), to MSC within 1 working day for immediate action.

16.4.10 Any queries raised are emailed to the PI for action

16.4.11 In case of urgency or if a particular significant trend in serious unexpected and related or unrelated events is observed on any trial a meeting may be held based on comments and action suggested by the Monitoring Subcommittee / IEC Secretary

16.4.12 The convener, Monitoring Subcommittee shall discuss the SAE in the subcommittee. After discussions, a report is finalized. The final report is signed by the convener and submitted to the Member Secretary, IEC. The original signed hard copy of the report is filed.

16.4.13 The IEC secretariat will send a formal letter signed by Member Secretary/Chairperson to the investigator(s) with instructions for specific actions as per the monitoring subcommittee decision.

16.4.14 In case a PI fails to respond to the MSC letter, the matter will be discussed at the next full board IEC meeting and a decision will be taken for specific action by simple majority.

16.4.15 All SAEs are listed in the next month IEC meeting agenda.

16.5 Responsibility of Sponsor : (Third Schedule, item 3 of the New Drugs and Clinical Trial Rules 2019 GSR 227E)

16.5.1 If study is discontinued, summary report to be submitted within 30 days

16.5.2 Forward the SAE report after analysis, within 14 days to the chairman of the IEC, Head of the institution & the LA.

16.5.3 In case of clinical trial related injury or death, sponsor to pay for medical management and financial compensation

16.5.4 Submit details of compensation paid, within 30 days of the order of DCGI

16.6 Actions to be taken by Chairperson

The Chairperson, IEC on basis of the information and comments received from the Member Secretary IEC and MSC, and applying his/her judgment will direct the IEC Secretariat to any one or more actions listed below, but are not limited to.

16.6.1 Soliciting opinion of one or more expert in writing. The information can be provided to expert after he/ she/ they agree(s) to the confidentiality clause and abide by the rules and regulations of IEC. The expert would be requested to provide an opinion in writing within 2-14 working days, depending upon the gravity and seriousness of the matter.

16.6.2 Calling for an emergency review by full board. This review should be initiated within 48 working hours (2 working days) of receipt of information.

16.6.3 Suspending all trial related procedures (except those intended for safety and well-being of the participant) till further review by the IEC

16.6.4 Suspending enrolment of new research participants till further review by the IEC

16.6.5 Direct the PI to inform participants already enrolled in the study about the SAE and request them to undertake additional visits, additional procedures, additional investigations, etc. as per recommendation

16.6.6 Direct the PI to inform participants already enrolled in the study about the SAE and obtain their consent regarding continuation in the research study, if necessary.

16.6.7 Recommend an amendment to the protocol, the Informed Consent Document, Participant Information Sheet, investigator brochure and/ or any other document.

16.6.8 Recommend whether or not compensation should be paid to the patient / his nominee for trial related injury / death as per institutional policy.

16.6.9 The IEC shall decide to suspend activities

- Suspend certain activities under the protocol (while going on with activities intended to protect the safety, well-being of participants who have already been enrolled)
- Suspend enrolment of new research participants
- Suspend the study till amendments requested for by the IEC are accepted Terminate the study
- Any other action

16.7 Responsibilities of the IEC in case of studies that have required approval of the CDSCO: In case of death occurring to the clinical trial subject, the IEC shall forward it's report on the serious adverse event of death, after due analysis, along with its opinion on the financial compensation, if any, to be paid by the sponsor or his representative to the Chairman of the Expert Committee constituted by the CDSCO, with a copy of the report to the CDSCO within thirty calendar days of the occurrence of the serious adverse event of death. In case of serious adverse event other than death occurring to the clinical trial subject, the IEC shall forward its report on the serious adverse event after due analysis along with its opinion on the financial compensation, if any to be paid by the Sponsor or his representative, to the CDSCO, within thirty calendar days of the occurrence of the serious adverse event.

16.8 Responsibilities of the IEC in case of queries from DCGI : Principal Investigator informs the MSC about SAE query raised by Drugs Controller General India (DCGI) requesting IEC opinion for a SAE DCGI queries on SAEs which are already discussed in MSC and ratified in a previous IEC meeting will be answered based on the opinion and findings of the MSC and IEC at that time. IEC discussion or opinion at that time will be conveyed to DCGI and Principal Investigator.

17. Monitoring

This process applies to any visit off site/ on site monitoring of any study sites of IEC approved study protocols.

Monitor : Any IEC member tasked to perform monitoring visit and report their findings to IEC.

Monitoring Report : Reports should include a summary of what the monitor reviewed and the monitor's statements concerning the significant findings / facts, deviations and deficiencies, conclusions, actions taken or to be taken and / or actions recommended to secure compliance.

Monitoring subcommittee : The Monitoring Subcommittee shall be appointed by the Chairperson of IEC, consisting of not less than 2 existing IEC members with one designated as Convener amongst them

17 A. On site Monitoring

Onsite Monitoring visit : The IEC or its representatives visit study sites to assess how well the investigators are conducting research, taking care of participants, recording data and reporting their observations, especially serious adverse events found during the studies. Normally monitoring visit will be arranged with prior intimation to the Principal Investigator.

17.1 Clinical trials sponsored by external funding sources and industry are continually audited for compliance and monitored for progress. Institutional clinical studies without outside sponsorship are the focus of the monitoring system of this committee.

17.2 Selection of study sites :

Cause monitoring could be initiated, in any of the following conditions :

- High number of protocol deviations / violations
- Large number of projects carried out at the study site or by Investigator
- High number of SAE reports
- High recruitment rate
- Non-compliance or suspicious conduct
- Complaint reported to IEC by participants
- Any alleged misconduct of approved studies
- Any adverse media report or any other source
- Any other cause as decided by IEC

Non-cause monitoring could be initiated as a routine audit of process or procedure

17.3 The Member Secretary will inform the PI regarding the scheduled monitoring visit and Monitoring Subcommittee and PI will coordinate the monitoring visit. The subcommittee member

will also notify the site about the scheduled visit.

17.4 The Subcommittee will look into all aspects of monitoring of the identified site

17.4.1 Review the informed consent document to make sure that the site issuing the current, approved version

17.4.2 Review randomly the participant's source files for proper informed consent documentation.(usually about 10%, or may be higher)

17.4.3 Observe the informed consent process, if possible

17.4.4 Check investigational product accountability is adequately controlled and documented throughout the product flow at the study site (arrival, dispensing, use, return from the subject and return/ destruction after the study). Storage times, conditions and expiry dates must also be acceptable and sufficient supplies available wherever applicable.

17.4.5 Review the study files to ensure appropriate documentation

17.4.6 Verifying that the investigator follows the approved protocol and all approved amendment(s), if any.

17.4.7 Ensuring that the investigator and the research team are adequately informed about the study

17.4.8 Verifying that the investigator and the research team are performing the specified study functions, in accordance with the approved protocol and any other written agreement between the sponsor and the investigator / institution, and have not delegated these functions to unauthorized individuals.

17.4.9 Verifying that the investigator is enrolling only eligible participants.

17.4.10 Verifying that source documents and other study records are accurate, complete, kept up-to-date and maintained.

17.4.11 Checking the accuracy and completeness of the CRF entries, source documents (with specific reference to the documentation of informed consent process in detail) and other study related records against each other.

17.4.12 Determining whether all Serious Adverse Events (SAEs) are appropriately reported within the time periods required by GCP / Regulatory agencies, the protocol, the IEC, the sponsor, and the applicable regulatory requirement(s).

17.4.13 Case Record Forms would be checked to review the safety data, Adverse Events (AEs) and Serious Adverse Events (SAEs) for the volume or severity of adverse events.

17.4.14 Collect views of the study participants, if possible.

17.5 After the monitoring site visit

17.5.1 The subcommittee Convener will make a report and present it to the IEC

17.5.2 The report will be reviewed by Chairperson / Member Secretary, queries if any are sent to PI and the form is forwarded to IEC for action

17.5.3 The convener / member of the subcommittee will present the monitoring visit findings in the next regular full board meeting of the IEC.

17.5.4 Full board recommendations to change the study / premature termination /

continuation of the project will be informed to the Principal Investigator in writing within 14 days of the meeting.

17.6 Steps to ensure timely reporting :

17.6.1 The IEC shall facilitate reporting of each adverse event by creating awareness about the need among the investigators.

17.6.2 The IEC while issuing the certificate shall clearly indicate the need for reporting as per regulatory guidelines

17.7 Any complaint/suggestion may be sent to the member secretary at the following address:

The Member Secretary
IEC Secretariat
Room 22, Ground floor
KMC Faculty Rooms (adjacent to KMC Administrative Block / Office)
Kasturba Medical College, Manipal - 576 104
Phone : +91 820 29 33522
E-mail : iec.kmc@manipal.edu
Intranet webpage : www.khinfo.edu (Knowledge base - Ethics Committee)

Complaints/suggestions may be anonymous and done orally or in writing.

17 B. Off site Monitoring

Off Site Monitoring : A convened meeting by the Monitoring Subcommittee of the IEC at a common meeting venue, where the Principal Investigator will produce documents to support the Responsible Conduct of Research activity. The meeting schedule will be intimated in advance to the Principal Investigator.

The purpose of offsite monitoring is to verify if the investigators are conducting the research activity as per the protocol approved by the IEC.

17.8 Day : Fourth Thursday of the month (unless otherwise notified). If the fourth Thursday is a holiday, the IEC meeting schedule will be intimated to each Principal Investigator by e-mail. The decision for calling additional meetings rests with the Convener of the Monitoring Subcommittee.

17.9 Time : 2.00 PM (unless otherwise notified)

17.10 Venue : Research Cell, Ground Floor, KMC Faculty Room Complex, KMC Administrative Building, Kasturba Medical College, Manipal. Any change in venue will be notified by the Member Secretary to the investigator and members of the monitoring subcommittee by e-mail.

17.11 Process: Projects already approved by the IEC earlier will be randomly selected for monitoring. Any of the IEC approved study projects may be monitored during the approved study

period or even up to 3 years after the closure of the study.

17.11.1 The selection of project for monitoring is based on As a routine audit of process or

- Procedure representative sample from department / institution type of the study Quantum of risk involved to the participant
- Number of studies carried out by Principal Investigator Any alleged misconduct of approved studies
- Non-compliance or suspicious conduct Complaint received by the IEC
- High number of SAE reports
- Any other reason decided by IEC

17.11.2 The Convener of the Monitoring Subcommittee will identify projects that are to be monitored. The list will be communicated to the Member Secretary. The Member Secretary will inform the PI regarding the scheduled monitoring meeting by e-mail.

17.12 Documents that will be evaluated during the off site monitoring : Original IEC approval certificate

- Approved current protocol of the study
- Verify and document protocol deviations and violations
- Permission letters obtained from any authorities
- Approved current version of Participant Information Sheets (including translations)
- Informed consent forms signed by participants
- Filled up Data sheets / Proformas / CRFs - verify completeness and accuracy
- Documents to support current recruitment status
- Documents to support current status of recruited participants
- Any published documents related to the study
- Any other study related documents.

17.13 Conduct of meeting : The Monitoring Subcommittee consisting of atleast2 existing IEC members, with one designated as convener will be present. The convener will present the agenda and conduct the meeting.

17.13.1 All the documents will be carefully evaluated to ensure that proper documentation is done. The Monitoring Subcommittee will evaluate the documents related to the study, to assess how well the investigators are conducting research, ensuring adequate informed consent process, ensuring safety of study participants, recording data and reporting their observations, reporting deviations and violations of approved protocol and reporting serious adverse events and adverse events found during the conduct of the study. The PI / CoI will be asked to explain non-conformances / deviations / violation, if any and these will be documented in the report.

17.13.2 The Convener of the Monitoring Subcommittee will document all the findings at the meeting.

17.14 Decision making during protocol deviations and non-compliances : The purpose of this procedure is to elaborate on the process of decision making in instances of deviation, non-compliance

17.14.1 The IEC in its Interim Annual Report Form and Final Closure Report Form encourages researchers to notify any deviations from the IEC approved protocol citing reasons.

17.14.2 It is the responsibility of the PI to submit the pilot / Interim / Annual and Closure reports. In case of projects where the student is the PI, if the PI is not available (left the institute) the Guide is responsible for filing the report.

17.14.3 It is the responsibility of the Monitoring Sub Committee to review the project interim reports and closure report and notify it at the full board meeting or request for further information from the PI, if required.

17.14.4 The IEC shall identify non compliances through monitoring of the projects, feedback and complaints from investigators and participants.

17.14.5 The IEC can pursue one or any of the following (based on potential risk exposure to participants) when deviations and non-compliances are noted in the project :

17.14.5.1 The protocol deviations and non-compliances in the project are noted in the monitoring report for notification at the full board meeting. The PI is informed of the deviations and non-compliances to ensure that in future these are minimized

17.15 Actions for protocol deviations and non-compliances :

17.15.1 Suspension of the on-going project. Continuation of suspended project will be permitted only after approval at the full board meeting

17.15.2 Suspension of all on-going projects by any or all investigators involved. Continuation of suspended projects will be permitted only after approval at the full board meeting

17.15.3 Non-compliance may be noted in the original IEC approval certificate

17.15.4 The Head of Department / Institution may be informed of noncompliance for appropriate administrative action

17.15.5 Exclusion of any collected data as per the deviation

17.15.6 Restriction on Publication of such projects

17.15.7 Withdrawal of the IEC certificate and approval status

17.15.8 Recommendation for undergoing training courses with an intention of sensitizing the researcher on ethical aspects before continuing/ initiation of new project.

17.16 Full board recommendations regarding non-compliance to attend the offsite monitoring meeting and/or submission of study related documents in time will result in the IEC pursuing one or any of the following:

17.16.1 Closed projects - New projects submitted by any of the investigators will be taken up for review by the IEC only if the investigator submits the closure report of the study to the satisfaction of the IEC Monitoring Subcommittee

17.16.2 Ongoing projects - New projects submitted by any of the investigators will be taken up for review by the IEC only if the investigator presents the ongoing monitoring report of the study at the full board meeting

17.16.3 Suspension of all on-going projects by any or all investigators involved. Continuation of suspended projects will be permitted only after approval at the full board

meeting

17.16.4 Non compliance may be noted in the original IEC approval certificate

17.16.5 The Head of Department / Institution may be informed of noncompliance for appropriate administrative action

17.17 After the offsite monitoring meeting :

The Convener shall prepare the minutes and present it in the next full board meeting of the IEC. The convener / member of the subcommittee will present the findings of the offsite monitoring meeting in the next regular full board meeting. If there is no further action required and the report is accepted by the full board, these will be filed. If any follow up action is to be taken by the PI / CoI of the project, a report of the findings will be sent to the investigator for appropriate action.

17.18 Any complaint/suggestion may be sent to the member secretary at the following address:

The Member Secretary
IEC Secretariat
Room 22, Ground floor
KMC Faculty Rooms (adjacent to KMC Administrative Block / Office)
Kasturba Medical College, Manipal - 576 104
Phone : +91 820 29 33522
E-mail : iec.kmc@manipal.edu
Intranet webpage : www.khinfo.edu (Knowledge base - Ethics Committee)

Complaints/suggestions may be anonymous and done orally or in writing.

18. Interim Annual Report

The purpose of Interim Annual Report is to monitor the progress of the study which was previously approved; not only for the changes but also to ensure continued protection of the rights and welfare of research subjects.

18.1 This process applies to conducting continuing review of studies involving human subjects at intervals appropriate to the degree of risk but not less than once a year. Depending upon the degree of risk to the participants, the nature of the study, the vulnerability of the study participants and duration of the study, IEC may choose to review the study more frequently.

18.2 It is the responsibility of the Monitoring Sub Committee to review the annual status report and notify it or request for further information, if necessary. The monitoring subcommittee is appointed by the chairperson from the IEC Members with one member designated as the convener for this subcommittee.

18.3 Procedure

18.3.1 It is the responsibility of the PI to communicate the annual status report to the IEC Secretariat. Investigators must plan ahead to meet the required timelines. The Annual Status Report has to be received before the completion of one year (365 days) of the study approval date. If an investigator fails to submit Annual Status Report in time (365 days from date of approval of study), all research procedures must stop.

18.3.2 If the IEC Secretariat does not receive the said report, the secretariat shall send reminders to PIs regarding the submission of Annual Status Report.

18.3.3 All the approved studies will be reviewed at least annually. IEC is responsible for determining if the project will be reviewed more frequently than annually, including specific criteria used to make these determinations (e.g., an IEC may set a shorter approval period for high risk projects or projects with a high risk: potential benefit ratio).

18.3.4 IEC is primarily responsible for reviewing the study progress, the occurrence of unexpected events or problems, and the rate of accrual of participants. The protocol, informed consent documents and assent documents are examined to ensure that the information remains accurate.

18.3.5 The monitoring of Annual Status Report will be done by the Monitoring Sub Committee. The IEC has the same options for decision making on an Annual Status Report as for an initial review application.

18.3.6 Principal Investigator should submit soft copy of the annual report. Upon receipt of the annual report, the IEC Secretariat will forward it to the Sub Committee.

18.3.7 The Sub Committee will review and will record their findings and the same will be presented in the IEC Meeting. The IEC members could arrive at any one of the

following decisions at the IEC meeting : Approval to continue the study / Not approved. The decision regarding the approval disapproval will be noted and documented in the minutes of the meeting and communicated to the PI. If necessary clarifications will be sought by the Sub Committee before the IEC Meeting.

18.3.8 The IEC secretariat will file the annual status report in master file of the research study (in soft copy) and archived year wise in hard copy.

18.3.9 For all regulatory trails, the IEC shall archive the report with the master file of the project.

19. Final Closure Report

It is the responsibility of the PI to submit Final Closure Report in the model format available at the IEC webpage. The Final Closure Report is to be submitted as soon as the project procedures are completed i.e after the last intervention on the last participant. Timely submission ensures compliance with regulatory requirements. Delay in the submission of Final Closure Report till after data analysis / inferences / conclusions are arrived at or when ready for submission of dissertation / publication is inappropriate.

19.1 Procedure

19.1.1 It is the responsibility of the PI to submit the completion report, suo moto and in time (after the last intervention on the last participant / after collection of data is completed).

19.1.2 The IEC shall send an alert to the PIs IEC Interface, 7 days before the due date for Annual and Closure Reports

19.1.2 In case of projects where the student is the PI, if the PI is not available (left the institute) the CoI / Guide is responsible for filing the report.

19.1.3 The IEC can take punitive actions in future submissions by the same PI / Co-investigators / Department which has failed to comply with the requirements of closure, including but not restricted to, not be permitted to submit any new proposal for review by the IEC nor undertake any other research projects until such reports are furnished to the satisfaction of the IEC.

19.1.4 The IEC secretariat will receive a copy of the Study Completion Reports from the PI. The Monitoring Sub Committee shall review the Final Closure Report Forms and Interim Annual Report Form and notify it or request for further information, if necessary.

19.1.5 The Sub Committee should review a copy of the completion report. The report is presented in the IEC meeting. If appropriate to the discussions, the chairperson may call for consensus to accept it or request further information or take any other action.

19.1.6 The secretariat will note the decision in the meeting minutes. In case, further information / action is requested, the same should be followed by the PI and communicated to the IEC office within 30 days. This update will be tabled in the full board meeting of IEC.

19.1.7 Once the report is accepted by IEC, study will be considered as closed and the secretariat will file the report in the study (in soft copy) and archived year wise in hard copy.

19.1.8 For all regulatory trails, the IEC shall archive the report with the master file of the said project.

20. Dealing with requests and complaints

This provides the processes for ensuring participant rights, responsibilities and wellbeing. It also lays out the guidelines for dealing with and accommodating requests by participants / patients regarding the rights as a participant or to resolve their complaints in any approved research study.

20.1 Rights of participants involved in any research project :

The Ethics Committee shall follow documented procedures for protection of the rights of research participants.

20.1.1 Right to Information : Participants have the right to receive information about the study, its objectives, methodology, what to expect, duration of study, possible benefits and side effects, alternate treatment options, information about any compensation, funding source, any alteration / compromise in standard treatment, cost implications of being in study and how to address any concerns they may have regarding the study. All potential participants have the right to receive a Participation Information Sheet, prior to enrolment in any study. Participant Information Sheet shall contain all relevant information in the language that participants comprehend. Participants have the right to retain a copy of the Participant Information Sheet for their reference.

20.1.2 Right to Consent : Participants have the right to give or withhold their consent for any proposed research project. They have the right to consult or seek a second opinion before giving their consent. They have the right to refuse consent for participation in any research. All potential participants have the right to receive a consent document, in the language they comprehend. Participants have the right to retain a copy of the signed consent document. Participants aged between seven and eighteen years have the right to assent, in addition to parental / guardian consent.

20.1.3 Right of Choice : Participants have the right to know all their options (eg. treatment, non participation) and the implications of participation in the research. They have the right to voluntarily participate in the study without any pressure or coercion from anyone conducting / associated with the study.

20.1.4 Right to Privacy : Participants have the right to confidentiality and privacy. They have the right to protection of personal, healthcare and any other information obtained as part of a research activity. Information concerning the participant may only be disclosed with their consent, except when required in terms of any law or an order of the court.

20.1.5 Right to Respect : Participants have the right to respect regardless of race, culture, religion, caste, age, gender, sexuality, income or physical ability and not to be subjected to any kind of discrimination or neglect.

20.1.6 Right to Quality : Participants have the right to quality in research conduct in accordance with standards such as Ethical Guidelines for Biomedical Research on Human Participants by ICMR, New Drugs and Clinical Trial Rules 2019 and ICH – GCP

20.1.7 Right to seek Clarification : The participant, while enrolled in a study, has the

right to ask questions or raise concerns on any aspect of the study, that may influence their decision to continue in the study.

20.1.8 Right to receive Remuneration for Participation : Research participants have the right to receive remuneration for participation in accordance with Ethical Guidelines for Biomedical Research on Human Participants by ICMR and New Drugs and Clinical Trial Rules 2019, as indicated in the protocol and Participant Information Sheet.

20.1.9 Right to Compensation for Injury : Research participants have the right to compensation for injury in accordance with New Drugs and Clinical Trial Rules 2019 (eg. free medical treatment, monetary compensation for disability / death)

20.1.10 Right to Withdraw : Participants have the right to withdraw their consent at any stage of the study, without giving any reason. Participants have the right to receive standard clinical care even after withdrawal of consent.

20.1.11 Right to Raise Concerns : Research participants have the right to get the contact details (email, telephone number and office hours) of the Institutional Ethics Committee to raise any concerns or complaints.

20.1.12 Right to Redressal : Participants have the right to receive a response from the IEC regarding their concerns / complaints within a period of 45 working days in compliance with current regulatory guidelines

20.2 Responsibilities of participants involved in any research project :

20.2.1 Participants in any research study must read the Participant Information Sheet and Informed Consent form and ask the Principal Investigator any questions they have, so that they can understand what will happen during the study before agreeing to participate. They should keep a copy of the Participant Information Sheet and the signed consent document for their records.

20.2.2 It is the responsibility of the participant to ask questions or raise concerns with the Principal Investigator if any detail of the study is not clear to them.

20.2.3 A research participant and her/ his attendants have the responsibility to provide complete and accurate information if they decide to take part in a study.

20.2.4 They should inform the Principal Investigator if they anticipate any problem in the prescribed treatment or are considering alternative therapies.

20.2.5 Participants are responsible for their decision to take part in a research study. They are required to follow all the study requirements including follow up appointments as mentioned in the Participant Information Sheet, till completion of study / withdrawal from study.

20.2.6 Participants are responsible for intimating the Principal Investigator when they decide to withdraw from a study to which they had consented

20.2.7 Research Participants are responsible for reporting any adverse events / any detriment experienced after their enrollment in the study

20.3 It is the responsibility of the IEC Member Secretary to provide the required information to the research participants / research participant's representatives / patient, in the case of queries received.

20.4 It is the responsibility of the Member Secretary / Chairperson to initiate a process of giving information to the participants or identifying and addressing any injustice that has occurred, if complaints are received from research participants.

20.5 When the IEC secretariat / member receives a request from a research participant (or research participant's representatives) or public (faculty, students or any other interested person):

20.5.1 The request / complaint and information will be received in writing. However the IEC may also initiate enquiry even when the complaint is made orally or suo moto based on complaints received by any IEC member.

20.5.2 The Chairperson will direct the Member Secretary to consider the matter for discussion.

20.5.3 The Chairperson / Member Secretary / designated IEC members will enquire the situation and the final enquiry report will be tabled at the next regular IEC meeting.

20.5.4 The final decision of the matter will be taken at the full board meeting. This decision will be recorded as part of the minutes.

20.5.5 A decision about the complaint will be sent to the complainant by the Member Secretary.

21. Record keeping

This describes instructions concerning procedures for record keeping / archiving.

21.1 The following documents shall be kept in secure lockers under lock and key and be access restricted to the IEC secretariat and regulatory bodies only. The keys to the records shall be under the custody of the Secretary and access shall be authorized by the Member Secretary / Chairperson

- The old and new versions of SOPs of the IEC
- The copy of the circular appointing members of the IEC - old and new Constitution and composition of the IEC
- Signed and dated Curriculum Vitae (CV) of all members of KMC & KH IEC including of alternate members, if any
- Training records of IEC members Signed confidentiality agreements
- Signed conflict of interest declarations of members Registration and accreditation documents
- Copy of all existing relevant national and international guidelines on research ethics and laws along with amendments
- Regulatory notifications
- Meeting-related documents (Agenda, comments form, minutes of full committee meetings and Monitoring Sub committee reports) duly signed by the Chairperson and Member Secretary or Convener as appropriate**.** All draft copies prepared during the meeting, in hand written form, will be securely shredded after the Member Secretary verifies the typed transcripts.
- Copy of all correspondence with members, researchers and regulatory bodies
- Financial records of EC
- IEC document request forms
- All communications received or made by the IEC Register of disposal of documents

21.2 The Member Secretary shall physically inspect the premises, cupboards and their contents (archived projects) periodically. The periodic inspections will certainly be at least every 6 months.

21.3 The projects that have completed the regulatory period of archiving (7 years for regulatory device studies, 5 years for regulatory drug studies and 3 years for non regulatory studies) will be disposed off by the Member Secretary securely. Soft copies of projects will also similarly be deleted by the Member Secretary after completion of the regulatory period of archiving (7 years for regulatory device studies, 5 years for regulatory drug studies and 3 years for non regulatory studies).

21.4 The Member Secretary may present statistical data of projects at any quality indicator audits of either Kasturba Medical College, Kasturba Hospital or Manipal Academy of Higher Education or other administrative meetings with institutional heads always ensuring confidentiality of individual projects submitted / approved by the IEC.

21.5 The Member Secretary may also forward any report / list of projects / minutes of the meetings to any regulatory body upon receiving a written request from the appointing authority.

22. Archival, retrieval and disposal of documents

This provides instructions for preparation and maintenance of active study files and other related documents approved by the KMC & KH IEC, and storage / archival of closed files and retrieval of documents. It applies to all active protocol / study files, closed files and their related documents that are maintained in the IEC office and archival site.

Active study file : Any approved protocol, supporting documents, records containing communications and reports that correspond to each currently approved study.

Closed study file : Any approved protocol, supporting documents, records containing communications and reports that correspond to a study which is completed or terminated or discontinued or suspended or not initiated.

22.1 It is the responsibility of IEC staff to ensure that all study files are prepared, maintained, and kept securely for a period of three years, five years and seven years after the closure of the project for non regulatory projects and regulatory clinical trials drugs and devices respectively (under a proper system that ensures confidentiality and facilitates retrieval at any time).

22.2 Active study files maintenance & archival of closed files

A Study Master File is the file comprising all essential documents and correspondence related to the study/protocol. Study master files shall include :

22.2.1 The study files are assigned unique identifiers (serial project no / year.)

22.2.2 The project files (original, modifications and amendments) will be archived, clearly labeled with the project number

22.2.3 The project SAE reports, AE reports, protocol deviations/violations, progress reports, continuing review activities, site monitoring reports, record of notification issued for premature termination of a study with a summary of the reasons, final closure report of the study and publications shall be archived in a single Project Master File for all regulatory projects.

22.2.4 A register shall be maintained separately for all regulatory projects

22.2.5 For Academic / Investigator Initiated Studies, separate folders for the print versions of closure / annual reports, amendments and additional documents shall be filed using the IEC Project Number for easy retrieval. The soft copies shall however be archived in a single Project Master File for all Academic / Investigator Initiated Studies also.

22.2.6 All active files are kept in a secured file cabinet with controlled access. Only the IEC Secretary, IEC Member Secretary and IEC Chairperson will have access to the files. Any member who wishes to go through the project / master files hard copy may request the Member Secretary to provide the same stating reason (eg.monitoring) for the requisition and the Member Secretary shall duly authorize the same.

22.2.7 The project files are confidential and access to the files should be restricted to the IEC and the regulatory authorities.

22.2.8 The electronic (soft) copy records are stored in the hard disk of 2 desktops (IEC Member Secretary and the IEC Secretary).

22.2.9 The electronic (soft) copy records will be archived in an external hard disk, at least every 6 months. The external hard disk would be stored in a secure cabinet under lock and with access permissions as for the original master files.

22.2.10 The e-submissions Master Files and related electronic records shall also be archived in an external hard disk for a period of seven years and five years from the completion of the study for regulatory device and drug trials and for three years for non- regulatory trials.

22.2.11 E-submissions of all study Master Files, with enclosed documents, annual status reports, SAEs and study closure report will be printed and archived for a period of seven years and five years from the study closure date for regulatory device and drug clinical trials and for three years for non-regulatory projects.

22.2.12 All print versions and electronic records shall be deleted / shredded at the end of a period of three years, five years and seven years after the closure of the project for non regulatory projects, regulatory drug and device clinical trials respectively.

22.3 Accessibility / Retrieval

22.3.1 For administrative purposes, the IEC Member Secretary and Chairperson can retrieve archived file(s). For this purpose the IEC Member Secretary can authorize the IEC Secretary to physically retrieve a file.

22.3.2 Master files will be made available for inspection and copying by authorized representatives of regulatory authorities after receiving the request in writing.

22.3.3 In case any investigator needs a copy of any document from the master file, he / she should make a written request to the Chairperson. Only the PI or the other investigator of the original team can make a request for a copy of the study files. Requests made by persons other than the investigators will not be processed.

22.3.4 The request for a copy should be accompanied by a processing fee equivalent to the fee charged for issuing a duplicate certificate.

22.3.5 The IEC staff will furnish a copy of the required document within 15 days with the IEC Member Secretary's approval.

22.3.6 Whenever an item is retrieved and a copy is provided to anyone for any purpose other than for review or verification within the IEC secretariat, the date, item and person requesting, person retrieving the item, date returned and number of copies made should be documented in the register.

22.4 The master files will be disposed off by the IEC secretariat after the archival period of three years and five years after the closure of the project for non regulatory projects and regulatory clinical trials respectively. A formal written off register will be maintained, providing details of the documents being written off / disposed off after notification at the full board of the IEC.

23. Review of the procedures of the IEC

The IEC will periodically review its procedures and guidelines in keeping with developments in the field of research on human subject and associated development in the field of ethics. Any changes in the procedures and guidelines will be communicated to the Head of the Institution (KMC & KH) for wider dissemination. The IEC will also itself be open to peer review in accordance with any guidelines that may come up in this direction from the ICMR, DCGI or any other national and / or international regulatory or advisory authorities at present or in future.

23.1 Evaluation of the functioning of the IEC

23.1.1 The Member Secretary shall audit the functioning of the IEC annually. The audit report shall be presented at the next regular board meeting of the IEC and corrective action for improving the functioning of the IEC shall be recorded.

23.1.2 Each member of the IEC shall do a self assessment, at 6 monthly intervals. The assessment report shall be filed at the Secretariat. Areas for improvement of functioning of IEC / member / staff shall be identified and steps taken to achieve the same.

23.1.3 The IEC shall have a provision for researchers to give their feedback on any aspect of the IEC functioning and SOP. The option of anonymous filing of complaints shall be permitted, by providing the option on the IEC webpage. The Member Secretary shall notify the full board on all such feedback and initiate appropriate corrective action in compliance with existing regulations and guidelines.

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