INSTITUTIONAL REVIEW BOARD

Standard Operating Procedures

MALABAR CANCER CENTRE

(An Autonomous Institute under the Government of Kerala)

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Preface

The Institutional Ethics Committee (IEC) established in 2013 is responsible for the scientific, ethical and regulatory oversight of research conducted at Malabar Cancer Centre, and serves to protect the rights and welfare of human subjects.

Standard Operating Procedures (SOP) of IEC provide guidance to the members of IEC, Data Safety Monitoring Subcommittee, Investigators and other stake holders involved in research. Adherence to these guidelines would help to promote and maintain the standards towards ethical conduct of research, and protect the rights and wellbeing of research participants and communities.

Various national and international bodies have developed and promulgated guidance documents for the ethical conduct of clinical research. The cornerstone of these ethical guidelines is that research should be subject to prior ethical review by a competent Institutional Ethics Committee. The present SOPs draw reference to these guidelines and documents and have been framed considering the variability in expertise, experience, training and capacity of IEC members at Malabar Cancer Centre. A set of SOPs have been developed to maintain consistency in the process of review and continuous monitoring of research proposals by the IEC.

The current set of revisions in the IEC SOPs has been made to update the existing SOPs, taking into account the changing laws, regulations and guidelines for the conduct of medical research involving human participants as well as identifiable human material and data. All future revisions of the IEC SOPs will be made to reflect the changes in the national laws and guidelines and to keep pace with the international advances in the field of bioethics. The ultimate mandate of these SOPs will be to further the cause of conduct and adherence to the highest standards of human research.

DIRECTOR

Date 22-09-2021

Place Thalassery

LIST OF ACRONYMS

Acronyms	Description
AAHRPP	Association for the Accreditation of Human Research Protection Programs
ACTREC	Advanced Centre for Treatment, Research and Education in Cancer
ADR	Adverse Drug Reaction
AE	Adverse Event
AIIMS	All India Institute of Medical Sciences
ASU	Ayurveda, Siddha, Unani.
BA	Bio-availability
BARC	Bhabha Atomic Research Centre
BE	Bio-equivalence
BIS	Bureau of Indian Standards
CDC	Center for Disease Control and Prevention
CDSCO	Central Drugs Standard Control Organization
CFR	Code of Federal Regulations
CIOMS	Council for International Organizations of Medical Sciences
CoI	Conflict of Interest
CONSORT	Consolidated standards of reporting trials
CRF	Case Record Form
CRO	Contract Research Organization
CRS	Clinical Research Secretariat
CTA	Clinical Trial Agreement
DAE	Department of Atomic Energy
DBT	Department of Biotechnology
DCGI	Drug Controller General of India
DCR	Drugs and Cosmetic Rules, 1945
DGFT	Directorate General of Foreign Trade
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
DSMSC	Data Safety Monitoring Sub Committee
DST	Department of Science and Technology
DTAB	Drugs Technical Advisory Board
ELSI	Ethical, Legal and Social Issues
FDA	Food and Drug Administration
FDC	Fixed Dose Combination

LIST OF ACRONYMS
(Contd.)

Acronyms	Description
GCP	Good Clinical Practice
GMP	Good Manufacturing Practices
HIPAA	Health Insurance Portability and Accountability Act
HMSC	Health Ministry's Screening Committee
IAEA	International Atomic Energy Agency
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Committee on Harmonization
ICJME	International Committee of Medical Journal Editors
ICMR	Indian Council of Medical Research
IDE	Investigational Device Exemption
IEC	Institutional Ethics Committee
IMDRA	Indian Medical Devices Regulatory Authority
IND	Investigational New Drug
IRB	Institutional Review Board
ISI	Indian Standards Institute
MCC	Malabar Cancer Centre
MoU	Memorandum of Understanding
MTA	Material Transfer Agreement
NAC-SCRT	National Apex Committee for Stem Cell Research and Therapy
NCE	New Chemical Entity
NDA	New Drug Application
NIH	National Institutes of Health
NOC	No-objection Certificate
OHRP	Office for Human Research Protections
PI	Principal Investigator
RCT	Randomized Controlled Trial
SAE	Serious Adverse Event
SOPs	Standard Operating Procedures
SRC	Scientific Review Committee
WHO	World Health Organization
WMA	World Medical Assembly

CHAPTER 1

Preparing Standard Operating Procedures (SOPs)

1.1 PURPOSE

This SOP defines the process for writing, reviewing, distributing, and amending SOPs within the Institutional Review Board (IRB). The SOP also defines procedure for documentation, archival, retrieval, destruction of SOP to ensure that the latest SOPs are followed, Malabar Cancer Centre (MCC).

The SOPs will provide clear, unambiguous instructions to conduct activities of the IRB in accordance with the ICMR guidelines, Indian GCP Guidelines, New Drugs & Clinical Trials Rules 2019, WHO Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants, and International Council for Harmonization, Guidance for Industry E6-R2 Good Clinical Practice: Consolidated Guidance, Code Federal Regulations Title 21

1.2 SCOPES

This SOP covers the procedures of writing, reviewing, distributing, and amending SOPs within the Institutional Review Board (IRB) of Malabar Cancer Centre (MCC).

1.3 RESPONSIBILITIES

It is the responsibility of Member Secretary of the Institutional Ethics Committee (IEC) of MCC along with the consent of the Director, MCC, to appoint the SOP Team to formulate the SOPs. SOP team will prepare the draft of the SOPs. The draft SOPs will be reviewed and approved by the Member Secretary or the IRB members. SOP team will be responsible to amend the SOPs as and when required. It is the responsibility of the IEC Member Secretary and administration staff/IEC Secretariat for maintaining control on all the SOPs.

The IRB Secretariat is responsible for ensuring that the current approved version of the SOP is available on the Institutional website. The SOP will bear the effective date and validity.
The IEC Secretariat will notify all concerned user via email of document updates (recent version). For the user, electronic access will be limited to a read-only format, thereby protecting against unauthorized changes made to the document

When SOPs are revised, the IEC secretariat will inform the IT department to remove obsolete copies from the website and upload the current approved version of the SOP

SOPs will be reviewed by the members of IRB, i.e. members of Committees constituting IRB in MCC. The Chairperson of IEC, MCC will give final approval of the SOPs. The SOPs will then be signed by Director.

The SOP team will consist of Member secretaries of IRB-IEC and one or two Scientific Review Committee members and/or Academic staffs of MCC. No other person without the written consent from authorized member of IRB, is entitled to make any changes in SOP's. The office of IRB/Members or the concerned SOP team will not be responsible for any natural/ill-intentional torturing in SOPs. The SOP team will-

- Assess the request(s) for SOP revision in consultation with the Member-Secretary of IEC and Chairperson, IEC
- Select the format and coding system for the SOPs
- Propose a new, or modification in existing SOPs as needed
- Draft the SOP after formatting and suitable coding
- Review the draft SOP
- Submit the draft for approval to Chairperson (Ethical Committee)

IEC Member Secretary

- Appoint one or more SOP Teams
- Sign and date each of the approved SOPs, as approver.

IEC members

- The delegated/designated member or Member Secretary will review the draft SOPs and sign as Reviewer.
- Return all out-of date SOPs to IEC office

Secretariat of IEC

- Co-ordinates activities of writing, reviewing, distributing, and amending SOPs.
- Maintains on file all current SOPs and the list of SOPs.
- Maintain a file of all SOP amendment requests
- Maintains an up-to-date distribution list of each SOP circulated to IEC members and ensure that each member is trained on the SOPs.
- Maintain a record of the investigators to whom SOPs are distributed against a requisition if any
- Ensures that all IEC members and involved administrative staff have access to the SOPs
- Ensures that the IEC members and involved staff are working according to current version of SOPs
- Maintain a file of all previous SOPs of the IEC
- Assist in the formulation of SOP procedure
- Ensure SOP revisions as and when required to comply with national regulations

1.4 DETAILED INSTRUCTIONS

1.4.1 Identify the need for new or amendment to the SOP

Any member of the IRB or member of Office of IRB or Academic Council Member or Investigators/ Researchers, can make a request for revision or notices an inconsistency/ discrepancy / has any suggestions on how to improve the existing SOPs or requests to design an entirely new SOP. The request can put forth by using the Request Form for Formulation of new SOP/ Revision of an SOP Form (*ANX5-VER2/SOP01/VER2)*. This Formulation of new SOP/ Revision of an SOP Form (*ANX5-VER2/SOP01/VER2)* is submitted to the Chairperson, IEC. The Member-Secretary of IEC will inform all IRB (both SRC & IEC) members about this request in a regular full meeting.

If IRB members agree to the request, the Chairperson/ Member Secretary of IEC will appoint an appropriate SOP team comprising of Member Secretary and suitable members of both committees and/or Academic staffs of MCC. This designated team will proceed with the task of revision / formulation process of the SOP.

If IRB members do not agree to the request, no further action will be taken.

The Member-Secretary of IEC must inform the person/ IRB member who made the request for modification of the SOP in writing about the decision.

1.4.2 Appoint of SOP Team

The Chairperson/Member Secretary will constitute an SOP team consisting of the Member-Secretary and two or more members from SRC & IEC who have a clear understanding of the scientific and ethical review process& qualities. The SOP writing team will carry out the subsequent steps (1.4.3 to 1.4.8)

1.4.3 List of relevant SOPs

- All the procedures of the IRB must be written down systematically and step by step
- Organize, devise and name each process
- Make a list of SOPs with coding format (e.g. *ANX1-VER2/SOP01/VER2)*

1.4.4 Format and Layout designing

Each SOP must be given a number and a title that is self-explanatory and is easily understood.
A unique code number with the format **SOP xx / VERy** will be assigned to each SOP. 'xx' is a two-digit number assigned to a specific SOP. "*VER*" refers to version of the SOP and "y" is a number identifying the version e.g. SOP01/VER2 is SOP number 01 with VER= Version Number 2

Each Annexure (ANX) is unique code with format **ANXn–VERp/SOP xx/VERy**. **e.g.** *ANX1–*

VER2/SOP01/VER2 indicates ANX is Annexure, 1 is Annexure number, VER2 is version 1,belonging to the SOP 01/VER2

Each Appendix will be given unique code with the format **APNn / VERy** e.g. APN1/VER2 indicates APN is Appendix, 1 is Appendix no 1, VER2 is Version no.1.

Each SOP will be prepared according to the template for Standard Operating Procedures (ANX2 – VER2/*SOP01/VER2)*. Each page of the SOP will bear a header with the effective date which isthe date of approval of the SOPs by the Chairperson, IEC and the Director, MCC.

The SOP number will be on the left-hand corner of the header. The title of the SOP will be on the left-hand corner of the footer. The page number will be listed as Page—of—Total pages on the right-hand corner of the footer.
The first two pages of each SOP document will be signed and dated by the authors/editors/ SOP team members, the IRB members who have reviewed the SOPs, IRB-IEC Chairperson and Director, MCC.

1.4.5 Write, Review and Approve SOP

With reference to section 1.4.1 and 1.4.2 the draft SOP will be prepared by the SOP team

Review by Consultation

- The draft SOP will be discussed with members of IECs and administrative staff and final review will be done by Member Secretary/delegate.
- The final version will be forwarded to the Chairperson for approval

1.4.6 Preparation and submission of final draft

- All the members of SRC & IEC will review the draft / revised SOP
- During respective IRB meetings, members can put forth their suggestions / comments on the draft / revised SOP
- The suggestions agreed upon unanimously by all IRB members will be incorporated and the final draft SOP will be formulated
- The SOP team would stand automatically dissolved once the IRB takes final decision regarding the SOP.

1.4.7 Final Approval of New / Revised SOP

The final version will be presented to the Chairperson, IEC, MCC for review and approval. The Chairperson will sign. This approved document will then be submitted to the Director, MCC for acceptance. This date of approval will be declared as the effective date for implementing the SOPs.

1.4.8 Implementation, distribution and filing of SOPs

- Approved SOPs will be implemented from the Effective Date. The Member Secretary will discussthe approved SOPs with the administrative staff and instruct them to implement the SOP accordingly.
- Approved SOPs will be distributed to IRB members, Head of the Departments, Medical Librarian, Administrative authorities and IRB staff and members according to the distribution list (*ANX4 – VER2/SOP 01/VER2).*
- When revised version is distributed, the old version will no longer be effective. A copy of the old version will be archived in a master file.
- One complete original set of current SOPs will be archived in the SOP master file, by the IRB Secretariat/Office of IRB and maintained in Malabar Cancer Centre.
- Soft Copy (Scanned & PDF of the existing SOPs Master File will be maintained in the individual offices of Division of Clinical Research & Biostatistics, Division of Cancer Registry, Office of the System Manager, Office of the Director and Medical Records division for sudden back up.
- Photocopies made from the paper versions of the SOP will be considered official only if stamped and signed by Member Secretary or authorized individual. A distribution log should be maintained *(ANX6 –VER2/SOP 01/VER2)*

1.4.9 Review and request for revision of an existing SOP

- Any member of the IEC, secretariat or administrative staff or investigators or administration who notices that current SOPs have some lacunae or have any suggestions to improve a procedure should make a written request, using a form (ANX5-VER2/SOP01/VER2)
- If IEC agrees with the request, the Chairperson will appoint an appropriate team for the revision process. If the committee does not agree, the Chairperson will inform the concerned individual who made the request for revision. Revised SOPs will be reviewed and approved as per Section1.4
- The Member Secretary initializing the review and the Secretariat assists the Member Secretary of the SOP at least once in every 2 years and records the dates of review in the SOP master file. SOPs will be reviewed once in every 2 years.

1.4.10 Document Control

IRB Secretariat will prepare the master copy / controlled copy / uncontrolled copy. The issuance of controlled and uncontrolled copies will be with the permission of the Member Secretary.
Archival / Retrieval / Disposal will be as per IEC SOP 10

Master copy- shall be an approved original copy of documents and will have a stamp/watermark of "Master copy". Master copy shall be kept in the IRB office with access control.

Controlled copies- shall be a copy of the master copy with a stamp / watermark of "Controlled copy". Controlled copies shall be kept in the IRB with access control. Controlled copy is a reference copy of master copy for the IRB members and IRB staff.
5 hard copies of the controlled copy of the IRB SOP will be maintained in the IRB office with restricted access for ready reference of the IRB Secretariat. A controlled copy of IRB SOPs shall be circulated to the IRB members at the time of reconstitution of the IRB.

Uncontrolled copies - shall be copy of master copy with a stamp / watermark of "Uncontrolled copy". Uncontrolled copies shall be kept in the IRB with access control. Uncontrolled copy is a reference copy of the master copy for the users such as researchers/research staff, sponsor, regulators and any other stake holders in research. It will be open on the institutional website (public domain) for reference.
Uncontrolled copies shall be distributed only on request. The issuance log of uncontrolled copies will be maintained.

1.4.11 Manage and Archive old SOPs

All the old SOPs should be retained and clearly marked "***SUPERSEDED***" and archived in a file by the Office of IRB. The process of evolution of previous SOPs of the IRB will be documented in a defined format (*ANX3 –VER2/SOP01/VER2*).

***** A PDF version of the approved SOPs must be put to the Institution's Website& the System Manager& other staffs of Health IT division, MCC, must be aware of and with any amendment done in SOPs.***

ANX1-VER2/SOP01/VER2

List of SOPs of Institutional Review Board (IRB), Malabar Cancer Centre (MCC)

Sr. No.	SOP Title		SOP Code
1	Preparing Standard Operating Procedures (SOPs)		SOP01/VER2
2	2a	Constitution of Institutional Review Board	SOP02a/VER2
	2b	Constitution of Data Safety and Monitoring Unit (DSMB)	SOP02b/VER2
3	Management of Research Study Submission		SOP03/VER2
4	4a	Full board Review of Submitted Protocol	SOP04a/VER2
	4b	Expedited Review of Submitted Protocol/Documents	SOP04b/VER2
	4c	Exemption from the Review for Research Projects	SOP04c/VER2
5	Preparation of Agenda, Procedures for conducting Meetings, Minutes recording		SOP05/VER2
6	Review of Amended protocol/ Protocol related documents		SOP06/VER2
7	Continuous Protocol Review		SOP07/VER2
8	Review of Protocol Deviation/ Violation/ Waiver/ Non-compliance		SOP08/VER2
9	Review of Reports on Serious Adverse Events (SAEs)		SOP09/VER2
10	Maintenance of Active project Files, Disposal/Archival of Closed project, Documents Retrieval		SOP10/VER2
11	Documentation of IRB Activities		SOP11/VER2
12	Study Completion Report Review		SOP12/VER2
13	Management of premature Termination/ Discontinuation/ Suspension of the Studies		SOP13/VER2
14	Review of request for waiver of Written Informed Consent		SOP14/VER2
15	Site Monitoring		SOP15/VER2
16	Dealing with patients'/ study participants' Requests or Complaints		SOP16/VER2
17	Reviewing Research Protocols Involving Vulnerable Populations		SOP17/VER2
18	Review of Academic Clinical Trial		SOP18/VER2
19	Training for IRB		SOP19/VER2
20	Assessment and Audit of IRB		SOP20/VER2
21	Review of proposals for conducting research in urgent / emergency situations		SOP21/VER2

ANX2-VER2/SOP01/VER2

Template for Standard Operating Procedures (SOP), IRB-MCC

Institutional Review Board (IRB), MCC	
Title: *Title which is self-explanatory& easily understandable*	
SOP No.: SOPxx/ VERy	Page:
SOP Code: SOPxx/VERy Effective Date: DD/MM/YYYY Authors: xxxxxxxx Reviewed By: xxxxxxxxx Approved By: xxxxxxxxx	

ANX3-VER2/SOP01/VER2

Document History of the SOP, IRB-MCC

Name of the Author	Version	Effective Date (DD/MM/YYYY)

Details of Superseded SOP, IRB- MCC

Name of the Team/Group	Version	Type (Final/Draft)	Date DD/MM/YYYY	Describe the Main Page

ANX4-VER2/SOP01/VER2

Log of IRB Members receiving SOPs

Serial No.	Name of the Recipient	Designation	SOP Code No..	No. of Copies	Signature	Date
1		Chairperson, IEC				
2		Member-Secretary, IEC				
3		Member, SRC &IEC				
4		Member, SRC &IEC				
5		Member, SRC &IEC				

ANX5-VER2/SOP01/VER2

Request for Formulation of New SOPs / Revision of SOPs

This form is to be completed by any member whenever a problem or a deficiency in an SOP is identified with the SOP until an authorized replacement is in place

SOP No.:	
Title:	
Details of problems or deficiency in the existing SOP	
Need to formulate an entirely new SOP (i.e. SOP not existing previously)	Date: (DD/MM/YYYY)
Identified By:	
Discussed in IRB (both SRC & IEC) Meeting held on: -	
SOP Revision Required: ☐ YES ☐ NO	
New SOP to be formulated: ☐ YES ☐ NO	
If Yes, to be carried out by Whom?	
If No, why not?	
Date of SOP Revised:	
Date of SOP Approved:	
Date of SOP becomes effective:	

ANX6-VER2/SOP01/VER2

Log of SOPs Recipients

(Other than SRC &IEC members)

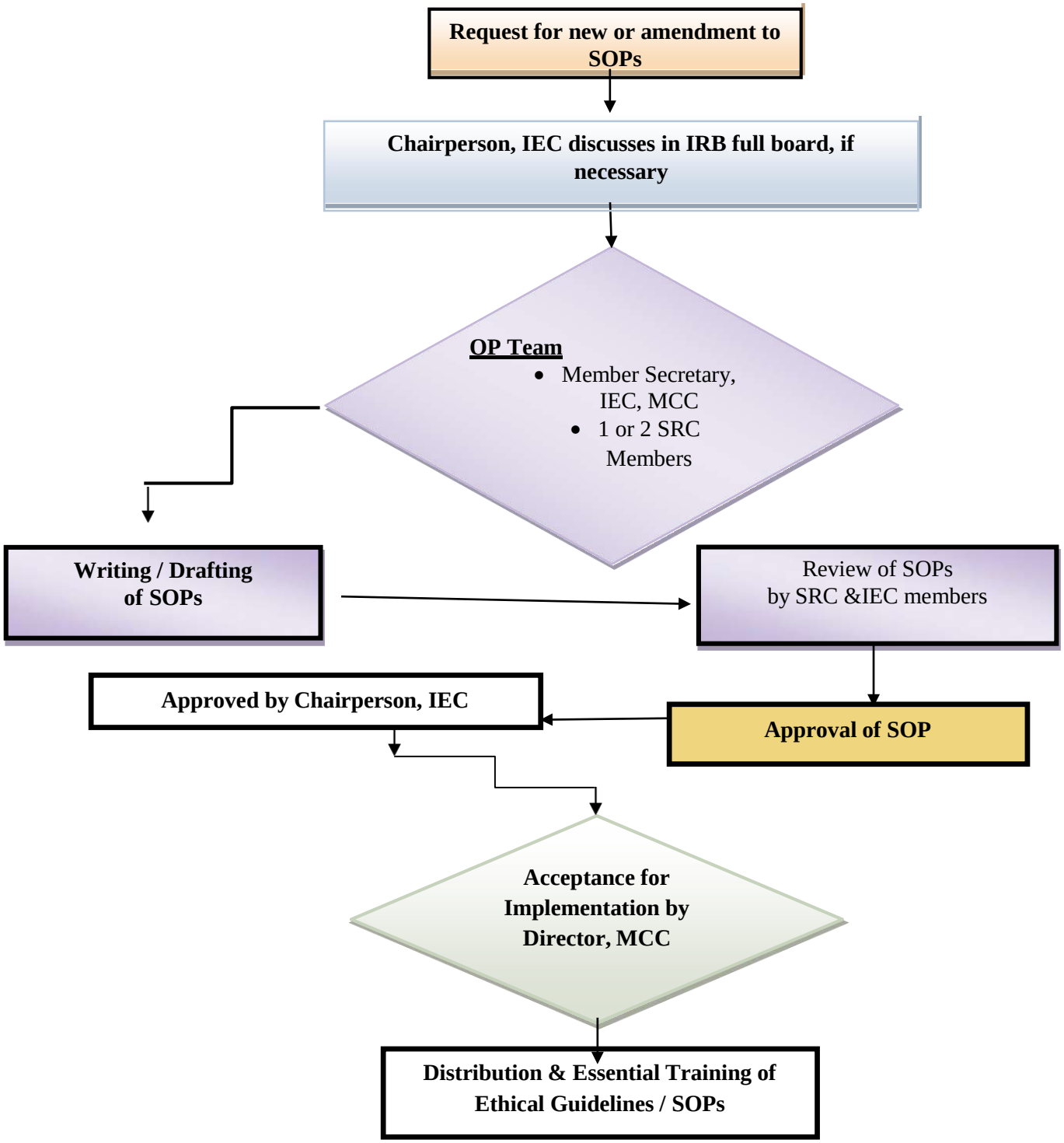
Serial No.	Name of the Recipient	Designation	SOP Code No..	No. of Copies	Signature With Date
1	XXXX	XXXX			
2	XXXX	XXXX			
3					
4					
5					

ANX7-VER2/SOP01/VER2

List of obsolete documents

Sr. No.	Name of Document and Number	Signature /Date
1.		
2.		

FLOW CHART


Request for new or amendment to SOPs
Chairperson, IEC discusses in IRB full board, if necessary
OP Team
Member Secretary, IEC, MCC
1 or 2 SRC Members
Writing / Drafting of SOPs
Review of SOPs by SRC &IEC members
Approved by Chairperson, IEC
Approval of SOP
Acceptance for Implementation by Director, MCC
Distribution & Essential Training of Ethical Guidelines / SOPs

CHAPTER 2a

Constitution of Institutional Review Board

INTRODUCTION

Malabar Cancer Centre (MCC), an autonomous institution under Health and Family Welfare Department of Government of Kerala, thrives for excellence in the field of early detection, diagnosis and treatment of cancer. The Institution is being developed as a State of Art cancer centre with equal thrust on Clinical Care, Education and Research. MCC has a clear vision to establish and evolve itself as a hub for Core Research on Oncology through investigator-initiated trials, multi-centric clinical trials,intervention studies, and development of newer technologies, experimental medications, therapeutics, processes and scientific techniques to fight against cancer.

The Institution is committed to continue oncology-based research by adhering to the internationally accepted ethical norms and scientific foundations. This requires impeccable and efficient management of its research activities and clinical trials to ensure the protection of human rights as mandated by Indian law (New Drugs and Clinical Trials Rules), and to satisfy public scrutiny, and public scrutiny.

Keeping the above in view, the Institutional Ethics Committee (IEC) of MCC was formally established in August 2013 as per the Annexure VIII of Schedule Y. All research proposals are subjected to ethical review by Institutional Ethics Committee (IEC), after scientific evaluation and approval by the Scientific Review Committee (SRC).The **Scientific Review Committee (SRC)** and the **Institutional Ethics Committee (IEC)**, together, constituted ***the Institutional Review Board (IRB)*** in MCC.

Timely review and systematic maintenance of ethical standards formed the basis ofthe IRB review process in MCC. These are essential for clinical research including Doctoral research, collaborating academic research with MoU undersigned, student research, investigator-initiated research, extramural, intramural funded research, multi-centric multinational research, CRO/SMO based clinical trials etc.

In view of the emerging demands for clinical research in the institution, the Director, MCC, constituted IRB to function with the specified purposes and SOPs, to expedite the review process. *All research proposals are scientifically evaluated and approved by Scientific Review Committee, before ethical review is taken up*.

A Board, named Data Safety & Monitoring Board (DSMB), is also been formed to assist

IRB for monitoring patient safety and assessing data during the course of the study in a manner that contributes to the scientific and ethical integrity of study**.**

The Institutional Review Boards (IRB) is constituted by the Director, Malabar Cancer Centre (MCC) under authority vested by the Executive Council and the Governing body of the centre.

2a.1 PURPOSE

The IRB in MCC was established to give legal status and specify Institution's commitment to the development and promotion of high quality scientific and ethical standards in Research, Education and Patient Safety & Care.

2a.2 MANDATE

The Institutional Review Board (IRB) through its delegated sub-committee(s) functions independently for maintaining a systematic, reliable and consistent scientificas well as in an ethical framework for patient care and research, and for communicating and integrating ethical values into organizational activities and practice.

I. The purpose of the IRB is to cultivate comprehensive and well-formalized exchange of scientific and ethical values and concerns, and to analyze them while looking for possibilities and scopes to enrich the scientific and ethical integrity and honesty of the Institution.

II. The mandate of the IRB essentially is to promote patient care and services through a scientific and ethical approach to research and education. The Terms of Reference for the IRB, MCC are as follows:

1) To ensure the highest scientific and ethical standards of research at MCC
2) Review, approve and manage proposals for clinical, basic or translational research projects (Intramural and Extramural) for scientific and ethical content
3) To function as a Medium to advise the administration in case of any ethical issues that may arise from patients or from families or from public
4) To create and sustain in leadership as a National Standard of reference in the field of oncology treatments, Care, Research &Professional Education.
5) To issue and periodically, update and revise SOPs and guidelines for effective functioning of IRB as and when necessary
6) Continuing education in clinical research bioethics and ethical aspects of clinical practice by National/International Seminars/Conferences, Workshops and interactive discussions for all categories of staff members including Nursing and Paramedical staffs.
7) To initiate research studies on ethical aspects of practice in MCC
8) Improve ethical standards and issue guidelines on ethical dilemmas related to patient care services.
9) To endeavor to be a national standard of reference
    - The IEC endeavors to provide guidance on a broad range of topics such as disclosures of diagnosis, diagnosis of brain death,indications for stopping resuscitation, informed consent, etc.
    - The committee does not address or interfere in matters of administration, nor does the committee function as a grievance cell for staff members.

The committees under IRB do not address or interfere in matters of administration, nor function as a grievance cell for staff members of MCC.

2a.3 SCOPE

This SOP applies to the formation of the IRB at Malabar Cancer Centre, Thalassery.

2a.4 RESPONSIBILITY

The IRB has the responsibility, within the Institution, for the following objectives:

- To ensure the competent review and evaluation of all scientific and ethical aspects of research projects received, compliance with the appropriate laws, and welfare of subjects.
- Consultations for clinical science and ethics
- Education of professional, administrative, and support staff about ethical issues.
- Creation, development, revision and implementation of guidelines for the IRB (SOPs).
- Initiate research studies in ethics.
- Continuing education and training programs to ensure that IRB members are regularly acquiring knowledge & well updated qualification to perform their specific duties.

2a.5 SCIENTIFICAND ETHICAL BASIS

- The committee consists of members who collectively have the qualification sand experience to review and evaluate the scientific, medical and ethical aspects of a proposed research project.

- The IRB recognizes that the protocols approved may also be approved by national and/ or local ethics committees and concerned regulatory bodies prior to their implementation in specific localities.

- In evaluating protocols and ethical issues, the IRB is aware of the diversity of laws, cultures and practices governing research and medical practices in various countries around the world

- The IRB also seeks to be informed, as appropriate, by national / other local ethics committees and researchers of the impact of the research it has approved.

- The IRB establishes its own Standard Operating Procedures based on the ICMR guidelines, New Drugs and Clinical Trials Rules 2019, WHO Standardsand Operational Guidance for Ethics Review of Health-Related Research with Human Participants, Indian GCP Guidelines and ICH-GCP E6-R2 Guidelines and their updates as and when they occur.
- The IRB is guided in its reflection, advice and decision by the Ethical principles expressed in the Declaration of Helsinki and CFR 45 (USFDA)

- It makes further reference to the International Ethical Guidelines for e.g. The Nuremburg Code (1945), the Belmont Report 1979, the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Geneva 2002), and the European Convention on Human Rights and Biomedicine
- IRB seeks to fulfill the requirements for international assurances and is established and functions in accordance with the national law and regulations

2a.6 COMPOSITION OF IRB

Institutional Ethics Committee (IEC)

- IEC will be multidisciplinary and multi-sectorial in composition. IEC is composed of a minimum of *seven*, and maximum of *fifteen* members. The members are selected to have an equitable representation of all specialties in Malabar Cancer Centre. It includes scientific and non-scientific members, clinicians and non -clinicians, a clinical pharmacologist, members of the community, a lawyer-expert in ethics, a social worker / layperson / patient representative to represent different points of view.
- The committee will comprise of a Chairperson, a Member Secretary, and 4-12 other active members who represent an appropriate balance of professional, ethical, legal, cultural, educational, and community interests
- The committee should have adequate representation of age, gender, community, etc. to safeguard the interests and welfare of all sections of the community /society. Members are expected to be aware of local, social and cultural norms, as this is the most important social control mechanism
- The members should have various backgrounds to promote complete and adequate review of research activities commonly conducted by MCC.
- IEC shall consist of at least fifty percent of its members who are not affiliated with the institute.

Composition of IEC

The composition should be as follows:-

No	Position	Affiliation status
1.	Chairperson	(not – affiliated to MCC)
2.	Member Secretary	Institutional Staff Member)
3.	Basic medical scientist	Institutional or non affiliated to MCC
4.	Clinicians	(not – affiliated to MCC)
5.	Pharmacologist	(not – affiliated to MCC)
6.	Social Scientist	(not – affiliated to MCC)
7.	Legal Expert	(not – affiliated to MCC)
8.	Lay person	(not – affiliated to MCC)

2a.6.1 SCIENTIFIC REVIEW COMMITTEE (SRC), MCC

2a.6.1 (a) Constitution:

The Scientific works under the Institutional Review Board, MCC and it is an independent sub-committee to review research project proposals in scientific point of view. The committee is formed by the Director, MCC, after a consultation with Chairperson, IRB-IEC and Academic Council of MCC.SRC reviews the scientific and technical aspects of the study proposals. It works as a first phase screening committee of IRB, MCC.

SRC will have the authority to approve a study proposal if the majority of membersare agreed in a SRC meeting and recommend the study proposal to exemption from review, Expedited review, full board review of Institutional Ethics Committee (IEC). IEC will reviewing ethical issues, and scientific aspects if any. The IEC need not approve the scientific aspect even if SRC approved.

2a.6.1 (b) Composition of Scientific Review Committee (SRC), IRB, MCC

The scientific Review Committee (SRC) of MCC is constituted by the Director of MCC with the following composition :

- Chairperson: Director of MCC
- Vice-Chairperson : Three Senior Professor or Clinical HoD)
- Members: Faculty members with or above the ranking of Associate Professor inacademic divisions, MCC
- 2 Biostatistics Faculty Members from MCC to see the Statistical bases for the studyproposals
- Invited experts from other major institutions as per the requirement

.

Quorum:

- Chairman- If the Chairman is not available- Any of the Vice Chairmen should be available
- Member-One Associate Professor from a Department or Division- if multiple Associate Professors available in a Department they can alternate
- Biostatistics faculty- Arrangement can be made from the Department/Division level
- 50% of the members should be available including chairman/Vice chairman SRC meets on every 2nd and 4thSaturday of amonth.

2a.6.2 MEMBERSHIP OF IRB-IEC, MCC

The Director, MCC appoints the Chairperson, IRB-IEC. The Director, MCC, will appoint all members of the IRB-IEC, after having a discussion in the Academic Council. The Executive Committee shall be informed or shall approve thecomposition. The Director of MCC shall nominate the Member Secretary for IRB- IEC.

❖ **Criteria for selection of members:**

i. Members are selected on their personal capacities, based on their interest, ethical and/or scientific knowledge and expertise, experience in the domain field and profile.
ii. Conflict of interest will be avoided while making appointments, but where unavoidable, there will be transparency with regard to such interests.
iii. New members will be identified according to the requirement i.e. as per the composition specified in Section 2.6. of this SOP and provided the potential member fulfils the conditions of appointment as defined in 2.6.4 of this SOP.

2a.6.3 Terms of Appointment

2a.6.3. (A) Duration

- The members of the IRB, MCC will be appointed for a duration of5years
- The appointment procedure for membership will be followed so that it allows for continuity, development and maintenance of expertise within the review board, and the regular input of innovative ideas and dynamic approaches.
- Generally, the members can be continued for a period of two terms, butextended periods can be permitted by suitable bodies of the institution. Extension of membership will be based on the recommendation of the Chairperson and Member Secretary of the IEC.
- In case of the resignation/discontinuation of a Member Secretary, Chairperson, vice chairperson or member, a replacement may be newly appointed by the Director, MCC before the completion of the tenure of the existing appointed committee. This appointment will be effective for the remaining tenure of the existing committee

2a.6.3. (B) Renewal

➢ The membership will be renewed after the stated term of 5 years.
➢ The process of renewal will be as follows: Selection of Chairperson and other members should be done at least 3months and 1 month in advance respectively. Member secretary designate should be inducted into the IRB as an observer before he/she takes on the mantle in the new IRB.
➢ Designated members of the IRB who wish to attend IRB meetings as observers should read, understand, accept and sign the agreement contained in the Confidentiality / Conflict of Interest form *(ANX2– VER2/SOP02/VER2)* at the beginning of the IRB meeting and/or beforescientific and ethical review tasks of the IRB commence
➢ The members who have resigned may be replaced at the discretion of the institutional Director. IEC members who decide to resign must provide the institutional Director, and Chairperson, IEC, the written notification/email of their proposed resignation date at least 30 calendar days prior to the next scheduled meeting. In case of resignation, Director, would appoint a new

2a.6.3. (C) Resignation / Replacement procedure

The members who have resigned may be replaced at the discretion of the Director, MCC. IRB members who decide to resign must provide the Director, MCC, and Chairperson, IEC, the written notification of their proposed resignation date at least 30 calendar days prior to the next scheduled meeting. In case of resignation, Director, MCC would appoint a new member, falling in the same category of membership e.g. "NGO representative" with "NGO representative". Recommendations may be sought from there signing member. Appointments may be made in consultation with Academic Council members and /or Chairperson of IEC.

2a.6.3. (D) Termination / Disqualification procedure

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

- Conduct unbecoming for a member of the IRB, MCC
- Failure to attend more than 3 consecutive meetings of the IRB without prior information and subsequent to review of the membership by the IRB; if deemed necessary, the IRB may decide to terminate the membership and the Chairperson, IEC may make a recommendation to the Director, MCC, for necessary action.
- Relocation to another city or any such matter

In all such situations/circumstances, Director, MCC will serve a letter of termination to the member. Documentation of the termination will be recorded in the minutes of the next duly constituted IRB meeting and the IRB membership roster and circulars will be revised.

2a.6.4 Conditions of Appointment

1. Name, gender, profession, and affiliation of IEC members will be publicized on the institutional website.
2. Members must accept the appointment in writing.
3. Members must submit a one page CV and training certificates in Ethics and/or GCP.
4. Members must apprise themselves of the New Drugs and Clinical Trials Rules, GCP for clinical trials in India, ICH GCP guidelines and the ICMR guidelines and institutional IEC SOPs.
5. Members are required to sign the Confidentiality / Conflict of Interest Agreement (AX1- V6/SOP 02a/V6) and Financial Disclosure at the start of their term. The confidentiality agreement protects the privacy and confidentiality of all parties whose information may be disclosed to the IEC in the course of its work. All IEC members shall disclose in writing to the IEC allconflicts of interest for themselves and their spouses/domestic partners and dependent children. For purposes of this policy, a conflict of interest may be identified as either financial in nature (such as when an IEC member holds an economic interest in the research) or non-financial in nature (such as when an IEC member or consultant participates in the research or will be included as a co-author on a publication from the research), either of which could affect or

appear to affect the design, conduct, oversight, or reporting of the research project. Financial interests that require disclosure include but are not limited to:

6. Ownership interest, stock options, or other economic interest related to the research, Board, scientific officer, or executive relationship related to the research, regardless of compensation for that position
7. An investigator can be a member of the IRB. However, the investigator-as member cannot participate in the review and approval process for any project in which he or she is present as a PI, Co-PI or CI or has any other potential conflict of interest.

2a.7 OFFICE BEARER OF IRB-IEC

The IEC will have the following office bearers who have the expertise and professional qualifications to review the proposals submitted.

2a.7.1 Chairperson, IRB-IEC

The IEC Chairperson should be a highly respected individual preferably from outside MCC, fully capable of managing the IEC and the matters brought before it, with fairness and impartiality. The task of making the IRB a respected part of the institutional community will fall primarily on the shoulders of this individual. The IRB must be perceived to be fair and impartial, immune from pressure either by MCC's administration, the investigators whose protocols are brought before it, or other professional and non-professional sources. The IEC Chairperson will respect the diverse backgrounds, perspectives, and sources of expertise of all IRB members, especially the contributions of the non-scientists, and must have the ability to foster such respect among the IRB members.

Co-Chairperson- The IEC Co-Chairperson should be a highly respected individual preferably from outside MCC, with the same capabilities of the Chairperson so as to manage the IRB and the matters brought before it with fairness and impartiality, in the absence of the Chairperson.

2a.7.2 Member-Secretary, IRB-IEC

The Member Secretary will be nominated by the Director of MCC, committed to the task of coordinating and managing the activities of the committee. He/she will be responsible for scheduling the meetings, describing the agenda and ensuring that the function of the committee is conducted as per the norms and policies described in this SOPs.

Specific roles of Member Secretary (As per ICMR Guidelines 2017)

- Member Secretary will be responsible to ensure training of EC secretariat and EC members
- Ensure SOPs are updated as and when required
- Ensure adherence of EC functioning to the SOPs
- Prepare for and respond to audits and inspections

- Ensure completeness of documentation at the time of receipt and timely inclusion in agenda for EC review.
- Assess the need for expedited review/ exemption from review or full review
- Finalizes the agenda for each meeting.
- Prepare the final minutes of the meeting.
- Issues communication to the PIs whose proposals were reviewed.

In the absence of a Member Secretary of IEC for any scheduled IRB meeting, Director, MCC must authenticate some distinguished staff of MCC to act as Member- Secretary (with having a decision-making power) for that particular meeting only. The Chairperson/Vice-Chairman will take the help of the mentioned MCC staff for coordinating and managing the activities of the IRB for that meeting.

2a.7.3 The IRB Secretariat/ Office of IRB, MCC

The Secretariat is composed of the Member Secretary, IEC, and the administrative supporting staff. The supporting staff consists of staff members of MCC appointed by the Director, MCC.
The secretariat shall have the following functions:

- Organization of an effective and efficient tracking procedure for each proposal received.
- Preparation, maintenance and distribution of study files.
- Organization of regular IRB meetings. .
- Preparation of the agenda and the minutes of the meetings,
- Maintenance of the IRB records and archives.
- Communication with IRB members and PIs.
- Arrangement of training for personnel and IRB members.
- Provision of the necessary administrative support for IRB related activities to the Member-Secretary, IEC.
- Receipt of IRB processing fees for pharma-funded projects and the issue of official receipts for the same.

❖ **The IRB Administrative Staff**: ***Working Rules***

1. There will be one or two faculty of *Clinical Research & Biostatistics Division* and attendant/s /helpers who will help the IEC Chairperson and/or Member-Secretary in executing functions of the IRB.
2. Additional staff may be appointed and duties assigned as and when required by the IRB. The eligibility criteria for new staff to be appointed will be laid down depending on the required job profile. The need for appointment of administrative staff, job profile and qualifications may be recommended by IRB members during regular IRB meeting and will be recorded in minutes. These will be forwarded to the Director, MCC.
3. The administrative staff will be appointed by conducting formal interviews as per MCC policy.

Duties of the administrative officers/staffs:

i. Organizing an effective and efficient tracking procedure for each proposal received.
ii. Organizing IRB meetings regularly, Preparing the agenda and minutes of the meetings
iii. Maintaining IRB records and archives. Providing necessary administrative support for IRB related activities to the Member-Secretary, IEC.
iv. Arranging training for personnel and IRB members.
v. Receiving IRB processing fees and issuing official receipts for the same.
vi. Corresponding with the IRB members, external experts and investigators.
vii. Preparing, maintaining and distributing study files. Communicating with IRB members and PIs.

2a.8 ROLES& RESPONSIBILITIES OF IRB MEMBERS

- The members' primary responsibilities will be determining the scientific and ethical validity of the research and the protection of the safety, rights and confidentiality of the research subjects.
- Participate in the IRB meeting & review and discuss research proposals assigned for evaluation.
- Review progress reports and monitor ongoing studies. Monitor SAEs and recommend appropriate action(s).
- Maintain confidentiality of the documents and deliberations of the IRB meetings. Declare conflict of interest, if any - IRB members shall disclose to the IRB all conflicts of the IRB member, their spouse/domestic partner, and their dependent children with regard to a research project involving human participants. Such disclosure shall be sufficiently detailed and timely to allow the IRB Administration to transfer the project to another IRB member or allow time for an alternate member to attend the IRB meeting to meet quorum. The IRB member/consultant shall evaluate whether a conflict of interest exists, and he/she shall disclose any identified conflicts to the IRB at the next IRB meeting. If an IRB member discovers that he/she has a conflict of interest during the conduct of a study over which the IRB provides oversight, the IRB member/consultant shall report the conflict to the IRB. IRB members shall cooperate with the IRB and other officials in their review of the conflicts of interest issues and shall comply with all requirements of the IRB.
- Declare conflict of interest, if any.
- Carry out work delegated by the Chairperson and/or Member-Secretary of IRB-IEC.
- Participate in continuing education activities in biomedical ethics and biomedical research.
- Provide information and documents related to training obtained in biomedical ethics and biomedical research to the IRB secretariat.

2a.9 QUORUM REQUIREMENT

All research projects for approval by the full board of the IRB shall be reviewed at convened meetings at which a majority of the members of the IRB are present,

including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of the majority of those members present at the meeting. The presence of the following five (5) members is required to form part of the quorum without which a decision regarding the project **should not** be taken.

Specific roles and responsibilities of the members (As per ICMR Guidelines)

2a.9.1Clinician:

- 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 car, management and compensation.

Thorough review of protocol, investigators brochure (if applicable) and all other protocol details and submitted documents.

2a.9.2 Basic Medical Scientist :

- Scientific and ethical review of the protocols 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 and pharmaco dynamics.
- Review of the Investigator Brochure and any related information about the study drug/interventions, as applicable.

2a.9.3 Legal experts:

- 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.
- Review the SAEs and comment on the causality assessment and the compensation payable.

2a.9.4 Social Scientists/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.

2a.9.5 Layperson:

- 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
- Review the SAEs and comment on the causality assessment and the compensation payable.

In the absence of the Chairperson, the nominated member by the Chairperson will chair the meeting. In the absence of both, a member who is independent of the institution will chair the meeting as the Acting Chairperson.

2a.10 EDUCATION OF IRB MEMBERS

The Member-Secretary, IEC, in consultation with the Chairperson, IEC, shall prepare an annual activity report of the IRB for submission to the Director, MCC and accreditation. The IRB office staff members will provide all necessary help to the Member-Secretary, IEC. This shall include:

- A Quantitative Evaluation (QE) of the activities of the committee on a yearly basis.
- List of the research proposals reviewed and approved in a year.
- Status of each research proposal.

The Annual Activity Report will be immediately put in the MCC website after the approval from Director, MCC.

2a.11 ANNUAL ACTIVITY REPORT

The Member-Secretary, IEC, in consultation with the Chairperson, IEC, shall prepare an annual activity report of the IRB for submission to the Director, MCC and accreditation. The IRB office staff members will provide all necessary help to the Member-Secretary, IEC. This shall include:

- A Quantitative Evaluation (QE) of the activities of the committee on a yearly basis.
- List of the research proposals reviewed and approved in a year.
- Status of each research proposal.

The Annual Activity Report will be immediately put in the MCC website after the approval from Director, MCC.

2a.12 HONORARIUM

All external non-MCC members should be given honorarium according to MCC norms & recommendations.

ANX1-VER2/SOP02/VER2

CONFIDENTIALITY & CONFLICT OF INTEREST FORM
(For IRB-IEC Members Only)
INSTITUTIONAL REVIEW BOARD
Malabar Cancer Centre, Thalassery- 670 103, India

"In recognition of the fact, that I, Dr/ Mr./ Mrs ..... herein referred to as the "Undersigned", have been appointed as a member of the Institutional Review Board and would be asked to assess research studies involving human subjects in order to ensure that they are conducted in a humane, scientific and ethical manner, with the highest standards of care according to the applied national, local regulations, institutional policies and guidelines; Whereas, the appointment of the undersigned as a member of the IRB is based on individual merits and not as an advocate or representative of a home province/ territory/community nor as thedelegate of any organization or private interest; Whereas, the fundamental duty of an IRB memberis to independently review research protocols involving human subjects and make a determination and the best possible
objective recommendations, based on the merits of the submissions under review;
Whereas, the IRB must meet the highest ethical standards in order to merit the trust and confidence of the communities with respect to the protection of the rights and well-being ofhuman subjects; The undersigned, as a member of the IRB is expected to meet the same high standards of ethical behavior to carry out its mandate.
This Agreement thus encompasses any information deemed Confidential or Proprietary provided to the Undersigned in conjunction with the duties as a member of the IRB. Any written information provided to the Undersigned that is of a Confidential, Proprietary, or Privileged natureshall be identified accordingly.
As such, the Undersigned agrees to hold all Confidential or Proprietary trade secrets ("information") in trust or confidence and agrees that it shall be used only for contemplated purposes, shall not be used for any other purpose or disclosed to any third party. Written Confidential information provided for review shall not be copied or retained. All Confidential information (and any copies and notes thereof) shall remain the sole property of the IRB.
The Undersigned agrees not to disclose or utilize, directly or indirectly, any Confidential or Proprietary information belonging to a third party in fulfilling this agreement. Furthermore, the Undersigned confirms that my performance of this agreement is consistent with MCC's policies and any contractual obligations it may have to third parties."

…….. ……
Undersigned Signature **Date**

Conflict of Interest

It has been recognized that the potential for conflict of interest will always exist but has faith in the IRB-IEC of MCC and its Chairperson to manage the conflict issues so that the ultimate outcome is the protection of human subjects. In accordance of the policy of the IRB-IEC, I shall not

participate in the review, comment or approval of any activity in which I have a conflict of interest, except to provide information as requested by the IRB-IEC.

The Undersigned will immediately disclose to the Chairperson of the IRB-IEC any actual or potential conflict of interest that I may have in relation to any particular proposal submitted for review by the committee, and to abstain from any participation in discussions or recommendations in respect of such proposals.
If an applicant submitting a protocol believes that an IRB member has a potential conflict, the investigator may request that the member be excluded from the review of the protocol.
The request must be in writing and addressed to the Chairperson. The request must contain evidence that substantiates the claim that a conflict exists with the IRB member(s) in question. The IRB may elect to investigate the applicant's claim of the potential conflict. When a member has a conflict of interest, the member should notify the Chairperson/IRB and may not participatein the IRB review or approval except to provide information requested by the Committee.

Examples of conflict of interest cases may be any of the following:

1. *A member is involved in a potentially competing research program.*
2. *Access to funding or intellectual information may provide an unfair competitive advantage.*
3. *A member's personal biases may interfere with his or her impartial judgment*.

Agreement on Confidentiality and Conflict of Interest

In the course of my activities as a member of the IRB, I may be provided with confidential information and documentation (which we will refer to as the "*Confidential Information*").
I agree to take reasonable measures to protect the Confidential Information; subject to applicable legislation, including the access to it, as per the right to Information Act, not to disclose the Confidential Information to any person; not to use the Confidential Information for any purpose outside the IRB's mandate, and in particular, in a manner which would result in a benefit to myself or any third party; and to return all Confidential Information (including any minutes or notes Ihave made as part of my Committee duties) to the Chairperson upon termination of my functionsas a Committee member.

……..
Undersigned Signature **Date**

Whenever I have a conflict of interest, I shall immediately inform the committee not to count me toward a quorum for consensus or voting.

I, Dr./Mr./Mrs.....have read and I accept the aforementioned terms and conditions explained in this Agreement.

……
Undersigned Signature **Date**

……..
Director of MCC **Date**

ANX2-VER2/SOP02/VER2

CONFIDENTIALITY AGREEMENT FORM- A
(For Independent Consultant)
INSTITUTIONAL REVIEW BOARD
Malabar Cancer Centre, Thalassery- 670 103, India

(A) For Independent Consultant

I,……
……(Name and Designation) as a non-member of IRB understand that the copy (ies) given to me by the IRB is (are) confidential. I shall use the information only for the indicated purpose as described to the IRB and shall not duplicate, give or distribute these documents to any person(s) without permission from the IRB.
Upon signing this form, I agree to take reasonable measures and full responsibility to keep the information as confidential.

……
……..
Undersigned Signature **Date**

…… ……..
Member-Secretary, IRB-IEC **Date**

CONFIDENTIALITY AGREEMENT FORM- B
(For Independent Observer)
INSTITUTIONAL REVIEW BOARD
Malabar Cancer Centre, Thalassery- 670 103, India

(B) For Observer

I, ... understand that I am allowed to observe IRB activities and attend the IRB-SRC/ IRB-IEC meeting/ scheduled on …….at .....am/ pm as an Observer.

In the course of the observer ship / meeting of the IRB some confidential information may be disclosed or discussed.
Upon signing this form, I ensure to take reasonable measures to keep the information and discussion as confidential.

Signature of the Observer **Date**

…… …….. ……..
Member-Secretary, IRB-IEC **Date**

I, ……..(Enter name) acknowledge that I have received a copy of this Agreement signed by Member-Secretary, IRB-IEC, MCC, and me.

Signature of the recipient **Date**

CHAPTER 2b

Data Safety Monitoring Board (DSMB)

Data Safety Monitoring Board (DSMB) shall comprise independent members and shall be constituted by the respective funding agency for all clinical trials involving human subjects in case of extramural funding or by the institutions/industry for in-house supported clinical trials.

2b.1 Purpose of DSMBs

DSMBs are considered to have "Stewardship" of a trial. Board has responsibilities to both subjects (in terms of safety and the sponsor (in terms of trial credibility). Specifically, the purpose of a DSMB includes:

- Protecting participant safety
- Ensuring the credibility and integrity of the trial for future subjects
- Ensuring the timely conclusions of a trial so its results can be disseminated
- Identify protocol violations that suggest clarification changes to protocol are needed
- Identify unexpectedly high dropout rates that threaten trials ability to produce credible results
- Ensure the validity of study results

2b.2 Types of Studies Requiring DSMB Oversight

All clinical studies require safety monitoring throughout the duration of the research, but not all studies require monitoring by a DSMB.

A DSMB is often considered relevant in the following kinds of studies:

1. **Controlled studies with mortality and/or severe morbidity** as a primary or secondary end-point
2. **Randomized controlled studies** focused on evaluating clinical efficacy and safety of a new intervention intended to reduce severe morbidity or mortality
3. Early studies of a **high-risk intervention** (risk of non preventable, potentially life-threatening, complications; or risk of common, preventable adverse events of interest [especially type A drug reactions]), whether or not randomized
4. Studies in the early phases of a novel intervention with very limited information on **clinical safety** or where prior information raises concern regarding **potential serious adverse outcomes**

5. Studies where the design or expected data accrual is complex, or where there may be ongoing questions with regard to the impact of accrued data on the study design and participants' safety, particularly in studies with a long duration.
6. Studies where the data justify its early termination, such as the case of an intervention intended to reduce **severe morbidity or mortality,** which might turn out to have adverse effects or lack of effect, resulting in increased morbidity or mortality.
7. Studies carried out in **emergency situations**.
8. Studies which involve **vulnerable populations**

2b.3 The functions of DSMBs

- To review and approve the scientific methodology and safety of a study prior to the research commencing.
- To provide written recommendation to the sponsor as to whether a protocol should be amended prior to the study proceeding.
- To provide independent, competent, efficient and timely review of the data from an ongoing study by evaluating the safety and clinical efficacy of data collected during the study and by assessing reports on cumulated serious adverse events (SAEs).
- To conduct emergency reviews of data to assess safety and futility related issues.
- To provide written recommendation to the sponsor as to whether the study should proceed, be suspended or prematurely terminated.
- To review and recommend appropriate amendments to the DSMB charter and SOPs in order to ensure optimal DSMB functioning.

2b.4 Constituting a DSMB

- When required by the nature of a study, a sponsor should establish a DSMB to ensure the broadest possible coverage of potential research participants, and the validity and scientific integrity of the data.
- The sponsor is responsible for establishing the DSMB's charter, which should be included (or referred to) in the study protocol.
- This may be undertaken with advice from investigators or other parties involved in the study.

Who should be on the DSMB?

- The **PI or trial sponsor** generally appoints the DSMB
- When appointing individuals to a DSMB, the following should be considered: **relevant expertise, experience in clinical trials, experience as a member of other DSMBs, and a lack of conflict.** A DSMB may **consist of as few as 3 members**, but this number should be large enough to include a representation of all needed skills and experience.

Who is typically included in a DSMB?

- Clinicians with expertise in relevant clinical specialties
- At least one biostatistician knowledgeable about analysis of trial data

Who might also be included in a DSMB?

- Medical ethicist
- Other types of scientists (i.e., clinical pharmacologist, toxicologist, epidemiologist, laboratory scientist, etc.)
- Members should not be affiliated with the sponsor, investigator(s), ethics committee(s), regulatory authority (ies), site(s) or study staff.
- Members should also not have vested conflicts of interest (e.g. a financial or other interest in an intervention or product similar to the intervention being studied)

2b.5 Terms of appointment

A procedure should be established identifying the terms of appointment for members of the DSMB, including

1. The duration of appointment
2. The policy for renewal of an appointment
3. The disqualification procedure
4. The resignation procedure
5. The replacement procedure

2b.6 Conflicts of Interest

- Conflicts of interest may be financial, intellectual, or emotional in nature, as in situations where there is competition for grants or scientific recognition

2b.7 DSMB Member Responsibilities

DSMB responsibilities are typically described in the charter. While the most critical responsibilities involve issues concerned with safety and efficacy data monitoring, additional responsibilities may include:

- **Reviewing the draft study protocol** and procedures to identify and resolve any potential concerns members have about monitoring the trial as indicated
- Identifying any potential scientific or ethical issues that might arise during the conduct of the study
- **Reviewing the basic soundness of the study design**, including, for example, the recruitment process, the informed consent, appropriateness of primary endpoints and, if relevant, making key recommendations to improve the overall design of the study
- **Review the study procedure** to become familiar with the data management and quality control procedures
- **Monitoring trail conduct issues,** such as compliance with trail eligibility restrictions, participants adherence to trail regimens, and the accuracy and completeness of the data

2b.8 Quorum requirements

The DSMB charter should establish specific quorum requirements for reviewing, and making recommendations on, the study, which should include:

- The minimum number of members required to compose a quorum (e.g. more than half the members).
- The professional qualifications required (e.g. physician, biostatistician, paramedic, ethics).
- A quorum should include at least one physician with experience in the medical field of concern, and one biostatistician

2b.9 Meeting procedures

Procedures for organization of the meetings should be developed in accordance with the meeting requirements.

1. **Organizational meeting**:
   - This initial meeting should be attended by the DSMB members and representatives of the sponsor; members of the study staff and the investigator(s) may also be invited.
   - The DSMB members should review and discuss the DSMB charter, including the role and responsibilities of the DSMB, the protocol safety monitoring plan, and the statistical methodology
2. **Early safety review meeting**
   - During the early stages of implementation of a study, a meeting may be held to review early safety information and factors relating to quality of conduct of the study.
3. **Periodic review meetings**
   - The expected frequency of these meetings should be specified. The DSMB charter should indicate whether the meetings are to be held in person or by teleconference.
   - The meetings should review the efficacy and/or safety data generated during this period, and should include a progress report from the investigator, serious adverse events reports, and cumulative safety data.
   - The DSMB should take into account the quality of conduct of the study and the accuracy of the data.
4. **Final study closeout meeting**
   - At the termination or conclusion of a study, the DSMB may meet to consider the efficacy and/or safety data generated from the study and provide any final recommendation to the sponsor.
   - A final assessment report can be considered.

2b.10 Interactions with Other Groups

DSMBs interact with other groups, including:

- The sponsor
- The data analysis center (DAC) or Biostatistician
- The Institutional Review Board (IRB)/Institutional Ethics Committee (IEC)
- The FDA/DCGI or non domestic regulatory body

- Medical monitor

Interactions with the IRB/IEC

- DSMBs have responsibilities that complement with those of an institutional review board (IRB)/Institutional ethics committee (IEC), and the two work separately. Adverse events (AE) are reported to both DSMBs and IRBs/IEC, but at different intervals and in different formats.
- An IRB/IEC typically focuses on safety issues that pertain its own given study site, while the DSMB reviews aggregated data from all sites and according to study arm.
- PIs submit open DSMB reports or minutes to the IRB/IEC.

What are the essential elements of the DSMP?

The plan should describe processes for dealing with the following:

1. **Monitoring the Progress and Safety of the Trial**
   a) Assessment of potential risks for study participants. The screening process and how it will be used to protect participants
   b) Measures to protect participants against risk.
   c) Plan to monitor the trials, including the type of information that will be reviewed, the parameters for defining abnormal values, and review periods.
   d) Define the stopping rules for the study.
   e) Any specific procedures are in place for activities such as monitoring and reporting in multicenter trials, if applicable. Plan to manage potential Conflicts of Interest
2. **Reporting of Unanticipated Problems (UPs)**
   a) Define what events will constitutes a UP (include a definition, grading scale, and "study relatedness" criteria).
   b) Define the process for assessing and timeline for reporting of potential UPs.
3. **Reporting of Suspensions or Terminations**
   a) Define the actions (FDA, Sponsor, IRB, etc.) that will be reported and who will bear the responsibility for reporting.
4. **Assuring Data Accuracy and Protocol Compliance**
   a) Define how data accuracy and protocol compliance will be assured. (i.e., protocol compliance checks, external data audits, regular data verification, etc.).
   b) Define reporting obligations for protocol deviations/violations and noncompliance

Documents and Matters to be reviewed by the DSMB

Documents and matters to be reviewed by the DSMB include but are not limited to

- **The research protocol** in its entirety prior to the study commencing.
- **Interim/cumulative data** for evidence of study-related adverse events.
- **Interim/cumulative data** for evidence of efficacy or futility according to pre established statistical guidelines.
- **Data quality, completeness and timelines**.
- Adequacy of compliance with goals for recruitment and retention, including those related to the participation of vulnerable groups.
- **Adherence to the protocol**

- Factors that might affect the study outcome or compromise the confidentiality of the trial data.

2b.11 The Standard Operating Procedures (SOP) of DSMB

Procedures should be established for

- Selecting members, including the method of appointing a member.
- Identifying conflicts of interest and criteria for determining unacceptable conflicts of interests.
- Identifying the terms of appointment for members of the DSMB.
- Stating the conditions of appointment.
- Defining the support of the DSMB.
- Determining confidentiality of data, discussion and disclosure, and processes to make disclosures where ethically indicated.

Reports from the DSMB

A. Verbal Report: At the conclusion of a DSMB meeting, the DSMB should discuss its findings and recommendations with sponsor representatives and the study investigators.

B. Summary Report: The DSMB will issue a written summary report that identifies topics discussed by the DSMB and describes their individual findings, overall safety assessment and recommendations. The rationale for recommendations will be included when appropriate. This report will generally not include confidential information. The DSMB Chair or designee is responsible for drafting, circulating and obtaining approval from other DSMB members within **two (2) weeks of the meeting**.

C. Closed Session Report: The DSMB may also prepare confidential minutes that include details of closed session discussions.

D. Immediate Action Report: The DSMB Chair will notify the sponsor of any findings of a serious and immediate nature or recommendations to discontinue all or part of the trial.

CHAPTER 3

Management of Research Study Proposal Submission

3.1 PURPOSE

This SOP is designed to describe and act as a guideline for the IRB Secretariat/ Office of IRB to manage Research study submissions

3.2 SCOPES

The scope includes the following -

- ✓ Submission for initial review
- ✓ Resubmission of study with modifications
- ✓ Submission of protocol amendments and any other amendments.
- ✓ Submission of status reports/continuing review of the study
- ✓ Submission of Serious Adverse Events and Deviations/Violations
- ✓ Protocol amendments and any other amendments.
- ✓ Annual Status Reports/Continuing review of the study
- ✓ Study completion/termination report
- ✓ Submission of any other study related documents

3.3 RESPONSIBILITY

It is the responsibility of the IRB secretariat to receive, record and distribute the study documents for IRB review.

3.4 DETAILED PROCESS

3.4.1 Receive submitted packages

For the initial review of study, investigators should submit all study related documents to the IRB, no fewer than ten (10) days before the next scheduled meeting. Initially, the PI will be asked to give power point presentations of his/her research proposal in front of SRC & IEC members after a communication

and green signal from IRB Secretariat/Office of IRB. The PI should submit research proposal to the IRB for review and approval under any of the 5 categories mentioned below.

- Initial Review Application
- Resubmission of Study with Corrections
- Protocol Amendment or any other amendments
- Annual Status Reports /Continuing Review of the study
- Study Completion / Termination
- Submission of Serious Adverse Events and Deviations/Violations
  Any other documents

The IRB will accept new submissions from Principal Investigators only after ensuring that continuing review applications/status reports of the previously approved studies have been submitted by the Principal investigator in a timely manner. The IRB shall not process a new research proposal from the PI unless the PI has submitted continuing review application/status reports for ongoing IRB approved studies.

3.4.2 Verification of Submission

On the receipt of the study related documents at IRB Secretariat/Office of IRB:

- Check the submissions for initial review as per checklist, to ensure that all mandatory forms and documents are submitted. Submission should include
  I. Project proposal/protocol submission Form (*ANX1-VER2/SOP03/VER2*)
  II. Study Protocol/Study Proposal

- Check completeness of necessary information with signature at all designated places in the submission form
- Notify the investigators, if the submission is incomplete.
- Stamp, sign & date on the cover letter confirming receipt of the documents. Record the completeness of submission on document receipt log book and inform the investigators for necessary action
- Payment details of IRB processing fees, if applicable.
- Count for correct numbers of hard copies as per the type of study
  - Thesis/ Academic Projects: 12 hard copy + soft copy,
  - Investigator-initiated studies: 12 hard copies + soft copy
  - Pharma-sponsored studies: 15 hard copies + soft copy
- Store the hard copies and soft copy of the research project. The hard copies will be stored under controlled access storage in the Division of Clinical Research & Biostatistics. The soft copy of the study accepted will be stored electronically.
- The project file is numbered as in format given below:
  "Type of Trial/Field/Dept/Year/Serial Number/Continuous Number"
  e.g., IM/HNO/DSO/2013-01/350 will indicate –
  Intramural study (IM) from *Head & Neck Oncology (HNO)/Department of Surgical Oncology* (DSO) /of the *Year* (2013)-*serial number (01) project of the year 2013* and *running project Number* (350). This project number is for use in the IRB Secretariat / Office of IRB
- Running project number *will be labeled* on each project file by electronic IRB Management software.

- All correspondence for the projects, should quote only the running project number i.e.,**350** (**unique identity number**)

3.5 DETAILED DESCRIPTION: RESEARCH/ STUDY PROJECT SUBMISSION

The **Research proposal/Study protocol** should be accompanied with the following relevant supporting documents for Scientific and Ethical review. These are –

* Checklist ()

A. Project Submission Form

a. Grouping of Project
b. Project Fact Sheet
c. Investigator Declaration and Study Team Undertaking with Duties &Delegation
d. Financial Disclosure
e. Project Submission Overview
f. Budget Sheet for the Proposed Study

B. Essential Documents

a) Study protocol
b) Lay summary-Provide a non-scientific summary of the proposal, including a statement about the importance of the question the research application will address, the relevance of the research to your country or region, and the potential impact of the study results.
c) Case Record Form, Patient reported outcome tools (whenever applicable)
d) Informed Consent Documents- Participant Information Sheet & Informed Consent Forms (ICFs) for adults. For studies involving children, parent information sheet and consent form and child information sheet and assent form are mandated in case of children between age 7-18 years of age.
e) English and Malayalam (if applicable) ICDs are to be mandatorily submitted to IEC. ICDs in other languages may be submitted if required by the study [Refer (ANX4- VER2/SOP03/VER2)]. Certificates of Forward and Back translations of participant information sheet & informed consent forms will be required for vernacular languages (Site specific variations…)
f) Application for waiver of consent (if applicable)
g) Audio video informed consent (if applicable)
h) Investigator's Brochure (if applicable)
i) One page, recent, signed and dated curriculum vitae of the investigators indicating qualifications and relevant experience.
j) Agreement to comply with national and international GCP protocols for clinical trials
k) Regulatory clearance from appropriate regulatory authorities i.e. DCGI approval / ICMR /Health Ministry Screening Committee (HMSC) (if applicable)
l) For international/ national collaborative study Memorandum of Understanding (MoU)between the collaborating partners
m) Clinical Trial Agreement (if applicable)
n) Insurance/Indemnity policies, indicating who are covered (if applicable)
o) Participant recruitment and enrollment procedures/advertisement (if any)
p) Documentation of clinical trial registration on the CTRI site.
q) Recent valid MMC registration certificate of the investigators (if applicable)
r) Draft/Final Material Transfer Agreement (MTA) if applicable

s) Any other important information relevant to the study
t) Decision of other Ethics Committees (If required / asked for)

3.6 RESUBMISSION OF STUDY WITH CORRECTIONS AS PER IRB SUGGESTIONS

- For resubmission- the PI will submit 3 copies of the amended study related documents along with justification for amendment or modification, and clearly highlighted/demarcated sections which have undergone change.
- The Office of IRB will verify the completeness and reconfirm that the copies contain the modification highlighted with respect to the earlier submission.
- The Office of IRB will perform the steps 3.4.2. The unchanged study related documents need not be submitted.

3.7 RESEARCH PROTOCOL AMENDMENTS & OTHER STUDY RELATED DOCUMENTS

- The PI should submit 12 hard copies or 5 hard copies + soft copy of the amended documents.
- The Office of IRB will verify the completeness of the submission.
- The PI should highlight the modification/s in the amendment, along with a summary of changes. He should also indicate whether these changes would entail change in the ICF as per the form.
- The Member Secretary in consultation with Chairperson will decide whether to
  - Carry out an expedited review in case of minor administrative amendment.

OR

  - Table for discussion at the full board meeting.

3.8 POST APPROVAL –RESEARCH PROTOCOL AMENDMENTS AND OTHER STUDY RELATED DOCUMENTS

- Investigators who may wish to modify or amend their approved protocols and/or other study related documents must seek IEC approval for all amendments before implementing the changes. A post-approval amendment reporting form should be completed with the submission.
- The PI should submit 1 hard copy (+ soft copy, if applicable) of the amended documents. The IEC Secretariat will verify the completeness of the submission.
- The PI should highlight the modification/s in the amendment, and provide a summary of changes. The summary of changes should be submitted as a separate document other than that provided in the post approval amendment reporting form. PI should also indicate whether these changes would entail change in the ICF as per the form.
- The Member Secretary in consultation with Chairperson will decide whether to initiate:
  - Full board review or
  - Carry out an expedited review in case of minor administrative amendment. This process is further elaborated in SOP4b/VER2.

3.9 ANNUAL CONTINUING REVIEW FOR *APPROVED RESEARCH STUDIES*

- The IRB will send reminders for annual report to Individual PI at least 90 days prior to expiry of approval.
- The IRB will receive a copy of Annual Status/ Continuing Review Report in the prescribed format and related documents (as per *SOP 07/VER2* for the approved research study
- The Office of IRB will verify the completeness of the Continuing Review Application Form (*ANX1-VER2/SOP05/VER2*) Progress report/Request letter for extension of approval of the project. The office will sign and date the documents.
- The progress or continuing review report will be tabled in the expedited review meeting or full board meeting of IRB

3.10 COMPLETION/TERMINATION OF RESEARCH STUDY

- The IRB will send reminders for annual status report to Individual Principal Investigators.
- The IRB will receive a copy of Study Completion Report in the prescribed format (as per *SOP 12/VER2*) **termination.**
- The Office of IRB will verify the completeness of the Study Completion Report Form (*SOP12/VER2*) **termination** filled by the PI.
- The study completion/ **termination** report will be tabled in the board meeting of IRB.

3.11 SUBMISSION OF SERIOUS ADVERSE EVENTS AND DEVIATIONS/VIOLATIONS

- The IRB secretariat will receive a copy of SAE and Deviations and Violations in the prescribed format (as per SOP 8/VER2 &SOP9/VER2)
- The IRB Secretariat will verify the completeness of the SAE/Deviations and Violations (SOP 8/VER2 &SOP9/VER2) filled by the PI.
- The SAEs will be discussed in the DSMB meeting and the Minutes of the DSMB meeting will be forwarded to the IRBs.
- The SAE and Deviations and Violations will be discussed in the Full Board meeting of IRB for further action.

Further action should be detailed here right up to writing to DCGI with compensation recommendations and all activity of IRB will end once the PI confirms that the patient/Nominee received the money. If this is covered in another SOP on safety reporting, it is acceptable.

***Abbreviation used*:**

1. MCC : Malabar Cancer Centre
2. MOHFW-DHR : Ministry of Health & Family Welfare-Department of Health Research
3. ICMR : Indian Council for Medical Research

4. DBT : Department of Bio-Technology
5. DST : Department of Science & Technology
6. WHO : World Health Organization
7. BARC : Bhabha Atomic Research Centre
8. UGC : University Grant Commission

ANX1-VER2/SOP03/VER2

RESEARCH PROJECT PROTOCOL FORM
Institutional Review Board (IRB)
Malabar Cancer Centre (MCC), Thalassery - 670103, India.

(A) GROUPING OF RESEARCH PROJECT

Project No. (For Office Use Only)	
Project Title	
Name of the Principal Investigator (PI)	

Please complete the questionnaire for submitting the research proposal for IRB- MCC
Study Group
(Please circle the applicable Y/N neatly)

	Group	Detail	Yes	No
		Controlled Trials		
01.	A1 a	Is this a Randomized Controlled trial?	**Y**	**N**
02	A1 b	Is this a Non-Randomized Controlled trial?	**Y**	**N**
03	A1 c	Is this a controlled trial that seeks new indication for establishing drug, process or a procedure?	**Y**	**N**
		Uncontrolled Trials		
04	A2 a	Is this a prospective trial testing new intervention, drug, or device on patients?	**Y**	**N**
05	A2 b	Is this a prospective trial designed to test new (unproven) indication for established drug, process, procedure or device on patients?	**Y**	**N**
06	A2 c	Is this a pilot trial on new intervention, drug, and device on patients?	**Y**	**N**
		Trial involve transfer of data/ material from MCC		
07	A3 a	Is this a Multi-Centre trial?	**Y**	**N**
08	A3 b	Is this trial involves transfer of patients' data to another site (including industry)?	**Y**	**N**
09	A3 c	Is this trial involves transfer of patients' blood, serum, DNA, tissue to another site?	**Y**	**N**
		Intramural Funding		
10	A4 a	Are you seeking Intramural funding?	**Y**	**N**
11	A4 b	Does this trial use additional resources of MCC beyond the usual work-up (e.g., Molecular profiling, MRI or any other non- routine part of work-up)	**Y**	**N**
		Extramural Grants		

12	A5 a	Are you submitting application for extra-mural grant for this trial?	**Y**	**N**
13	A5 b	Is this trial partly or wholly supported by grants from sponsored industry?	**Y**	**N**
14	A5 c	Is this a phase IV/ marketing trial undertaken on behalf of the industry?	**Y**	**N**
		Modification in approved trials		
15	A6	Are you seeking modification/s in the IRB-MCC approved trial?	**Y**	**N**
		Patient to bear the cost of trial		
16	A7 a	Are patient going to bear the cost of experimental intervention or drug therapy?	**Y**	**N**
17	A7 b	Does patient has to undergo additional blood sample collection, biopsy, endoscopy, procedure etc.?	**Y**	**N**
18	A7 c	Whether the patient has to bear the cost of complications arising from experimental treatment?	**Y**	**N**
19	A7 d	For the trial purpose, does the patient has to spend Rs. 5000/- or more above the usual expenses (for any reason such as drug therapy, additional investigation, prolonged stay or repeated travel)?	**Y**	**N**
		Community or Screening trial		
20	A8 a	Will the trial be undertaken in the community?	**Y**	**N**
21	A8 b	Will the trial involve screening?	**Y**	**N**
		Trials involving genomics & proteomics		
22	A9	Does this trial involve conducting Genomics or Proteomics studies on patients' specimens?	**Y**	**N**
		Trials with conflict of interest		
23	A10	Will this trial involve development of a device, drug or test lead to profits or patent?	**Y**	**N**
24	B1	Is this a prospective follow-up study (documentation of parameters only) of patients being offered standard treatment at MCC?	**Y**	**N**
25	B2	Is this a phase II-IV trial restricted to standard intervention/ treatments?	**Y**	**N**
26	B3	Is this a feasibility study for introduction of new treatment, recently shown in major international studies, to be beneficial / superior and need to be started at MCC?	**Y**	**N**
27	B4	Is this a retrospective or prospective analysis of charts and audit of procedures / tests / treatments?	**Y**	**N**

28	B5	Is this a retrospective or prospective review of pathology specimen (may involve some additional staining techniques)?	**Y**	**N**
29	B6	Is this a retrospective or prospective review of radiology reports and their clinical correlation?	**Y**	**N**
30	B7	Is this a retrospective or prospective review of laboratory reports and their clinical correlation?	**Y**	**N**
Procedure / demonstration at workshops etc.				
31	B8	Are you demonstrating an experimental procedure which is '*not established standards of care*' at a workshop or a public meeting?	**Y**	**N**
32	B9	Are you performing a procedure in workshop at MCC by non-MCC staff member? (Please check other requirements also)	**Y**	**N**

Name of the PI

Signature with date

Project Submission Form for review by IRB, MCC

(B) PROJECT FACT SHEET

B1	Project No. (To be filled by the Secretariat)	
B2	Date of receipt by IEC	
B3	Project Title	
B4	Key Words title (2-4 options)	
B5	Principal Investigator Co-Principal Investigator Co-Investigator	
B6	Number and type of ongoing studies in which PI is involved? (as PI only)	Total- _____ **Interventional studies** • RCT-_____(state whether pharma sponsored/investigator initiated) • Non-RCT-_____(state whether pharma sponsored/ investigator initiated) **Observational studies** • Prospective - _____ • Retrospective -_____
B7	Contact number Principal Investigator	
B8	Site/sites where study is to be conducted	
B9	Tick the type of study (multiple options if applicable)	☐ Investigator Initiated study ☐ Pharmaceutical sponsored Study ☐ Thesis * If * thesis specify the name of the student_____ ☐ Investigator Initiated study + Thesis
B10	Funding Agency /* Sponsor	
B11	Total estimated budget in Rs.	
B12	Duration of the Project (months)	
B13	If this is a prospective study, mention total number of participants to be accrued in study	
B14	If this is a prospective study, mention Number of participants from institute to be accrued	

B15	a) If this is a retrospective study, mention time frame from which data is collected b) The total number of participants whose data is being analyzed	
B16	Will biological products/data be sent out of the country?(Yes/No) If yes attach the copy of regulatory clearance obtained [DCGI/ ICMR /Health Ministry Screening Committee (HMSC)]	Yes/No
	Signature of PI	
	Date of submission	

*** Sponsor means a person who takes responsibility for and initiates clinical research. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation/research unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators.**

Sponsor-Investigator means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.

(C) Investigators Declaration:

1. This research project (including collection of blood or tissues samples for research) will not be started until the final approval of the IRB has been obtained.
2. We agree to undertake research proposal involving human participants in accordance with the NDCT Rules 2019 (Drugs & Cosmetics Act 1940), ICH-GCP and ICMR ethical guidelines. We will not modify the research protocol, consent, etc. without prior approval by the IRB.
3. The investigators agree to obtain a properly informed and under stood consent for all trial subjects before their inclusion in the trial in the informed consent form that is approved by the IRB. Participants will receive an 'information sheet' which will detail the project design in simple understandable layperson's language.
4. The investigators agree to report within a week all serious adverse events (SAE) associated with the trial in the SAE form to the IRB. In the event of a death of the trial subject, the Secretary, IRB and DSMB will be informed within 24 hours.
5. The investigators agree to submit periodic 6 monthly progress report of the trial in the appropriate form. A final report will be submitted at the end of the trial.
6. Full details on funding and a proposed budget are included with the trial proposal. The proposed budget is presented on the specific budget sheet of this form.
7. We understand that the IRB is concerned about transparent financial transactions during the trial. A report on how the trial funds were utilized will be presented to the Academic Council of MCC along with the final project report at the end of the trial.
8. The investigators agree to transfer 8% of the total budget to MCC as service charges. This will not apply to intramural projects, those projects cosponsored by MCC/MOHFW-DHR and ICMR/CSIR-CDRI/ DBT /DST/WHO/BARC/UGC funded projects.
9. The investigators agree that the grant money will be spent in accordance with the budget proposal only. The funds will not use for any other purposes without prior approval from the IRB. Thirty percent of the surplus grant if left over at the end of the study will be credited to MCC. The

remaining 70% of the surplus grant money may be used by the investigators for conducting intramural research, improving teaching facilities in the department, providing financial assistance to investigators for conferences, etc… after obtaining permission from the MCC authority.

10. For all research proposals that are sponsored by a pharmaceutical or biomedical company, we the investigators will ensure that the Sponsor Company will underwrite all expenses such that neither the hospital nor the study participants are made to spend while participating in the trial. The

investigators will also ensure that in the event of complications arising directly due to the trial or litigation, the cost of management or legal fees will be borne by the Sponsor Company totally.

11. The investigators state that they do not stand to gain financially from the commercial sponsor and do not have conflict of interest in the drug or product by way of consultations, shareholding, etc.
12. The investigators will ensure that personnel performing this study are qualified, appropriately trained and will adhere to the provisions of the Institutional Ethics Committee (IEC). MCC, approved protocol.
13. All data and biological specimen collected during the research project, including those supported by commercial sponsors (e.g. pharmaceutical company), will remain the property of Malabar Cancer Centre.
14. The salaries to staff employed for the research project will be as shown in the budget sheet and at par with the prevailing MCC salary scales.
15. The case records (source documents) will be made available to members of the SRC or IRB any time for random verification and monitoring. The case records (source documents) will be preserved in the premises of MCC for at least 5 years after the last approval of application or publication.
16. The investigators promise to ensure that there is no falsification of data when compared to the source documents. We agree to clarify any doubts or discrepancies that may arise during the data monitoring evaluation.
17. All the findings and conclusions of the proposed project such as review of case records, analysis of forms of treatment, investigations, etc… will be first presented to the staff members of MCC before they are released or presented elsewhere. The investigators will submit a copy of the abstract to the SRC and IRB well in advance of any proposed presentation at national or international conferences or seminars.
18. The investigators will not issue any press release before the data and conclusions have been peer-reviewed by the MCC staff or published in a peer-reviewed journal.
19. All serious injuries arising from the trial will be the responsibility of the Investigators. The investigators agree to ensure that the sponsors undertake a product liability insurance to cover any expenses for injury or compensation arising from the study treatment.
20. The investigators will constantly inform the IRB about amendments in the study protocol, data collection forms, informed consent forms, budget expenses, salaries, other trial documents, etc. as and when they occur. No major changes in the treatment arms or the study protocol or randomization technique will be carried out without prior permission of the IRB.
21. The investigators realize that the IRB is particular that all aspects of the study are in accordance with the ICH-GCP and ICMR ethical guidelines, 2017. The investigators will comply with all policies and guidelines of the MCC and affiliating/collaborating institutions where this study will be conducted, as well as with all applicable laws regarding the research.

We the investigators of the proposed trial have read all the statements listed above and agree to observe / undertake these IRB requirements while conducting our proposed project/ trial

We understand that serious protocol violations and/or non-compliance during the trial by the investigators may result in withdrawal of project approval by IRB

Study team undertaking with duties & delegation:

	Investigator Name	Status (PI/Co-PI, CI etc.)	Role & Responsibility**	Conflict of Interest (Yes/No) If yes, please specify	Signature with date
1					
2					
3					

Please provide details (an one page CV) of Co-PIs, CIs, Clinical Research Coordinator, Research Nurse, Phlebotomist, other stuffs related to the study. Use separate sheets for each individual.
** Choose from the following list:

A. Concept B. Design C. Screening of patients D. Selection & Recruitment and consenting of patients E. Laboratory investigations F. Laboratory report interpretation G. Treatment decision H. Patient evaluation I. AE and SAE management, evaluation and reporting	J. Examination of patients on follow-up K. Data collection and monitoring of data L. Interpretation of data M. Statistical analysis & Interpretation N. Maintaining patients file and master file of project O. Drafting final report P. Publication Z. Any other, please specify

***Note**: Investigators may clarify any of the points in this undertaking with the IRB office of MCC.*

To
The Member Secretary
Institutional Ethics Committee
Institutional Review Board, Malabar Cancer Centre

Project Title…….. ……..
Name of PI:
Conflict of Interest

(Please tick in the appropriate box)

☐ I hereby declare that I have no conflict of interest in my project.

☐ I have following conflict of interest:

Signature of PI

Date

Consent of Head of the PI's Department

Date: DD/MM/YYYY……

I have reviewed the above project submitted by ..... Principal Investigator, from my Department/Institution.
I endorse the project and have 'no objection' for submission for consideration by Institutional Review Board.

I concur with the participants / investigators included in the study.

Signature & date:
Name:
Department:

OFFICE SEAL

ANX2-VER2/SOP03/VER2

Checklist of Documents

Item No.	Mandatory Documents	Yes	No	NA
1.	IEC processing fee **(applicable for pharma sponsored trials)**			
2.	Project Submission Form (both hard and soft copies) duly signed by the Principal Investigator			
3.	**A.** Grouping of Project			
4.	**B.** Project Fact Sheet Investigators Declaration Conflict of Interest Consent of Head of the PI's Department Consent from Working Group			
5.	**C.** Project Submission Overview			
6.	**D.** Budget Sheet for the Proposed Study Detailed Budget for the Proposed Study			
7.	Study Protocol			
8.	Lay summary			
9.	Participant Information Sheet & Informed consent forms (ICFs) in English & Malayalam (and if required any other language)			
10.	Back translations of ICFs (not mandatory for Malayalam)			
11.	Application for waiver of consent			
12.	Case Record Form			
13.	Questionnaire			
14.	Investigator Brochure			
15.	Package insert/label			
16.	Insurance policy			
17.	DCGI approval letter/ DCGI submission letter			
18.	NOC from DCGI /ICMR/HMSC			
19.	Undertaking By The Investigator			
20.	Clinical Trial Agreement (CTA)/Memorandum of Understanding(MOU)/Material Transfer Agreement(MTA) if applicable			
21.	Brief resume of Principal Investigators and Co-investigators (1 Page each)			
22.	Copy of Good Clinical Practice training certificate for all investigators			
23.	MMC of Principal Investigators and Co-investigators			
24.	Any Other			

ANX3-VER2/SOP03/VER2

Guidelines for devising Informed Consent Form
Institutional Review Board (IRB)
Malabar Cancer Centre (MCC), Thalassery-670 103, India

Guidelines for devising Participant Information Sheet and Informed Consent Form and Sample format of an Informed Consent Document.

Guideline for preparation of the informed consent document

While submitting your project to the IEC, ensure that you have included an informed consent document that is prepared as per the New Drugs and Clinical Trials Rules 2019, ICMR ethical guidelines, ICH-Good Clinical Practice (ICH–GCP) and the Declaration of Helsinki.

Kindly note:

- Informed consent documents in English and Malayalam are mandatory and any Language if applicable
- Font: Times New Roman and appropriate English & Malayalam
- Size:12
- All the consent documents must have Version No, Date, Page no in the footer
- Separate documents should be prepared when minors (children) are study participants; assent form for the mature minors (age 7-18 years) and consent document for the parents
- Glossary of technical words/medical terminology for participant understanding
- Schedule of investigations to be performed for the study as a chart.

The consent document template describes the minimal requirements. You are free to add additional information you wish to

Template for a "Participant Information Sheet & Informed Consent Form" (Include or exclude information, as applicable)

Participant Information Sheet & Informed Consent Form

[The simplified title of the project as per the project submission form with name of

Principal Investigator]

Name of the funding agency (if

applicable) Name of the

sponsor (if applicable) Address

of Research Site

Introduction:

You are invited to participate in a study/research/experiment. This document gives you a description of the study/trial in which you are being asked to participate. Your participation in this study is voluntary, and you can enquire about all details before giving your written consent to participate in the study.

This research study is approved by the Institutional Ethics Committee of Malabar Cancer Centre. A copy of the ICF will be given to you for your record.

Purpose:

The purpose of this study is to

…… …… …… …… ……

Statement that the study involves research and explanation of the purpose of the research Clear state

1. The Aim/ objectives of the study to be mentioned
2. Statement of type of cancer patients/healthy volunteers enrolled

…… …… …… …… ……

Information:

List all procedures, which will be carried out in the study. Clearly state experimental procedures and explain technical and medical terminology in simple, non-technical & direct language.

Graphics could be used if helpful in making the text meaningful to the research participant. If this is a randomized trial, details of both arms of the trial must be explained.

State the amount of time required by the participant for the study with clearly stating the total duration of the study.

Clearly state

i. The number of participants who will take part in the research

ii. Information concerning taping or filming (If applicable)
iii. For clinical studies which require regulatory approval – Please include
   a) A statement that there is a possibility of failure of investigational product to provide intended therapeutic effect
   b) A statement that in the case of placebo controlled trial, the placebo administered to the participants shall not have any therapeutic effect
iv. Statement of foreseeable circumstances under which the subject's participation may be terminated by the Investigator without the Subject's consent
v. Statement that the subject or subject's representative will be notified in timely manner if significant new findings develop during the course of the research which may affect the subject's willingness to continue participation will be provided
vi. Information regarding patients roles and responsibility (follow-up/ QOL assessment)

Alternative treatments:

Disclose appropriate alternative treatments available, if any.

Clearly state if you refuse to participate in the trial - Standard treatment will be given (if applicable)

Risks:

List the foreseeable risks, discomforts or inconvenience, if any, of each of the procedures to be carried out in the study and measures to minimize the risks or treatment in case of occurrence. Explanation of anticipated side effects, including rare side effects, or known idiosyncratic reactions.

A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently unforeseeable

Costs:

Describe the cost for participating in the study to the subject/participant. The information must be written in clear terms regarding the cost which will be borne bysponsors/Principal Investigator/s of the project, and study participant.

Reimbursement for Participation

Describe plan for reimbursement or amount for expenses incurred, time spent and any inconvenience. State clearly the details for travel reimbursement for trial participants &/or attendant.

Emergency Medical Treatment

(If applicable, add here)

In case of the physical injury to the participant during the course of research please state the name and contact details of the PI.

Describe available medical treatment in case of complications.

Benefits

List the anticipated benefits from this research, either to the participants, others, community, scientific community.

If no benefit is expected subject should be made aware of this

- May benefit other patients/society in future
- Information may help the doctor to learn more about disease condition, treatment etc…

Also mention that the many of the most effective treatments used today are the result of clinical trials done in the past.

Confidentiality

The information in the study records will be kept confidential and the clinical charts will be housed (specify the location).Data will be stored securely for a period of years and will be made available only to persons conducting the study and to the regulatory authorities. The data will not be made available to another individual unless you specifically give permission in writing. No reference will be made in oral or written reports which could link you to the study. Result of the study will not be communicated to the participant unless deemed necessary.

Compensation for study related Injury or death

(As per the DCGI directive for regulated studies, it is mandatory for sponsors to comply with the following requirement: in case of study related injury, sponsor should provide completed medical care as well as compensation for the injury (Death) as per the provisions of law and same should be included in ICF)

Compensation of participants for disability or death resulting from such research related injury;

Describe the details of compensation or insurance for study related injury to the trial participant. Explain who will bear the cost in case of trial related injury?

Research participants who suffer physical injury as a result of their participation in the research study are entitled to financial or other assistance to compensate them equitably for any temporary or permanent impairment or disability participant to confirmation from IEC. In case of death, their dependents are entitled to material compensation.

Statement describing the financial compensation and medical management as under

- In the event of an injury occurring to the clinical trial participant, such participant shall be provided free medical management as long as required or till such time it is established that the injury is not related to the clinical trial, whichever is earlier
- In the event of a trial related injury and death, the sponsor or his representative, whosoever has obtained permission from the Licensing Authority for the conduct of clinical trial, shall provide financial compensation for the injury or death

---

Contact

If you have questions at any time about the study or the procedures, (or you experience adverse effects as a result of participating in this study,) you may contact the researcher, [PI Name], at [Office Address], and [Office Phone Number].

If you have any questions about the informed consent process or your rights as a participant, contact the Member Secretary, IEC [], at [Office Address], and [Office Phone Number]

Participation

Your participation in this study is voluntary; you may decline to participate at any time without penalty and without loss of benefits to which you are otherwise entitled.

If you withdraw from the study prior to its completion, you will receive the usual standard of care for your disease, and your non participation will not have any adverse effects on your subsequent medical treatment or relationship with the treating physician.

If you withdraw from the study before data collection is completed, your data will not be entered in the study report.

If staff /student is involved - Your participation in this research will not bestow upon you any competitive academic or occupational advantage over other students or staff who do not volunteer, and we will not impose any academic or occupational penalty on those students or staff who do not volunteer."

Consent

Informed Consent form to participate in a clinical trial/research (main study)

Study Title:

Study Number:

Participant 'Initials:_____Participant's Name: Date of Birth :___/___/_____Age:_____

1. I understand that I am being invited to take part in the research study. I confirm that I have read/been read to and understood the information sheet dated for the above study and have had the opportunity to ask questions.
2. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I understand the risks and potential benefits of this research study that were explained to me. I freely give my consent to take part in research study described in this form.
4. I understand that the Sponsor of the research study, others working on the Sponsor's behalf, IEC and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.
5. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
6. I agree to take part in the above study.

I have read/have been read the above information and agreed to participate in this study. I have received a copy of this form.

Participant's name (print):	
Participant's Signature/Thumb impression &date:	
Address : Educational Qualification (please attach supporting documentation) (if applicable) _____ Occupation: Student / Self-Employed / Service / Housewife /Others (Please tick as appropriate) and attach supporting documentation (if applicable) Annual Income of the participant (please attach supporting documentation) (if applicable):_____	
Phone Nos:	
Legal Acceptable Representative name	
Legal Acceptable Representative Signature/Thumb impression &date (if applicable):	
Address (capital letters): Phone Nos:	
Impartial Witness's name :	
Impartial Witness's signature & date (if applicable):	
Address (capital letters): Phone Nos:	
Name of PI or Co-PI/Co-I:	
PI or Co-PI/Co-I sign & date:	

Guidelines for developing informed consent documents for Biological sample study:

The ICF for use of biological sample may include the following points:

- Foreseeable extent of information on possible current and future uses of the biological material and of the data to be generated from the research.

Other specifics are as follows:

a) Period of storage of the sample/data and probability of the material being used for secondary purposes.
b) Whether material is to be shared with others, this should be clearly mentioned.
c) Right to prevent use of her/his biological sample, such as DNA, cell-line, etc., and related data at any time during or after the conduct of the research.
d) Risk of discovery of biologically sensitive information and provisions to safeguard confidentiality.
e) Post research plan/benefit sharing, if research on biological material and/or data leads to commercialization.
f) Publication plan, if any, including photographs and pedigree charts.

Template of consent for Biological sample study

As part of this protocol the investigators may store your blood/tissue/serum samples for future research. The investigators may also store and use the tumor tissues that are removed as part of routine biopsy or surgery, for future research. The tissue could be either paraffin blocks or fresh tissue that is frozen at very low temperatures as part of the Hospital Tumor Tissue Repository. Such blood, plasma, serum or tissue samples could be used for pathology, immune histo chemical, genetic, genomic, proteomic, transcript to mic or other studies in the future. The investigators will maintain your confidentiality at all times and at no time point will your individual data be linked to youridentify.

If you are willing to participate in the biological study, kindly give your consent by ticking at appropriate box in this consent form.

You may choose not to let your sample be used for the additional research and still become part of this study. At any time during and after the study if samples are remaining with the sponsor, you have rights to discard the sample material or to take it back. If you choose to discard your samples or to take them back, please contact your study doctor.

Informed consent form to participate in a biological sample study

Study Title:

Study Number:

Participant 'Initials:_____

Participant's Name:_____

Date of Birth:__/__/_____Age:_____

Do you consent to biological sample study?

 YES, I consent ☐ NO, I do not consent

a) I understand that I am being invited to take part in the research study. I confirm that I have read/been read to, and understood the information sheet dated for the above study and have had the opportunity to ask questions.
b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
c) I understand the risks and potential benefits of this research study that were explained to me. I freely give my consent to take part in research study described in this form.
d) I understand that the Sponsor of the research study, others working on the Sponsor's behalf, IEC and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.
e) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
f) I agree to take part in the above study.

I have read/been read to, the above information and agreed to participate in this study. I have received a copy of this document.

Participant's name (print):	
Participant's Signature/ Thumb impression & date:	
Address : Qualification (please attach supporting documentation) (if applicable) _____ Occupation: Student / Self-Employed / Service / Housewife /Others (Please tick as appropriate) and attach supporting documentation (if applicable) Annual Income of the participant (please attach supporting documentation) (if applicable):_____	
Phone Nos.:	
Legal Acceptable Representative name	
Legal Acceptable Representative Signature/ Thumb impression & date(if applicable):	
Address (capital letters): Phone Nos.:	
Impartial Witness's name :	
Impartial Witness's signature & date(if applicable)::	
Address (capital letters): Phone Nos.:	
Name of PI or Co-PI/Co-I:	
PI or Co-PI/Co-I sign & date:	

Note to Investigators Regarding the Process of Obtaining Informed and Understood Consent

- The prospective participant should be given Participant Information Sheet first.
- The participant should then be encouraged to read the Information Sheet and think over, preferably for a period of 24 hours. Following which, the participant should be served a questionnaire to ensure that he/she is aware of his/her own rights as a participant in the clinical trial. The informed consent form should be served to the participant only after ensuring that the participant is now prepared for informed

decision making.

- The PIs are urged by the IEC to use the simple non-technical words or should add the glossary and follow the sample template of Participant Information Sheet & Informed Consent Form
- Use of alternative wording or different format may slow down the review process. The form should be written in second person ("You are invited..."). Use of first person ("I") can be interpreted as suggestive and coercive.
- The study participant should be explained all the details in a language she/he understands.
- The Informed Consent Document must have the name and Telephone No. of the Principal Investigator or of any other co-investigator in case of an emergency, or even to seek answers to their queries.
- The consent document must bear version no. &date.

A copy of the signed Informed Consent Document (ICD) must be given to prospective participant. A receipt of copy of ICF by the participant should be documented by the

investigator in the source documents. Copies of the consent document must be available in English, state language.

Please tailor your ICF to suit the needs of our Indian population, and if this is a multinational Pharma based project, an additional ICF specifically designed for the trial site may be used.

Separate forms should be prepared when minors are used; one for the mature minors (age 7- 18 years) and one for the parents.

If your document is more than one page, there should be a line at the bottom of each page for the participant's initials, except for the last page where the signature is obtained.

Be sure to include any elements of informed consent that are appropriate to your study. If they apply to your study, they must be included.

If informed consent form requires more than one page, print the informed consent document front to back.

Please make provision for the assent of the child to the extent of the child’s capabilities as is the case with mature minors and adolescents.

Please make provision on the form for signatures / thumb impression of the participant/parent or legal guardian, if minor and of the investigator, or person administrating the consent document, and of an impartial witness. If the LAR’s sign has been taken for medical reasons (e.g. patient is unconscious, then the patient has to be consented when conscious and able to grant consent and this should be documented.)

†The investigator, or a suitably qualified and trained person designated by the investigator

to conduct the informed consent process, must sign and date the form at the same time as the participant.

‡ Impartial Witness: A person, who is independent of the study, who cannot be unfairly influenced by people involved with the study, who attends the informed consent process if the participant or the participant's legally acceptable representative cannot read, and who reads the informed consent and any other written information supplied to the participant. Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance.

Legally Acceptable Representative (LAR): An individual or juridical or other body authorized under applicable law to consent, on behalf of a prospective participant, to the participant's participation in the clinical trial.

Note: Copy of the Participant Information Sheet and duly filled in Informed Consent Document should be handed over to the participant or his/her attendant

AX5-V6/SOP 03/V6

Child Information Sheet and Assent Form

Study title: "… ....."

Introduction- Background and Rationale would be more appropriate

We want to tell you about a study we are doing. This study is a "research" study. It is a special way to find out about something. We are trying to find out more about **[purpose of study in simple language].** You are being asked to join the study because **[insert the name of medical condition or other reasons for inclusion].** The reason why we are doing this need to do this is because [gap in knowledge in simple words]. This might help other children like you in future……

We invite you to participate in this study.

What will you have to do?

You are being asked to be part of this project. The project is about [insert general statement about study]. Your [parents or legal guardian, if applicable] have already been told about the project. Your accompanying parent / guardian will also sign a similar form called as the Parent Informed Consent Form Please read this form and ask the researcher any questions you have. You can decide whether or not to take part in the study. You can say no as well. It is your choice to be part of the project or not.

The assent form describes the research study and states that you have been explained the purpose and the nature of the study to your satisfaction by the attending doctor and you are ready to follow the study procedures.

List all study procedures. Point out any that are considered experimental/or otherwise, and explain technical and medical terminology in simple, non-technical & direct language.

Risks, discomforts & Side effects

If you experience any of these side effects, you can contact your doctor immediately.
The doctor will treat you

Dr. **Phone:**

(Describe in simple language provisions for treatment/hospitalization for side effects/injury)

We want to tell you about some things that might hurt or upset you if you are in this study. **[Describe risks – e.g., painful procedures, other discomforts, things that take a long time. For example: The needle we use to take the blood may hurt. You might get a bruise on your arm.]**

You and your parents will not bear the expenses regarding the therapy. If you follow the directions of the doctors in charge of this study and you are injured due to any substance or Procedure given under the study plan, the study doctor who is treating you will be responsible for paying for the medical expenses for the treatment of that injury.

Costs:

Describe the cost for participating in the study to the subject/participant. The information must be written in clear terms regarding the cost which will be borne bysponsors/Principal Investigator/s of the project, and study participant.

Reimbursement for Participation

Describe plan for reimbursement or amount for expenses incurred, time spent and any inconvenience. State clearly the details for travel reimbursement for trial participants &/or attendant.

Emergency Medical Treatment

(If applicable, add here)

In case of the physical injury to the participant during the course of research please state the name and contact details of the PI.

Describe available medical treatment in case of complications.

Benefits

If you are in the study it may or may not help you to get better or benefit you. But we hope to learn something that will help other children like you some day.

Confidentiality

The information collected about you during this study will be kept safely locked up. Data will be stored securely for a period of_____years. Nobody will know it except the doctor doing the research. The doctor will not tell your friends or anyone else.

The information will only be accessed by the doctor the Ethics Committee and the Regulatory authority

The study information about you will be given to your father/mother/guardian if required.

Right to refuse or withdraw

You do not have to be in this study, if you do not want to be. If you do not want to be in this study, we will tell you what other kinds of treatments there are for you. If you decide that you don't want to be in the study after we begin, that's OK too. Nobody will be

angry or upset. We are discussing the study with your parents and you should talk to them about it too.

Whom to contact

You can ask questions if do you do not understand any part of the study. If you have questions later that you don't think of now, you can call the doctor

<Name of PI > **Phone:** <Contact No.>

If you have any queries regarding your rights you may contact,

<Name of Member Secretary of IEC>

Phone: < Contact No>

Your responsibilities

It is the responsibility of your parent / guardian to come along with you to the hospital during the study period for all the visits unless you withdraw or do not continue to receive treatment/care as per the study. It is also your responsibility and your parent / guardian to report any side effects that you may experience while on the study.

It is also your responsibility and that of your parent / guardian to inform the doctor if you consume any other medication apart from the study treatment.

We expect your co-operation throughout the study.

Child Assent Form

I_____, agree to participate in the study. " ....."

I have been informed, to my satisfaction, by the attending physician, about the study. I know that my parents/guardians do not have to bear the expenses of the treatment if I suffer from any study related injury, which may be related to the study drug/ procedure/ device.

I am also aware of my right to not be part of the trial, at any time, without having to give reasons for doing so

_____

Name and Signature/ Thumb impression of the study participant Date:

_____

Name and Signature/ Thumb impression of Legally Acceptable Representative

Date:

_____

Name and Signature of Impartial Witness Date:

_____

Name and Signature of the attending Physician Date:

AX6-V6/SOP 03/V6

Parent Information sheet and Informed Consent Form

[The title of the project here exactly as it is in the project design with names of Principal Investigator and all other investigators.]

Introduction:

Your child is invited to participate in a study/research/experiment. This document gives you a description of the study/trial in which you are being asked to participate. Your participation in this study is voluntary, and you can enquire about all details before giving your written consent to participate in the study.

Purpose:

The purpose of this study is to ……

Participant Selection

Voluntary Participation

Indicate clearly that they can choose to have their child participate or not. State, if it is applicable, that they will still receive all the services they usually do if they decide not to participate. This can be repeated and expanded upon later in the form as well. It is important to state clearly at the beginning of the form that participation is voluntary so that the other information can be heard in this context.

Example: Your decision to have your child participate in this study is entirely voluntary. It is your choice whether to have your child participate or not. If you choose not to consent, all the services you and your child receive at this clinic will continue and nothing will change. You may also choose to change your mind later and stop participating, even if you agreed earlier, and the services you and/or your child receives at the clinic will continue

Information on the Trial Drug

Procedures and Protocol

Describe or explain the exact procedures that will be followed on a step-by-step basis, the tests that will be done, and the drugs that will be given. Describe very clearly which procedure is routine and which is experimental or research.

Duration

Include a statement about the time commitments of the research for the participant and for the parent including both the duration of the research and follow-up, if relevant.

Example: The research takes place over (number of) days/ or (number of) months in total. During that time, it will be necessary for you to come to the clinic/hospital/health facility (number of) days, for (number of) hours each day. We would like to meet with you six months after your last visit for a final check-up. Altogether, we will see you and your child 4 times over a year.

Side Effects

Parents should be told if there are any known or anticipated side effects and what will happen in the event of a side effect or an unexpected event.

Example: These vaccines can have some unwanted effects or some effects that we are not currently aware of. However, we will follow your child closely and keep track of these unwanted effects or any problems. We will give you a telephone number to call if you notice anything out of the ordinary, or if you have concerns or questions. You can also bring your child to this health facility at any time and ask to see [name of nurse, doctor, researcher].

We may use some other medicines to decrease the symptoms of the side effects or reactions. Or we may stop the use of one or more drugs. If this is necessary we will discuss it together with you and you will always be consulted before we move to the next step.)

Risks

A risk can be thought of as being the possibility that harm may occur. Explain and describe any such possible or anticipated risks. Provide enough information about the risks that the parent can make an informed decision. Describe the level of care that will be available in the event that harm does occur, who will provide it, and who will pay for it.

Example: By participating in this research it is possible that your child will be at greater risk than he/she would otherwise be. There is a possibility that_____may happen as a result of taking this drug. While the possibility of this happening is very low, you should still be aware of the possibility. If something unexpected happens and harm does occur, we will provide you with_____. [Explain the level of care that will be available, who will provide it, and who will pay for it. Inform the parent if there is a particular insurance in place.]

Discomforts

Explain and describe the type and source of any anticipated discomforts that are in addition to the side effects and risks discussed above.

Example: By participating in this research it is possible that your child may experience some discomfort such as the discomfort of the injections. There may be a slight hardening and/or swelling where the needle stick goes into the skin. This should disappear in one day. Your child may also be fussier than usual or more tired. These behaviors usually stop within one day but if you are concerned, please call me or come to the clinic.

Costs:

Describe the cost for participating in the study to the subject/participant. The information must be written in clear terms regarding the cost which will be borne bysponsors/Principal Investigator/s of the project, and study participant.

Reimbursement for Participation

Describe plan for reimbursement or amount for expenses incurred, time spent and any inconvenience. State clearly the details for travel reimbursement for trial participants &/or attendant.

Emergency Medical Treatment

(If applicable, add here)

In case of the physical injury to the participant during the course of research please state the name and contact details of the PI.

Describe available medical treatment in case of complications.

Benefits

Benefits may be divided into benefits to the individual, benefits to the community in which the individual resides, and benefits to society as a whole as a result of finding an answer to the research question. Mention only those activities that will be actual benefits and not those to which they are entitled regardless of participation.

Example: If your child participates in this research, he/she will have the following benefits: any interim illnesses will be treated at no charge to you. If your child falls sick during this period he/she will be treated free of charge.

There may or may not be any other benefit for your child but his/her participation is likely to help us find the answer to the research question. There may not be any benefit to the society at this stage of the research, but future generations are likely to benefit.

Confidentiality

Explain how the research team will maintain the confidentiality of data, especially with respect to the information about the participant, which would otherwise be known only

to the physician but would now be available to the entire research team. Because something out of the ordinary is being done through research, any individual taking part in the research is likely to be more easily identified by members of the community and is therefore more likely to be stigmatized. Data will be stored securely for a period of _____years.

Example: The information that we collect from this research project will be kept confidential. Information about your child that will be collected from the research will be put away and no- one but the researchers will be able to see it. Any information about your child will have a number on it instead of his/her name. Only the researchers will know what his/her number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except [name who will have access to the information, such as research sponsors, DSMB board, your clinician, etc].

Sharing of the results

Your plan for sharing the information with the participants and their parents should be provided. If you have a plan and a timeline for the sharing of information, include the details. Also inform the parent that the research findings will be shared more broadly, for example, through publications and conferences.

Example: The knowledge that we get from this study will be shared with you before it is made widely available to the public. Confidential information will not be shared. There will be small meetings in the community and these will be announced. Afterwards, we will publish the results in order that other interested people may learn from our research

Right to Refuse or Withdraw

This is a reconfirmation that participation is voluntary and includes the right to withdraw. Tailor this section well to ensure that it fits for the group for whom you are seeking consent. The example used here is for a parent of an infant at a clinic.

Example: You do not have to agree to your child taking part in this research if you do not wish to do so and refusing to allow your child to participate will not affect your treatment or your child's treatment at this Centre in any way. You and your child will still have all the benefits that you would otherwise have at this Centre. You may stop your child from participating in the research at any time that you wish without either you or your child losing any of your rights as a patient here. Neither your treatment nor your child's treatment at this Centre will be affected in anyway.

Alternatives to participating

Include this section only if the study involves administration of investigational drugs or use of new therapeutic procedures. It is important to explain and describe the established standard treatment.

Example: If you do not wish your child to take part in the research, your child will be provided with the established standard treatment available at the centre/institute/hospital.

People who have malaria are given….

Whom to Contact

Provide the name and contact information of someone who is involved, informed and accessible (a local person who can actually be contacted.) State also that the proposal has been approved and how.

Example if you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following: [name, address/telephone number/e-mail] This proposal has been reviewed and approved by [name of the IEC], which is a committee whose task it is to make sure that research participants are protected from harm. If you have any queries regarding your rights as a study participant, you may contact, the Member Secretary, of the Institutional Ethics committee,

Dr. _____

Phone:

Consent

The nature and the purpose of the above Research Study have been explained to my child and me; we have agreed to have my child participate in the research study. We also agree that my child's personal health information can be collected, used and shared by the researchers and staff for the research study described in this form. We will receive a signed copy of this consent form.

_____ _____

Name and Signature /Thumb impression of Parent/Guardian Date

_____ _____

Date

_____ _____

Name and Signature of Person Obtaining Consent Date

_____ _____

Name and Signature of Impartial Witness Date

CHAPTER 4a

Full Board Review of Submitted Protocol

4a.1 PURPOSE

The IRB should review and approve, every research study involving human participants and other forms of studies, before the research is initiated. The IRB should evaluate the scientific rationale, scope and, methodology, and the ethical/ legal aspects of the study. The committee should evaluate the possible risks to the participants with proper justification as well as the expected benefits to participants/community. The adequacy of documentation for ensuring privacy & confidentiality should also be reviewed.

The purpose of this Standard Operating Procedure (SOP) is to describe how the IRB members will review an initial submission of the research study for approval using the Study Assessment Form. The Study Assessment Form ANX1-VER2/SOP04a/VER2 is designed to standardize the review process andto facilitate reporting, recommendations and comments offered to each study.

4a.2 SCOPE

This SOP applies to the review and assessment of all studies submitted for initial review and review of revised and resubmitted protocols submitted for approval of the IRB. The specific elements in the Study Assessment Form must be adequately addressed in the protocol and/or protocol-related documents submitted for review. Relevant comments made during discussion and deliberation about a study should be recorded in the minutes of the meeting. The decision reached by the IRB will be communicated to the PI.

4a.3 CATEGORIZATION OF PROTOCOLS

The Member Secretary, IEC or secretariat shall screen the proposals for their completeness. Depending on the risk involved, the research proposals are categorized into three types, viz.

i. Full Board review
ii. Expedited review
iii. Exemption from review

The Scientific Review committee (SRC) may categorize protocol into the above three types. In case the PI wishes to apply for expedited review or exemption from review of the submitted research proposal, a standard request form needs to be filled out, providing justification for the same. Standard Request Forms for Expedited Review and Exemption from review are available as annexures ANX1-VER2/SOP04b/VER2 (SOP04b/VER2) and ANX1-VER2/SOP04c/VER2 (SOP04c/VER2) respectively. However, the decision to accept the request for Expedited Review /Exemption from review will be made by the Member Secretary, IRB.

This SOP describes the process of full board review of research proposals.

4a.4 Full board Review

All research proposals presenting more than minimal risk that are not covered under exempt or expedited review should be subjected to full committee review. Some examples are;

- Research involving vulnerable populations, even if the risk is minimal.
- Research with minor increase over minimal risk.
  - ❖ This includes increment in probability of harm or discomfort that is only a little more than the minimal risk threshold. This may present in situations such as routine research on children and adolescents; research on persons incapable of giving consent; delaying or withholding a proven intervention or standard of care in a control or placebo group during randomized trials; use of minimally invasive procedures that might cause no more than brief pain or tenderness, small bruises or scars, or very slight, temporary distress, such as drawing a small sample of blood for testing; trying a new diagnostic technique in pregnant and breastfeeding women etc. Such research should have a social value. Use of personal identifiable data in research also imposes indirect risks. Social risks, psychological harm and discomfort may also fall in this category.

- Studies involving deception of participants -Some types of research studies require deception due to the nature of research design. A true informed consent may lead to modification and may defeat the purpose of research. Such research may be carefully reviewed by the EC before implementation.
- 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.
- Amendments of proposals/related documents (including but not limited to informed consent documents, investigator's brochure, advertisements, recruitment methods, etc.) involving an altered risk.
- Major deviations and violations in the protocol.
- Any new information that emerges during the research for deciding whether or not to terminate the study in view of the altered benefit–risk assessment.
- 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.
- Prior approval of research on predictable emergencies or disasters before the actual crisis occurs for implementation later when the actual emergency or disaster occurs.

The primary task of the IRB is to review research proposals and their supporting documents with special attention to the scientific validity, competence of the investigators, informed consent and elements of the study covered in the submission form to evaluate the suitability and feasibility of the study.

4a.4.1 SCIENTIFIC DESIGN AND CONDUCT OF THE STUDY

- Paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this unmet medical need
- Is this an attempt to validate, prove or disapprove the validity of existing knowledge?
- Appropriateness of study design, work plan and structure to achieve the stated objectives: Are the conceptual or clinical framework, design, methods and analyses adequately developed, well integrated, well-reasoned and appropriate to the aims of the project?
- Relevance of the work in the context of contemporary translation or clinical cancer research:
- Does this study address an important research question or is it predominantly, a service proposal?
- If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced?
- What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventive interventions that drive this field?
- Appropriateness of the study design in relation to the objectives of the study.
- The statistical methodology (including sample size calculation), and the potential for reaching sound conclusions with the smallest number of research participants.
- The available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial.
- The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants and the concerned communities.
- The outcome of the research should be relevant to the health problems of the patient population of the site and to a greater extent the Indian population.
- The justification for the use of control arms.
- Potential of the work that would be conducted to lead to a larger and high impact study.
- Criteria for prematurely withdrawing research participants, and criteria for suspending or terminating the research as a whole. The adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a Data Safety Monitoring Board, if applicable
- Investigator's capability, availability of infrastructure and scientific environment to conduct the study within the time frame and carry it forward.
- The adequacy of the site, including the support staff, available facilities, and emergency procedures
- Study Reporting and publication of the research.
- Regulatory permission for conduct of the study if applicable, and HMSC clearance for academic international collaborative studies.
- MOU/CTA and MTA for national and international collaborative research to safeguard the interests of participants and ensure compliance while addressing issues related to confidentiality, sharing of data, joint publications, benefit sharing etc.

4a.5 FULL BOARD REVIEW-REVIEW PROCEDURE

The primary task of the IEC is to review research proposals and their supporting documents with special attention to the scientific validity, competence of the investigators, informed consent and elements of the study covered in the submission form to evaluate the suitability and feasibility of the study.

The following will be considered as applicable:

4a.5.1 SCIENTIFIC DESIGN AND CONDUCT OF THE STUDY

- Is the project original and innovative? e.g. Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this unmet medical need
- Is this an attempt to validate, prove or disapprove the validity of existing knowledge?
- Appropriateness of study design, work plan and structure to achieve the stated objectives: Are the conceptual or clinical framework, design, methods and analyses adequately developed, well integrated, well-reasoned and appropriate to the aims of the project?
- Relevance of the work in the context of contemporary translation or clinical cancer research:
- Does this study address an important research question or is it predominantly, a service proposal?
- If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced?
- What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventive interventions that drive this field?
- Appropriateness of the study design in relation to the objectives of the study.
- The statistical methodology (including sample size calculation), and the potential for reaching sound conclusions with the smallest number of research participants.
- The available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial.
- The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants and the concerned communities.
- The outcome of the research should be relevant to the health problems of the patient population of the site and to a greater extent the Indian population.
- The justification for the use of control arms.
- Potential of the work that would be conducted to lead to a larger and high impact study.
- Criteria for prematurely withdrawing research participants, and criteria for suspending or terminating the research as a whole.
- The adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a Data Safety Monitoring Board, if applicable.

- Investigator's capability, availability of infrastructure and scientific environment to conduct the study within the time frame and carry it forward.
- The adequacy of the site, including the support staff, available facilities, and emergency procedures.
- Study Reporting and publication of the research.
- Regulatory permission for conduct of the study if applicable, and HMSC clearance for academic international collaborative studies.
- MOU/CTA and MTA for national and international collaborative research to safeguard the interests of participants and ensure compliance while addressing issues related to confidentiality, sharing of data, joint publications, benefit sharing etc…

4a.5.2 RISK BENEFIT ASSESSMENT

- The benefits accruing from the planned research either to the participants or to the community or society in general must justify the risks inherent in the research.
- Risks may be physical, psychological, economic, social or legal and harm may occur either at an individual level or at the family, community or societal level. It is necessary to first look at the intervention under investigation and assess its potential harm and benefits and then consider the aggregate of harm and benefits of the study as a whole.
- The IEC should review plans for risk management, including withdrawal criteria with rescue medication or procedures.
- The IEC should give advice regarding minimization of risk/ discomfort wherever applicable

4a.5.3 CARE AND PROTECTION OF RESEARCH PARTICIPANTS

- Qualifications and experience of the investigators for the conduct of the proposed study.
- Any plans to withdraw or withhold standard therapies for the purpose of the research, and the justification for such action.
- Plans to withdraw participants from the study by the investigator.
- Medical care to be provided to research participants during and after the course of the research.
- Adequacy of medical supervision and psycho-social support for the research participants.
- Steps to be taken if research participants voluntarily withdraw during the course of the research.

- Criteria for extended access to, the emergency use of, and/or the compassionate use of study products.
- Arrangements, if appropriate, for informing the research participant's general practitioner or family doctor, including procedures for seeking the participant's consent to do so.
- Description of any plans to make the study product available to the research participants following the research and description of any financial costs to research participants.
- Rewards and compensations for research participants (including money, services, and/or gifts).
- Provision for payment (in cash or kind or both) for incidental expenses and other inconveniences, free services and the processes involved without amounting to undue inducement.
- Provisions for compensation/treatment in case of injury/disability/death/lost wages of a research participant attributable to participation in the research (as per New Drugs and Clinical Trials Rules, institutional policy (2009)
-
- /ICMR guidelines/Insurance and indemnity arrangements

4a.5.4 PROTECTION OF RESEARCH PARTICIPANT CONFIDENTIALITY

1. A description of the persons who will have access to personal data of the research participants, including medical records and biological samples.
2. Measures taken to ensure the confidentiality and security of personal information concerning research participants.

4a.5.5 INFORMED CONSENT DOCUMENT

4a.5.5.1 ESSENTIAL ELEMENTS:

1. Statement that the study involves research and explanation of the purpose of the research in sufficient details in layman's (non-technical) language
2. Statement that the study is approved by IEC after evaluation of scientific and ethical validity.
3. Expected duration of the Participant's participation and total number of participants that will be accrued on the study.
4. Description of the procedures to be followed, including all invasive procedures
5. Description of any reasonably foreseeable risks or discomforts to the

Participant.

6. Description of any benefits to the Participant or others reasonably expected from research. If no benefit is expected from the study, whether the Participant is being made aware of this through the consent document.
7. Disclosure of specific appropriate alternative procedures or therapies available to the Participant.
8. Statement describing the extent to which confidentiality of records identifying the Participant will be maintained and who will have access to Participant's medical records.
9. Trial treatment schedule(s) and the probability for random assignment to each treatment (for randomized trials).
10. Compensation and/or treatment(s) available to the Participant in the event of a trial-related injury. ICD should include the statement, "free medical management shall be given as long as required or till such time it is established that the injury is not related to the clinical trial, whichever is earlier."
11. An explanation about whom to contact for trial related queries, rights of Participants in the event of any study related injury.
12. The anticipated prorated payment, if any, to the Participant for participating in the trial. In particular, the IEC must review payments to determine that:
    - The amount of payment and the proposed method and timing of disbursement neither is coercive nor presents undue influence.
    - In case any amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
13. Participant's responsibilities on participation in the trial.
14. Statement that participation is voluntary, that the participant can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the Participant is otherwise entitled.
15. Any other pertinent information.

ADDITIONAL ELEMENTS, WHICH MAY BE REQUIRED:

- Statement of foreseeable circumstances under which the Participant's participation may be terminated by the Investigator without the Participant's consent.
- Additional costs to the Participant that may result from participation in the study.
- The consequences of a Participant's decision to withdraw from the research and procedures for orderly termination of participation by Participant.
- Statement that the Participant or Participant's representative will be notified in a timely manner if significant new findings develop during

the course of the research which may affect the Participant's willingness to continue in the study.

- A statement that the particular treatment or procedure may involve risks to
- The Participant (or to the embryo or fetus, if the Participant is or may become pregnant), which are currently unforeseeable.
- Adequacy, completeness and comprehension of written and oral information to be given to the research participants, and, when appropriate, their Legally Acceptable Representative(s) (LAR) and/or Impartial witness (if applicable).
- Clear justification for the intention to include research participants who cannot consent, and a full account of arrangements made to obtain their consent /authorization/consent of LAR and/or Impartial witness (if applicable).
- Assurances that research participants will receive information that becomes available during the course of the research relevant to their participation including their rights, safety, and well-being.
- Provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project.
- Provision for audio-visual recording of consent process, if applicable, as per relevant regulations.
- The protocol meets the criteria for approval of application for consent waiver or verbal/oral consent request.
- Contact details of PI and Member secretary of IEC to be included in the ICD.

4 a.5.5.2 TYPES OF CONSENT PROCESSES AND THEIR IMPLICATIONS

- Blanket or broad consent: This is an open consent given only once to collect the sample, store it and use it for any research at any time in future without the need to revert to the individual for a re-consent. A consent model that allows for current and future access and use of samples or data for research without necessarily specifying what the focus of such studies might be.
- Tiered consent: This model of consent offers several options from which participants can choose. It includes an opt-in option for future use specifying general permission, or use only related to some aspects of research, sharing of bio specimens/data benefit sharing, etc. It also takes into consideration return of results for which options are also provided for consent.
- Specific consent: Consent is obtained for a specific research purpose. Participants are re contacted for every new use of their stored samples/data if

the scope of research is outside that for which they had originally given consent.

- Delayed consent: It may be administered in the post-medical procedure period when bio specimen or data may be collected for appropriate research from critically ill patients who may not have given prior consent for research. Consent may be taken from the participant or LAR when it is practical.
- Dynamic consent: This consent is different from one of static, paper-based consent and involves an ongoing engagement and interactions over time with participants to re-contact in response to changing circumstances using technology based platforms. It incorporates a flexible, configurable, technology-based design accommodating both participant and researcher needs. Modern longitudinal bio banks equipped with advanced technology strive for this type of consent.
- Implied consent: is consent which is not expressly granted by a person, but rather implicitly granted by a person's actions and the facts and circumstances of a particular situation for e.g a prospective participant is informed about a study where participation consists only of filling out an anonymous questionnaire. The person completes the questionnaire and, by doing so, agrees to participate in the research.
- Telephonic consent
- IEC may request for a telephonic consent to be made available and to be used in case of any studies which requires extra telephonic contact with the patient.
- Withdrawal of consent or destruction of sample: The donor has the right to ask for destruction of her/his collected sample(s) and discontinuation/withdrawal from participation in the research. In longitudinal studies, a participant may withdraw from one component of the study, like continued follow-up/data collection when withdrawal may be referred to as partial.
- Waiver of consent: While using anonymized (de-identified) samples/data, researchers should seek the approval of the EC of the institution or the repository for waiver of consent from donors.
- Re-consent: Secondary or extended uses of stored samples/dataset: In such an instance, one of the preliminary considerations for ECs must be to identify the circumstances under which the research requires re-use of collected identifiable biological material to generate the data or utilize the pre-existing identifiable dataset. This must also include review of the informed consent obtained originally to see if re- consent is warranted. There may be situations where consent would be impossible or impracticable to obtain for such research, in which case the research may be done only after independent evaluation by an EC (Declaration of Helsinki, October2013).
- Pediatric donors: In longitudinal studies once the child donor attains the legal

age of consent a re-consent should be sought for the storage and use of her/his tissue or sample. In pediatrics bio banks or bio banks with pediatric samples it is important to address the issue of children reaching legal age of consent. Sometimes re-contact may lead to withdrawal, resulting in limited data analysis. This may lead to bias or it could evoke emotional distress about past research. On the other hand, re-consent may give the participant the power to agree. A bio bank should decide the policy it would like to adopt for re-contact.

4a.5.6 COMMUNITY CONSIDERATIONS

- The EC should ensure that due respect is given to the community, their interests are protected and the research addresses the community's needs.
- The proposed research should not lead to any stigma or discrimination. Harm, if any, should be minimized.
- Impact and relevance of the research to the local community and the concerned communities from which the research participants are drawn.
- Steps taken to consult with the concerned communities during the course of designing the research.
- Influence of the community on the consent of individuals.
- Proposed community consultation during the course of the research.
- Extent to which the research contributes to capacity building, such as the enhancement of local healthcare, research, and the ability to respond to public health needs.
- A description of the availability and affordability of any successful study product to the concerned communities following the research.
- The manner in which the results of the research will be made available to the research participants and the concerned communities.
- It is important to examine how the benefits of the research will be disseminated to the community.

4a.5.7 RECRUITMENT OF RESEARCH PARTICIPANTS

- The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status, and ethnicity).

- The means by which initial contact and recruitment is to be conducted.
- The means by which full information is to be conveyed to potential research participants or their representatives.
- Inclusion criteria for research participants.
- Exclusion criteria for research participants.
- Students or staff recruitment in research.
- Healthy volunteers.
- Vulnerable groups
- Information contained in the advertisement and mode of its communication.

1. Final copy of printed advertisements.
2. Final audio or video taped advertisements.

4a.5.8 ADVERTISEMENTS

The IEC reviews advertising to ensure that advertisements do not:

1. State or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.
2. Include exculpatory language.
3. Emphasize the payment or the amount to be paid, by such means as larger or bold type.
4. Promise "free treatment" when the intent is only to say participants will not be charged for taking part in the investigation.

Advertisements are limited to the information prospective participants need to determine their eligibility and interest, such as:

- The name and address of the researcher or research facility.
- The purpose of the research or the condition understudy.
- In summary form, the criteria that will be used to determine eligibility for the study.
- A brief list of benefits to participants, if any. A statement that study specific expenses (other than standard care) will be borne by study budget.
- The time or other commitment required of the participants.
- The location of the research and the person or office to contact for further information.

4a.5.9 DISCLOSURE OF CONFLICT OF INTEREST

IEC evaluates each study in the light of any disclosed conflict of interest and ensure appropriate action is taken to mitigate this and makes appropriate suggestions for management, if conflict of interest is detected at the institutional or researchers level.

4a.5.10 SOCIAL VALUES:

The basic requirement for health research to be ethically permissible is that it must have anticipated social value. The outcome of the research should be relevant to the health problems of society. All stakeholders, including sponsors, researchers and ECs must ensure that the planned research has social value.

4a.6 RESPONSIBILITY

The IEC Secretariat is responsible for receiving, verifying, and managing the hard copies of the received submission. In addition, the Secretariat should create a study specific file, circulate the research proposals and other study related documents including the study assessment forms to the IEC members (lead discussants) for review, and communicate the review results to the investigators.

IEC members are responsible for receiving, verifying, and reviewing the research protocols.

4a.7 DETAILED INSTRUCTIONS

Investigator-initiated trials/studies seeking intramural grants, may be sent to IEC Full board review meeting. Projects requiring expert opinion may be sent to external review committee- Intramural Research fund (IMR), MCC.

DISTRIBUTION OF THE PROJECT DOCUMENTS

1. The distribution of the project documents for IEC review will be as follows:

E-copies of study documents to be reviewed in the full board meeting would be circulated along with Agenda to the Committee members preferably 7 days in advance of the scheduled meeting.

The reviewers can also access new research proposals and other study related documents such as CRAs, SAEs etc… through the online IEC portal.

The scientific member reviews the scientific, ethical, and informed consent issues and the Social scientist/NGO representatives/Ethicist/Lay Person has the responsibility ofreviewing the ethical aspects of the study and finalizing the informed consent documents which helps the PI to make the documents lucid and in simple language.

2. Legal expert will review legal documents which includes CTA/ MTA/ MOU etc. and advice on any legal matters such as data sharing, IPR and compensation issues. The lead discussants/Principal Investigator (as applicable) will present the research study at a regular full board meeting of the IEC.
3. The Investigator may be called for any questions or clarification required by the Committee.

The /PI is informed no less than 7 days prior to the meeting through the Agenda. In case the lead discussant is not in a position to review the assigned projects due to some reason, he/she should inform the Member Secretary, IEC at the earliest through written or email, so that

the research study can be assigned to another member. In the event of his/her absence, a lead discussant can send written comments on the research protocols to the Member Secretary, which will be tabled and discussed during the meeting. However, a final decisionon the research protocol will be arrived at, by a broad consensus at the end of discussion among attending members and not solely based on written comments.

4. It is the responsibility of the assigned to review the research protocols assigned to them thoroughly and communicate their observations, comments and decisions to the IEC during the meeting
5. All members are expected to read all protocols and submissions before a meeting, and to participate in meeting discussions.
6. The Member Secretary can invite an independent consultant (if necessary) for comments during the full board meeting.

RESPONSIBILITIES OF IEC MEMBERS

1. Check the meeting date to see if he/she is available to attend the meeting.
2. Check the contents of the e-copy of study documents received via email
3. Identify the project/study related documents assigned for review.
4. Notify the IEC secretariat immediately if there is any conflict of interest
5. Notify the IEC Secretariat 3 days prior to the convened IEC meeting regarding incomplete study document submissions, If any.
6. The lead discussants/PI should submit the Study Assessment Form and comments to the IEC Secretariat on day of the scheduled meeting or within 2 working days after the IEC meeting. In case an IEC member is not in a position to attend the scheduled meeting, the responsibility of submitting the study assessment form and comments would be that of the alternate IEC member assigned for review.
7. The non-medical member of the IEC shall specifically address ethical aspects of the study in the study assessment form such as study population involved, consenting process, waiver of consent etc.

4a.8 REVIEW THE PROTOCOL:

Review all elements as per section 4a.3, 4a.4, 4a.5. The protocol will be reviewed by lead discussants as per guidelines to review a study protocol described in VER2 ANX1-VER2/SOP04/VER2.

4a.9 USE OF STUDY ASSESSMENT FORMS AND SCORING SHEET

It is the responsibility of the IEC members (lead discussants) to use study assessment form as a checklist while reviewing each research protocol. The study assessment forms shall be submitted online. The study assessment form is designed to standardize the review process. The study assessment form (ANX1-VER2/SOP04a/VER2) helps to ensure that all elements of research study are

reviewed and are accordingly documented during the discussion/meeting. The lead discussant(s) of the research proposal shall complete the study assessment form for initial review and expedited review. The lead discussant needs to submit comments for the resubmitted projects via ANX2-VER2/SOP04a/VER2.

4a.9.1 COLLECTION OF THE STUDY ASSESSMENT REPORTS

The IRB Secretariat will collect the Assessment Forms ANX1-VER2/SOP04a/VER2 and the comments from each lead discussant and file them in the original set of the study file.

4a.10 GUIDANCE FOR ADDRESSING ETHICAL ISSUES RELATED TO RESEARCH (FOR BIOLOGICAL SAMPLES)

4a.10.1 ROLE OF THE IEC

IECs play a key role in oversight and use of the bio- and data repositories for research, scientific and public health programmes. Research proposals, which require bio repository services including material transfer and available data sets, should be reviewed by the IEC, either an institutional one or that of the bio repository.

4a.10.2 As per National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017, Bio banks 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.

4a.10.3 Ownership of the biological samples and data**:** The participant owns the biological sample and data collected from her/him and therefore, could withdraw both the biological material donated to the bio bank and the related data sent document.

Complete anonymization would practically make the original donor lose the right of ownership. Bio banks/institutes are the custodians or trustees of the samples and data through their ECs as their present and future use would be done under supervision of the respective ECs. Researchers have no claim for either ownership or custodianship.

4a.10.4 Transfer of bio specimens: An MTA 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 EC should oversee the process of the in-country and international material transfer. Mandatory regulatory clearances with appropriate MoU are required if bio specimens are to be sent overseas. Directorate General of Foreign Trade (DGFT) has issued a notification related to transfer of human biological material for commercial purposes.

4a.10.5 Secondary or extended uses of stored samples/re-consent: The EC will examine circumstances under which the biological material or the data were originally collected, and informed consent obtained. The decision about anonymization /informed consent waiver or re-consent will be made on a case-to-case basis.

The following must be considered when stored samples are to be used:

1. Whether the proposed use is aligned with the original consent given for the earlier research and scrutinizes the validity of the objectives of the new research.
2. Whether provisions for ensuring anonymity of the samples for secondary use are stated;
3. Whether the permission of LAR is obtained for post-mortem uses of samples.
4. Whether the consent form mentions retention and various possible future uses of tissues in the form of a tiered consent.
5. Whether provisions have been made for allowance of waiver of consent if the donor is not traceable or the sample/data is anonymized or it is impractical to conduct the research.

4a.10.6 RETURN OF RESEARCH RESULTS TO INDIVIDUAL/GROUPS

Results of the study should be communicated back to the providers of samples/ data. Wherever applicable, research findings in aggregate form (which does not reveal individual results) must be discussed with the community, especially when research involves vulnerable population.

In the absence of an appropriate mechanism to deal with informational harm that can occur if participants are provided feedback when they are not prepared to face it or if it is not actionable or when such information is unrelated, a lot of distress could be caused to participants concerned. At the time of sample collection, it may be a good approach to offer donors the choice of receiving the results of the research whether they are beneficial or not. Participants may also choose not to be contacted about their results. Another alternative is to give participants the option of receiving an aggregate report of all the results of the study which could become a shared benefit for the community. The aforementioned options may be incorporated in a tiered consent.

4a.10.7 BENEFIT SHARING

Biological materials and/or data have potential commercial value but the participants' contribution and their share in this benefit is very often not known to them. The informed consent document should emphasize this aspect with necessary clauses for clarity about benefit sharing. It is the responsibility of the IEC members to evaluate this aspect and its inclusion in the ICD.

Annexure

ANX1-VER2/SOP04a/VER

Study Assessment Form

Protocol Number :	Date (DD/MM/YY):
Protocol Title :	
Principal Investigator:	
Department :	
Application □New □Revised	
Total No. of Participants:	
Funding Agency:	
Duration of the Study:	
Lead discussant Name	

Type of the Study :	**Treatment studies /Interventional Studies** □Randomized controlled trial □Double-blind randomized trial □Single-blind randomized trial □Partial-Blind randomized trial □Open labeled □Adaptive clinical trial □Nonrandomized trial (quasi-experiment) □Interrupted time series design □Any other (please specify) comment:_____ □Pre-clinical □Phase-I, □Phase-II, □Phase-III, □Phase-IV, □NA **Feasibility Study:-**□Pilot □Pivotal □Pharmacokinetics □Pharmacodynamics **Observational studies** □Prospective cohort □Retrospective cohort □Time series study □Case-control study □Nested case-control study □Cross-sectional study □Community survey (a type of cross-sectional study) □Longitudinal study □Epidemiological study □Survey (others) □Others (please specify)_____

Research involves – □Less than minimal risk □Minimal risk □Minor increase over minimal risk or Low risk □More than minimal risk or High risk	
Review Type	□Full board □Expedited
Justification for expedited review	Comment:
CTRI Registration	□Applicable □Not Applicable

Academic clinical trial to be notified to CLA as per **GSR 227 (E).** **(If applicable)**	□Yes □No □N/A
Does this study require institutional insurance coverage	□Yes □No □N/A
Does this study require permission from regulatory authorities?	□Yes □No □N/A If Yes- □Central Licensing Authority □ICMR □other govt. Departments/Agencies
Are human biological material/data sent	□Yes □No □N/A
abroad?	Comment: If yes, permission required □Health Ministry's Screening Committee (HMSC) □Others, please specify
Description of the study in brief: (Study objectives/study hypothesis etc…) –	

Mark and comment on whatever items applicable to the study

Section A- To be filled by scientific lead discussants		
1	Need for human participants	□Yes □ No □N/A Comment:
2	Objectives of the study	□Clear □Unclear What should be improved?

3	Background information and data	□Sufficient □Insufficient Comment:
4	Availability of similar study / results	□Yes □No □N/A Comment:
5	Relevance of the work in the context of contemporary Translation or clinical cancer research: * Does this study address an important research question or is it a predominantly service proposal?* If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced?	□Yes □No □N/A Comment: (please specify)
6	Methodology:	□Clear □Unclear What should be improved?
7	Classify Risk/Benefit	□Less than minimal risk/ High Benefit □Less than minimal risk/ Low benefit □Minimal risk/ High Benefit □Minimal risk/ Low benefit □High Risk/High Benefit □High Risk/Low Benefit
8	Risk and benefit considerations a) Are both risks and anticipated benefits accurately identified, evaluated, and described? b) Have the risks and benefits of the research interventions been evaluated separately from those of the therapeutic interventions? c) Are the risks to subjects reasonable in relation to the importance of the knowledge from the study?	□Yes □No □N/A □Yes □No □N/A □Yes □No □N/A

	d) Are the risks (physical, psychological, legal, economic, and social) to subjects minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk?	☐Yes ☐No ☐N/A
	e) Are the risks minimized, whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes?	☐Yes ☐No ☐N/A
	f) Does the study define risk management plan?	☐Yes ☐No ☐N/A
9	Inclusion Criteria	☐Appropriate ☐Inappropriate Comment:
10	Exclusion Criteria	☐Appropriate ☐ Inappropriate Comment:
11	Discontinuation and withdrawal criteria	☐Appropriate ☐ Inappropriate Comment:
12	Does the study involve modified or new claims, namely, indications, dosage forms (including sustained release dosage form) and route of administration of already approved drugs and combination of two or more drugs	☐Yes ☐No ☐N/A
13	Study/Data collection Performa	☐Appropriate ☐ Inappropriate Comment:
14	Involvement of vulnerable participants	Yes ☐No ☐ N/A Comment: ☐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. ☐Terminally ill or are in search of new interventions having exhausted all therapies ☐Suffering from stigmatizing or rare

		diseases. □Economically and socially disadvantaged (unemployed individuals, orphans, abandoned individuals, persons below the poverty line, ethnic minorities, sexual minorities – lesbian/gay/bisexual and transgender (LGBT), etc.); □Have diminished autonomy due to dependency or being under a hierarchical system (students, employees, subordinates, defense services personnel, healthcare workers, institutionalized individuals, under trials and prisoners). □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. □Tribally 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; Comments on addressing vulnerability issues:
15	Sufficient number of participants?	□Yes □No □N/A Comment:
16	Control Arms (placebo, if any)	□Yes □No □N/A Comment:
17	Are qualifications and experience of the participating investigators appropriate?	□Yes □No □N/A Comment:
18	Is the duty delegations as per investigator's expertise and study design?	□Yes □No □N/A Comment:

19	Disclosure or declaration of potential conflicts of interest	☐Yes ☐No ☐ N/A Comment:
20	Facilities and infrastructure of MCC for conduct of the research	☐Appropriate ☐ Inappropriate Comment:
21	Is community consultation required	☐Yes ☐No ☐ N/A Comment:
22	Involvement of local researchers and institution in the protocol design, analysis and publication of results	☐Yes ☐No ☐ N/A Comment:
23	Contribution to development of local capacity for research and treatment	☐Yes ☐No ☐ N/A Comment:
24	Benefit to local communities	☐Yes ☐No ☐ N/A Comment:
Section B- To be filled by both scientific and non - scientific lead discussants		
25	Has the PI applied for waiver of consent?	☐Yes ☐No ☐N/A Comment:
26	Has the criteria for waiver of informed consent documentation been met?	☐Yes ☐No ☐ N/A Comment:
27	Is the waiver of consent granted?	☐Yes ☐No ☐N/A **Specify reasons for granting waiver of consent** ☐Research involves 'not more than minimal risk ☐There is no direct contact between the researcher and participant ☐Rights of the participants are not violated ☐Confidentiality of data and privacy of research participant are protected If No, **Specify reasons for not granting waiver of consent**

28	Does the study involve consenting of participants	□Yes □No □ N/A Comment:
29	Are procedures for obtaining informed consent appropriate?	□Yes □No □ N/A Comment:
30	Contents of the informed consent document	□Clear □Unclear Comment:
31	Language of the informed consent document	□Clear □ Unclear Comment:
32	Does the informed consent document address all the essential elements of consenting as per the regulations/guidelines?	□Yes □No □ N/A Comment:
33	Contact persons for participants mentioned?	□Yes □No □ N/A Comment:
34	Privacy & Confidentiality ensured?	□Yes □No □ N/A Comment:
35	Inducement for participation	□Unlikely □ Likely Comment:
36	Does the ICF provide explanations of the research to the participant with an accurate assessment of its risks and anticipated benefits?	□Yes □No □ N/A Comment:
37	Provision for Medical / Psychosocial Support	□Appropriate □ Inappropriate Comment:
38	Provision for treatment of study-related injuries	□Appropriate □ Inappropriate Comment:
39	Provision for Compensation	□Appropriate □ Inappropriate Comment:
40	Provision for post-trial access	□Appropriate □ Inappropriate Comment:
41	Provision for payments	□Appropriate □ Inappropriate Comment:

42	Provisions for monitoring the data to ensure the safety of participants	☐ Yes Comment:	☐ No	☐ N/A
43	Voluntary, Non-Coercive Recruitment of Participants	☐ Yes Comment:	☐ No	☐ N/A

Assessment Report

Project number:		
Project title:		
DECISION :	☐Approved ☐Revisions with minor modifications ☐Revisions with major modifications for resubmission ☐Not approved ☐Deferred	
Findings/ Modifications required :		
Is there any conflict of interest (scientific, service or financial) between you and that of the Investigators? ☐ Yes ☐ No ☐ N/A		
Signature :		Date**:**

Assessment Report

ANX2/SOP04a/VER2

Assessment of Resubmitted Protocol

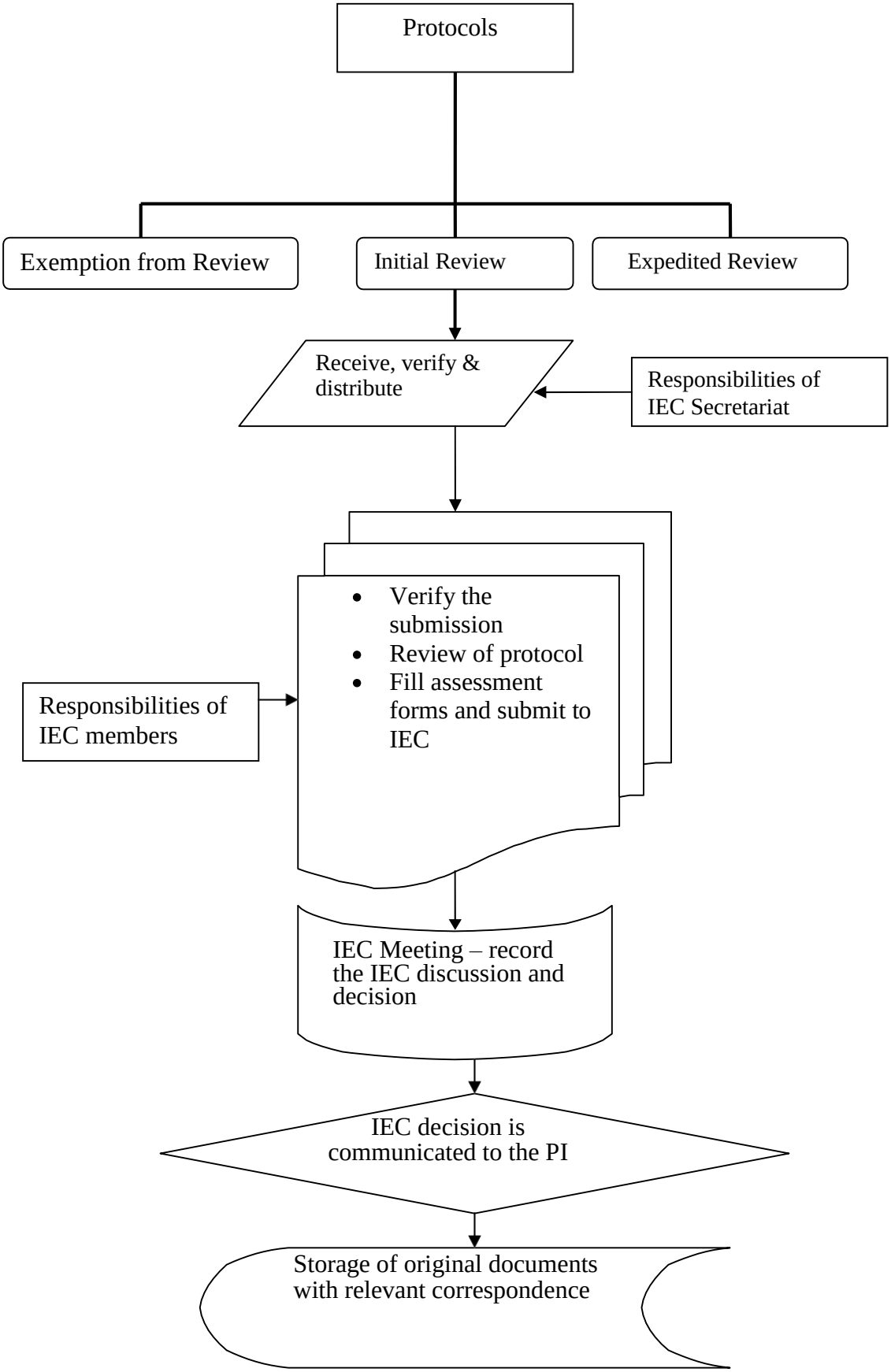
Protocol Number:	**Date (DD/MM/YY):**	
Protocol Title:		
Principal Investigator:		
Has the PI done the revisions/ modifications or provided justification (as applicable) according to the IEC recommendations: ☐ **Yes** ☐ **No** ☐ **Partial** **Findings/ Modifications required –**		
DECISION: ☐ **Approved** ☐ **Revisions with minor modifications** ☐ **Revisions with major modifications for resubmission** ☐ **Not approved** ☐ **Deferred**		
Is there any conflict of interest (scientific, service or financial) between you and that of the Investigators? ☐ **Yes** ☐ **No**		
Signature:		**Date:**

Comments or suggestions if any (Attach extra sheets, if necessary):

Is there any conflict of interest (scientific, service or financial) between you and the Investigators? Y/N

IEC member Signature & Name (below the line please):

FLOW CHART


Protocols
Exemption from Review
Initial Review
Expedited Review
Receive, verify & distribute
Responsibilities of IEC Secretariat
Verify the submission
Review of protocol
Fill assessment forms and submit to IEC
Responsibilities of IEC members
IEC Meeting – record the IEC discussion and decision
IEC decision is communicated to the PI
Storage of original documents with relevant correspondence

CHAPTER 4b

Expedited Review of Submitted Protocol/Documents

4b.1 PURPOSE

The purpose of this SOP is to provide criteria for those research studies which qualify for expedited review by IEC and describe the expedited review process in detail.

4b.2 SCOPE

This SOP applies to the review and approval of research studies and documents which qualify for expedited review by IRB.

4b.3 RESPONSIBILITY

It is the responsibility of the Member Secretary to identify the research studies or documents which are eligible for expedited review.

4b.4 CATEGORIZATION OF PROTOCOLS

The IRB-SRC will screen the study for its completeness and depending on the risk involved in the research study categories it into three types, viz.

I. Full board review (full board/regular review)
II. Expedited review
III. Exemption from review

An investigator cannot categorize his/her study into the above three types. An investigator may apply for expedited review for the study protocol using Expedited Review Application Form (ANX1-VER2/SOP04b/VER2).

However decision to accept the request will be made by the Member Secretary, IEC with permission from the Chairperson.

4b.5 EXPEDITED REVIEW

Expedited review is a procedure through which certain kinds of research proposals that pose no more than minimal risk may be reviewed and approved by a subcommittee (refer section 4b.6.2) without convening a meeting of the full Board for example;

- Research involving non-identifiable specimen and human tissue from sources like blood banks, tissue banks and left-over clinical samples.
- Research involving clinical documentation materials that are non-identifiable (data, documents, records).
- Modification or amendment to an approved protocol including administrative changes or correction of typographical errors and change in researcher(s), handover of trials or projects.
- Minor changes in previously approved research during the period covered by the original approval may be eligible for expedited review where:

a) The research is permanently closed to the enrolment of new subjects
b) All subjects have completed all research-related interventions

- Revised proposals previously approved through expedited review, full board review or continuing review of approved proposals.
- Minor amendments/corrections in the CRF, e-CRF, budget

  Minor deviations from originally approved research causing no risk or minimal risk;
- Continuing review of research previously approved by the convened IEC (e.g., not originally subject to expedited review) may be eligible for expedited review if
  a) The research is permanently closed to the enrolment of new subjects.
  b) All subjects have completed all research-related interventions.
  c) The research remains active only for long-term follow-up of subjects.
  d) Where no subjects have been enrolled and no additional risks have been identified.
  e) Where the remaining research activities are limited to data analysis.
- Expedited review of SAEs/unexpected AEs of minor nature will be conducted by SAE subcommittee.
- Premature Termination/Discontinuation/Suspension/Withdrawal of study before site initiation.
- Research on interventions in emergency situation–

  When proven prophylactic, diagnostic, and therapeutic methods do not exist or have been ineffective, physicians may use new intervention as investigational drug (IND)/devices/vaccine to provide emergency medical care to their patients in life threatening conditions. Research in such instance of medical care could be allowed in patients –

  I. When consent of person/patient/responsible relative or custodian/ team of designated doctors for such an event is not possible. However, information about the intervention should be given to the relative/ legal guardian when available later;
  II. When the intervention has undergone testing for safety prior to its use in emergency situations and sponsor has obtained prior approval of DCGI;
  III. Only if the local IEC reviews the protocol since institutional responsibility is of paramount importance in such instances.
  IV. If Data Safety Monitoring Board (DSMB) is constituted to review the data

THE EXPEDITED REVIEW PROCEDURE IS NOT APPLICABLE:

1. When the research involves more than minimal risk to the subjects;
2. Where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protection will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal;
3. For studies intended to evaluate the safety and effectiveness of medical devices, including studies of cleared medical devices for new indications.
4. When the research involves no more than minimal risk to the subjects but require funding

4b.6 DETAILED INSTRUCTIONS TO THE IRB SECRETARIAT:

4b.6.1 RECEIVE THE SUBMITTED DOCUMENTS

- Receive the application and documents submitted by investigators as described in SOP03/VER2

4b.6.2 EXPEDITED REVIEW

Procedure: The PI submits a completed protocol submission form along with the study protocol, waiver of consent form, case record form and any other documents as applicable-Document Checklist (ANX2-VER2/SOP 03/VER2)] to IRB. Principal Investigator may submit expedited review application form to IRB, if he/she feels the study meets the eligibility criteria for expedited review. Upon receipt of the application, IRB staff screens it for completeness and accuracy. Member Secretary, IRB makes a preliminary determination that the application/research proposal/documents meet the criteria for expedited review, including minimal risk, and identifies the research categories. If the application does not meet the criteria for expedited review, the study would be considered for full board review (as per SOP04a).

After deciding that the study or study documents qualify for an expedited review, Member Secretary informs the Chairperson. Member Secretary in consultation with the Chairperson forms a subcommittee comprising of the Member Secretary of the IRB, an external IRB member and one or two IRB members from MCC. The external member will chair the meeting in case of face to face meetings. The project documents will be provided to the lead discussant. Two lead discussants will be assigned. Review may be made either by circulation of comments, email, telephone discussion or meeting. The lead discussant should complete the online study assessment form (**ANX1-VER2/SOP04a/VER2).**
IRB members who are conducting expedited review must disclose to the IRB MemberSecretary any conflicts of interest related to the study under review, and must not review thoseitems. If IRB Member Secretary has any conflicts of interest related to the study under review,he must disclose the same to the IRB subcommittee Chair and must not review that project. Items identified to have a conflict of interest by the IRB
Member Secretary are marked to an IRB subcommittee Chair or designee who does not have a conflict with the study.
In reviewing the research, the sub-committee may exercise all the authorities of the IRB except that the sub-committee may not disapprove the research. If that is the case, it must go through full board review. The decision of the full board meeting will be communicated to the PI.

The lead discussants while reviewing the projects meeting the criteria for expedited
review are required to document in the study assessment form the justification for using the expedited procedure and document protocol-specific reasons justifying a waiver of consent for initial and continuing review of research, actions taken by the reviewer and any findings required by laws, regulations, codes, and guidance. The expedited review process should ordinarily be completed within 15 working days after it has been accepted and categorized for expedited review by the Member Secretary of the IRB. Although the project qualifies for expedited review, it may be reviewed in the full board meeting due to logistics or any other reason.

Research proposals that 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.

4b.6.3 COMMUNICATION BETWEEN THE IEC AND THE INVESTIGATOR

- The decision of the IEC subcommittee will be communicated to the Principal Investigator at the latest by one week of the expedited meeting. The minutes of expedited review will be ratified in the full board meeting.
- If the project is approved or has to be revised with minor modifications, this will be informed to the Principal Investigator in writing and the modifications submitted by PI will be reviewed by the Member Secretary or lead discussants for final approval. The PI will need to submit the modifications/revisions within 5working days of receipt of communication from the IEC.

Annexure 1

ANX1-VER2/SOP04b/VER2

Expedited Review Application Form

MCC IRB-SRC Project No.:_____*(To be filled by IEC Secretariat)*

1. Principal Investigator's Name: _____
2. Department/Division: _____
3. Title of Project: _____
4. Name of study team members:_____

_____

5. Brief description of the project:

_____

_____

6. State reasons why expedited review from IEC is requested? (Tick applicable)
   - ➢ Risks to subjects is no more than minimal
   - ➢ Research involving non identifiable specimen and human tissue from sources like blood bank, tissue banks, left over clinical samples
   - ➢ Research involving materials (data, documents, records, or specimens) which are non-identifiable that have been collected, for non-research (clinical)purposes

   Are children included in the study? ☐Yes ☐No

   Does the research involve vulnerable population? ☐Yes ☐No

Any other reasons:

_____

*Principal Investigator's signature:*_____

Recommendations by the IEC Member Secretary:

- Consider for expedited review, Reasons
- Cannot consider for expedited review, Reasons

_____

_____

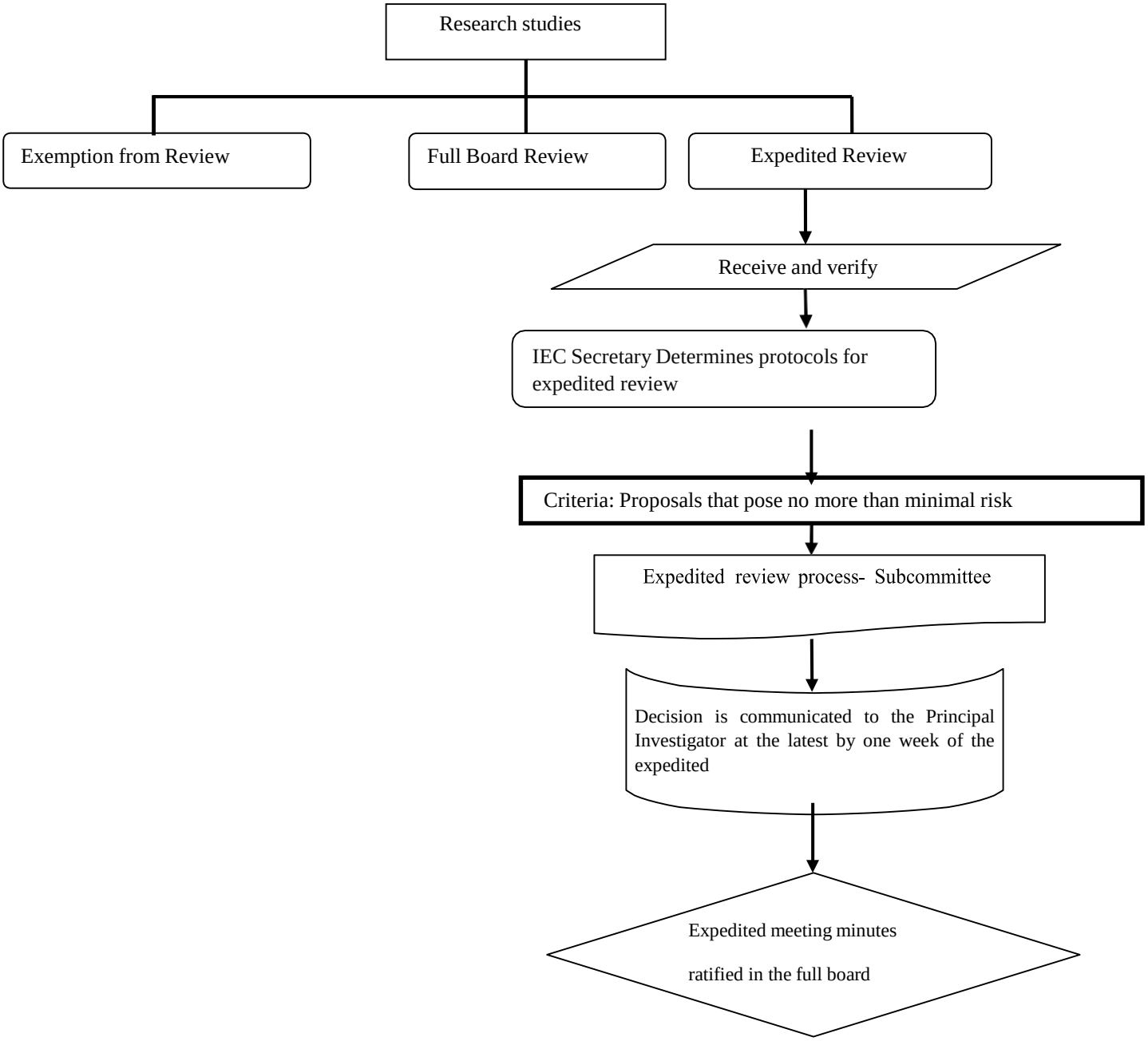
_____

Final Decision: ☐Expedited Review ☐ Full Board Meeting

Signature of the Member Secretary:

*Date-*_____

Flow Chart


Research studies
Exemption from Review
Full Board Review
Expedited Review
Receive and verify
IEC Secretary Determines protocols for expedited review
Criteria: Proposals that pose no more than minimal risk
Expedited review process- Subcommittee
Decision is communicated to the Principal Investigator at the latest by one week of the expedited
Expedited meeting minutes
ratified in the full board

CHAPTER 4c

Exemption from the Review for Research Projects

4c.1 PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to describe the IRB review exemption process and delineate the research studies that can be exempted from full board/expedited IRB review. The Exemption Form ANX1-VER2/SOP04c/VER2 is designed to standardize the process of exemption.

4c.2 SCOPE

This SOP applies to the studies submitted for exemption from review by the IRB. This SOP describes exemption from review in detail. The specific points in the Exemption Form shall guide the Member Secretary to determine whether the study qualifies for exemption from review. The decision should be taken by the IRB-SRC and in consultation with the Member Secretary. Member secretary in consultation with the Chairperson and should be informed to the members in the fourth coming IEC meeting.

4c.3 RESPONSIBILITY

It is the responsibility of the Member Secretary to record the decision in the Exemption Form with reasons. The IRB Secretariat is responsible for recording and filing the Exemption Form. The Member Secretary/Chairperson must sign and date, the letter conveying the decision. ANX1-VER2/SOP04c/VER2.

4c.4 CATEGORIZATION OF PROTOCOLS

The IRB-SRC, IEC-Member Secretary, or secretariat shall screen the proposals for their completeness and depending on the risk involved in the research proposals categorize them into three types, viz., Exemption from review, Expedited review and Full review.

An investigator may also apply for exemption from IRB review of the study protocol using Review Exemption Application Form (ANX1-VER2/SOP04c/VER2).However the decision to accept the request will be made by the Member Secretary, IRB with permission from the Chairperson.

4c.5 EXEMPTION FROM REVIEW

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

Minimal risk would be defined as probability of harm or discomfort anticipated in the research is not greater than that ordinarily encountered in routine daily life activities of a healthy individual or general population or during the performance of routine physical or psychological examinations or tests. However, in some cases like surgery, chemotherapy or radiation therapy, great risk would be inherent in the treatment itself, but this may be within the range of minimal risk for the research participant since it

would be undertaken as part of current everyday life. (ICMR)

Review Exemption: A research study is said to be exempt from review when it does not require the IRB approval for its conduct. Proposals that can be exempt from review include those with less than minimal risk where there are no linked identifiers such as;

- Research conducted on data available in the public domain for systematic reviews or meta-analysis.
- Observation of public behavior when information is recorded without any linked identifiers and disclosure would not harm the interests of the observed person.
- Quality control and quality assurance audits in the institution.
- Comparison of instructional techniques, curricula, or classroom management methods.
- Public health programs 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).

EXCEPTIONS:

a. When research on use of educational tests, survey or interview procedures, or observation of public behavior can identify the human participant directly or through identifiers, and the disclosure of information outside research could subject the participant to the risk of civil or criminal or financial liability or psycho social harm.
b. When interviews involve direct approach or access to private papers.

1. In circumstances where research appears to meet minimal risk criteria may need to be reviewed by the IEC. This might be because of requirements of:
   a. The publisher of the research.
   b. An organization which is providing funding resources, existing data, access to participants etc.
2. No research can be considered as minimal risk if it involves but is not restricted to the following:
   a) Invasive physical procedures or potential for physical harm
   b) Procedures which might cause mental/emotional stress or distress, moral or cultural offence
   c) Personal or sensitive issues
   d) Vulnerable groups
   e) Cross cultural research
   f) Investigation of illegal behavior(s)
   g) Invasion of privacy
   h) Collection of information that might be disadvantageous to the participant
   i) Use of information already collected that is not in the public arena which might be disadvantageous to the participant
   j) Use of information already collected which was collected under agreement of confidentiality
   k) Participants who are unable to give informed consent

l) Conflict of interest e.g. the researcher is also the lecturer, teacher, treatment-provider, colleague or employer of the research participants, or there is any other power relationship between the researcher and the research participants.

m) Deception

n) Audio or visual recording without consent

o) Withholding benefits from "control" groups

p) Inducements

q) Risks to the researcher

4c.6 DETAILED INSTRUCTIONS TO THE IRB SECRETARIAT:

4c.6.1 RECEIVE THE SUBMITTED DOCUMENTS

- The Secretariat will receive the Review Exemption Application Form ANX1-VER2/SOP04c/VER2, Protocol and other documents submitted by the investigators.
- Acknowledge the submitted documents
- Hand over the received documents to the Member Secretary, IEC.

4c.6.2 DETERMINE PROTOCOLS ELIGIBLE FOR EXEMPTION FROMREVIEW

The *IRB*-Member Secretary will determine whether a protocol qualifies for exemption from review based on criteria explained in section 4c.5.

4c.6.3 EXEMPTION PROCESS

- If the protocol and related documents satisfy the criteria as listed in 4c.5, the IRB Member Secretary in consultation with the Chairperson will review the brief summary of the project and the Exemption Form.
- The Member Secretary will record the decision on the Exemption Form.
- The Secretariat will communicate the decision to the investigator.
- The Member Secretary will inform the IRB about the decision at the next full board meeting.
- In case the study does not qualify for exemption from review, the Member Secretary/ Chairperson will refer the study for full board/expedited meeting as appropriate.
- Exempt research should fulfill organization's ethical standard, such as:

  - The research should hold less than minimal risk to participants.
  - Selection of participants should be equitable.
  - If there is recording of identifiable information, there should be adequate provisions to maintain the confidentiality of the data.
  - If there are interactions with participants, the IRB should determine whether there should be a consent process that will disclose such information's:
    a) That the activity involved in the research.
    b) A description of the procedures.
    c) That participation is voluntary.

d) Name and contact information of the researcher.
e) There are adequate provisions to maintain the privacy and interests of participants.

Exempt research does not require continuing review or submission of status report. Thecompletion report is not expected.

4c.6.4 COMMUNICATION BETWEEN THE IRB AND THE INVESTIGATOR

- The decision regarding request for exemption from review, signed by the IRB Member Secretary/Chairperson, will be forwarded by the Secretariat to the Principal Investigator within 15 days after the decision regarding the exemption is taken.
- The Member Secretary will inform the IRB of the decision at the forthcoming regular meeting and minute it in the meeting notes.

Annexure 1

ANX1-VER2/SOP04c/VER2

Review Exemption Application Form

IRB-SRC Project No.:_____(To be filled by IRB Secretariat)

1. Principal Investigator's Name:

2. Department/ Division

_____

3. Title of Project:

4. Names of study team members:

_____

5. Brief description of the project:

Please give a brief summary (approx. 300 words) of the nature of the proposal, including the aims/objectives/hypotheses of the project, rationale, study population, and procedures/methods to be used in the project.

Please check that your application / summary includes:

- Procedures for voluntary, informed consent
- Privacy &confidentiality
- Risk to participants
- Needs of dependent persons
- Conflict of interest
- Permission for access to participants from other institutions or bodies
- Inducements

6. State reasons why exemption from IRB review is requested (Tick applicable)

- ☐ Audit of educational practices
- ☐ Observation of public behavior when information is recorded without any linked identifiers and disclosure would not harm the interests of the observed person;
- ☐ Quality control and quality assurance audits in the institution;
- ☐ Comparison of instructional techniques, curricula, or classroom management methods;
- ☐ Research on microbes cultured in the laboratory

- Research on immortalized cell lines
- Research on cadavers or death certificates which reveals no identifying personal data
- Analysis of data freely available in the public domain for systematic reviews or meta-analysis;
- Consumer acceptance studies related to taste and food quality; and
- 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).
- Any other (please specify) ___

*Principal Investigator's signature:*_____ *Date*_____

Forwarded by the Head of the department: Name:_____**Signature:**_____**Date:** _____

Recommendations by the IRB –SRC Chairman:

- Exemption,
  Reasons
  _____
- **Cannot be** exempted,
  Reasons
  _____

_____

- Discussion at full board

Signature of the Member Secretary:

- *Date* _____

Final Decision:

- Exemption
- Cannot be exempted,

Reasons

_____

_____

- Discussion at full board

*Signature of the Chairperson:*_____*Date* _____

Final Decision at Full Board meeting held on_____

NOTE: No research can be counted as minimal risk if it involves:

1. Invasive physical procedures or potential for physical harm
2. Procedures which might cause mental/emotional stress or distress, moral or cultural offence
3. Personal or sensitive issues
4. Vulnerable groups
5. Cross cultural research
6. Investigation of illegal behavior(s)
7. Invasion of privacy
8. Collection of information that might be disadvantageous to the participant
9. Use of information already collected that is not in the public arena which might be disadvantageous to the participant
10. Use of information already collected which was collected under agreement of confidentiality
11. Participants who are unable to give informed consent
12. Conflict of interest e.g. the researcher is also the lecturer, teacher, treatment-provider, colleague or employer of the research participants, or there is any other power relationship between the researcher and the research participants.
13. Deception
14. Audio or visual recording without consent
15. Withholding benefits from "control" groups
16. Inducements
17. Risks to the researcher

This list is not definitive but is intended to sensitize the researcher to the types of issues to be considered. Minimal risk research would involve the same risk as might be encountered in normal daily life.

Please check that your application / summary has discussed:

- Procedures for voluntary, informed consent
- Privacy &confidentiality
- Risk to participants
- Needs of dependent persons
- Conflict of interest
- Permission for access to participants from other institutions or bodies

- Inducements

In some circumstances research which appears to meet minimal risk criteria may need to be reviewed by the IEC. This might be because of requirements of:

- The publisher of the research
- An organization which is providing funding resources, existing data, access to participants etc.

ANX2-VER2/SOP04c/VER2

Template of the decision letter/communication of decision regarding exempt from review

Date:

PI Name,
Principal Investigator,
PI Dept
Malabar Cancer Centre

Ref: Project No.____-Request for exemption from review.

Dear Dr. PI,

Your application dated_____for **P.No._____- Project Title** "_____"was

Reviewed by the Chair person on_____.

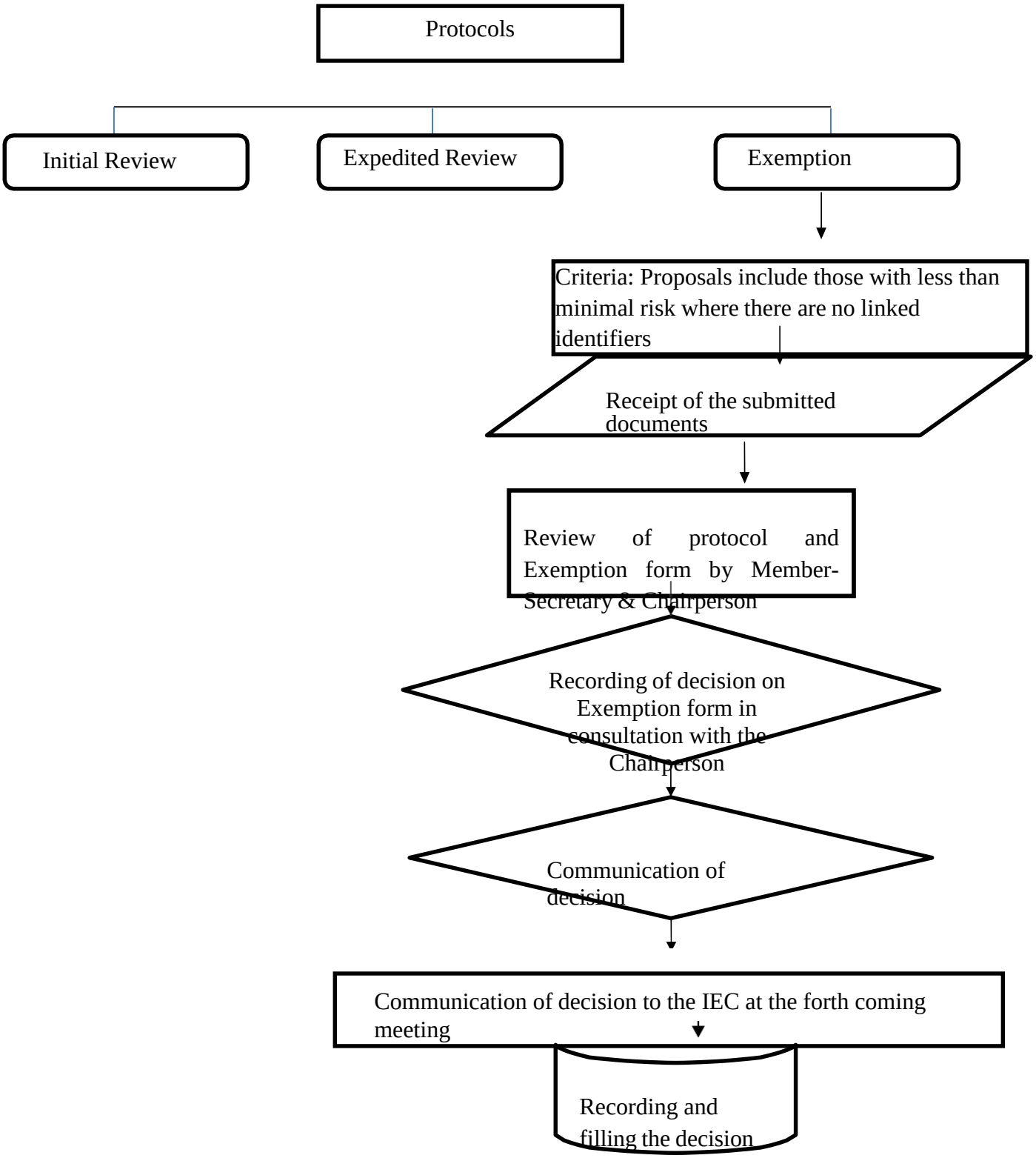
Status: Exempted

Thanking you
Yours faithfully

Member Secretary

Institutional Ethics Committee

FLOW CHART


Protocols
Initial Review
Expedited Review
Exemption
Criteria: Proposals include those with less than minimal risk where there are no linked identifiers
Receipt of the submitted documents
Review of protocol and Exemption form by Member-Secretary & Chairperson
Recording of decision on Exemption form in consultation with the Chairperson
Communication of decision
Communication of decision to the IEC at the forth coming meeting
Recording and filling the decision

CHAPTER 5

Preparation of agenda, procedures for conducting Meetings, minutes recording

5.1 PURPOSE

The purpose of this procedure is to elaborate administrative process and provide instructions for preparation, review, approval, and distribution of meeting agenda, minutes, and notification letters of IRB, MCC meetings.
The day, time, and venue of IRC meetings for both committees (SRC and IEC) are specified as follows:

SRC meets at 10:00 am on the 2nd and 4th Saturday of every month or as when required
IEC meets at on every three months and/or as and when required.

5.2 SCOPE

This SOP applies to administrative processes concerning the conduct of the IRB meetings.

5.3 RESPONSIBILITY

It is the responsibility of the Chairperson, SRC and Member Secretary of IEC and Office of IRB staffs to prepare for the respective meetings.

5.4 DETAILED INSTRUCTIONS

5.4.1 BEFORE IRB MEETING

SRC Meeting:
Prepare the agenda of the SRC meeting at least 3 days prior to avoid last minute rush or mistakes.

- Prepare the agenda of the IEC/SRC meeting.
- Investigators are advised to submit proposals at least 7-14 days before the scheduled meeting date to ensure that their projects would be reviewed in the

meeting scheduled in a given month as applicable depending on site IEC SOPs..

- No limit is placed on the number of items on the agenda. The number of items is based on available expertise (members and consultants), urgency, order of submission to the IEC and IEC workload.

  Lead discussants will be assigned as necessary taking into account conflicts of interests of members. In addition, the IEC Administrator will check the agenda prior to the meeting to identify IEC members who may have a conflict of interest due to their participation as key personnel on a current or proposed research project. If a conflict of interest is identified, the study is assigned to another member who does not have a conflict of interest. An IEC member who has a conflict of interest with regard to a research project that will be reviewed at a convened IEC meeting must notify the IEC office of the conflict prior to the meeting. Once the IEC office receives notice of recuse, the IEC Member Secretary will seek an alternate IEC member to join the meeting for the review of that project if necessary to meet quorum

- It is general practice (but not required policy) that IEC Chairs are not assigned lead discussant responsibilities except in circumstances when their expertise is the most appropriate.

IEC Meeting:

Prepare the agenda of the IEC meeting (*ANX-VER2/SOP05/VER2*)
Schedule protocols on the agenda on a first come first serve basis. MCC has constituted one IEC, so the protocols are not assigned randomly to the committee. However, in case
PI is a member of one of the IEC, the protocol is referred to the IEC Chairperson to avoid bias.

5.4.2 DISTRIBUTION OF PROTOCOL/DOCUMENT PACKAGES TO IRB MEMBERS

Distribute copies of the protocols to the SRC members by electronic mail (mail ID; ***irbmcctly@gmail.com***) at least 7 days prior to the scheduled meeting date.
Distribute copies of the protocols to the IEC members by either electronic mail or by courier preferably 10 days in advance of the scheduled meeting.

Verify (verbally, by e-mail, by fax or by mail) with the members whether the protocol
Packages are received. It is the responsibility of the IEC member to verify items of the parcel on receipt and in the event of any missing items, intimate the IRB office immediately so that the relevant documents could be made available to the members before the meeting.

5.4.3 MEETING PREPARATION

- Reserve the IEC meeting room on the scheduled meeting date and time. The meeting will be held in the meeting room of IEC, unless otherwise specified. In case of meetings held via video-conference, the necessary arrangements would be made with IT support.
- Ensure that the room, equipment (projectors, recorder, etc) and facilities are

available in good working conditions

- All original files of studies on the agenda are kept for ready reference before the meeting
- E-copy of SOPs, new CT Rules, ICMR guidelines are kept available for ready reference
- Secretariat informs the scheduled meeting date and time to the Principal Investigators.
- The meeting will be re-scheduled or canceled if it becomes apparent that meeting requirements (quorum, sufficient expertise) will not be met.

5.4.4 MEETING CONDUCT

1. The members should gather in IRB Meeting Venue on scheduled time.
    - In case of any emergency delay of a committee member for attending the meeting, he or she must immediately inform to the Chairperson of that Committee by the Office of IRB, provided the concerned member does not do it intentionally.
    - The Office of IRB may ask the members who do not come for the regular IRB meetings without any prior intimation for a written explanation and everything will be recorded as minutes.
2. The Chairperson should determine that the quorum (*SOP02/VER2 section no. 2a.9*) requirements are met, otherwise he/she may wait for a maximum period of 30 minutes, and otherwise the meeting will be called as "*cancelled due to lack of quorum*". To avoid such cancellation of IRB meetings, members of both the committees must intimate (by mail or by phone call) their presence and absence (with proper cause) well in advance to the Office of IRB.
3. The Chairperson of SRC and IEC should ask for declaration of conflict of interest either verbally or written on any protocol for discussion.
4. If any IEC member has conflict of interest involving a project then he / she should declare the same, before the meeting commences and leave the meeting room before the discussion on the same. This should be recorded in the minutes
5. The Member Secretary of IEC should table the minutes of the previous meeting and present the agenda for discussion
6. The IEC may invite investigators to attend the full board meeting related to their studies, and clarify doubts, if any.
7. The meeting proceeds in the sequential order of the agenda; however the Chairperson may change the order, if the situation so demands
8. The Member Secretary will request the lead discussant to discuss the research protocol.
9. The lead discussant will submit the duly filled study assessment form at the end of the discussion or at the conclusion of IEC meeting.
10. Amendment will be reviewed by previously assigned lead scientific discussant.
11. In case the lead discussant cannot attend the meeting, Member-Secretary, IEC or any other IEC member may brief the IEC about the research protocol and also discuss the written comments/duly filled study assessment form, if provided by the lead discussant.

12. The Member Secretary, IEC/IRB staffs minutes/records the proceedings of the SRC and IEC meetings.

5.4.5 DECISION MAKING PROCESS

IEC completes the adequate review of the research studies submitted. The committees will review new studies, amendments, annual /continuing review of ongoing studies, SAE reports, any other documents and assess final reports of all research activities through a scheduled agenda.

- An IEC member will withdraw from the meeting for the decision procedure concerning the study where conflict of interest exists.
- 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.
- Decision may only be taken when sufficient time has been allowed for review and discussion of study in the absence of non-members (e.g., the investigator, representatives of the sponsor, independent consultants) from the meeting, with the exception of IEC staff
- Decisions will only be made at meetings where a quorum (SOP02a/V6) is present
- The documents required for a full board review of the application should be complete and the relevant elements considered before a decision is made.
- Only IEC members who attend the meeting will participate in the decision.
- Decisions will be arrived at through consensus/unanimous consent or majority opinion amongst the voting members of IEC. The decision-making is thus concerned with the process of deliberating and finalizing a decision. When a consensus is not possible, the IEC will vote.

  Voting Procedure;

  1. This may be in the form of voice vote, show of hands, or by secret ballot, as determined by the Chairperson, IEC.
  2. All members of the IEC excluding the Chairperson have the right to vote/express their decision and should exercise this decision. In case of a tie, the Chair will have a casting vote.
  3. The concurrence / voting of the members will be recorded in the minutes as - Agreed / Disagreed / Abstained /Recused.
     - Agreed: in favor
     - Disagreed-Against
     - Abstain: Present but formally decline to vote either for or against a proposal
     - Recused: Listed under "Members Present" but not present for

the discussion and decision on the study due to conflict in the proposal..

- Types of decision
  - **Approved**- The study is approved in its present form
  - **Revision with minor modifications/amendments** - refers to minor modifications that do not alter the risk-benefit assessment for the research and do not require substantial changes in protocol and informed consent document.

    The revisions will be reviewed by the Member Secretary, IEC or in some cases, by the respective lead discussant on behalf of the full board. Such revised proposals may not be taken up for the full board review, however in some cases these studies may be referred for a full board review. If revisions are found satisfactory, approval will be granted.

    Examples may include but are not limited to- minor, non-substantive changes in the protocol and consent form(s), Correction of typos, grammatical errors, minor wording clarifications (in informed consent forms).

  - **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 board meeting.

    Resubmit refers to major modifications that may alter the risk-benefit assessment for the research and require substantial changes in protocol and informed consent document.

    Examples may include but are not limited to- significant changes in the protocol (research methodology, study design) and consent form(s), and modification affecting participant

  - **Not approved**- The study is not approved in its current form. A negative decision on an application will be supported by clearly stated reasons. If the investigator wishes to appeal to the decision, he/she may do so by contacting the IEC Secretariat

- **Deferred-** The decision cannot be arrived at present and therefore postpone to next meeting. Grounds for this: lack of quorum, lack of expertise etc..
- **Noted-** Study documents that are notified to IEC
- **Query**- Further clarification/ modification required

- An IEC may decide to reverse its positive decision on a study if it receives information that may adversely affect the risk/ benefit ratio/ safety of participants.
- Any advice by the IEC that is non-binding will be appended to the decision.
- The discontinuation of a trial will be recommended if the IEC finds that the goals of the trial have already been achieved midway, unequivocal results are obtained or if the IEC feels the continuation of the trial may potentially harm participants.
- If necessary, the investigator may be invited to present the protocol or offer clarifications in the meeting. Representative of the patient groups or community can be invited during deliberations to offer their view point.
- Subject expert/s may be invited to offer their views or their review comments would be considered. The expert/s should not participate in the decision making process. However, his / her opinion must be recorded.
- The proceedings of the IEC meetings will be documented and the meeting minutes will be signed by the Chairperson/Member Secretary, IEC.

After the IEC meeting

Preparing the minutes and the decision letters

- The IRB Administrators will 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.
- The minutes of the meeting will then be finalized by the Member Secretary preferably within 15 working days
- The minutes will record whether the decision was unanimous, or whether a vote was taken for the decision. 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 basis for requiring changes in or disapproving research; and a written summary of the discussion of controversial issues and their resolution must be recorded.

Approval of the minutes and the decision

- The minutes will be circulated to all the members for comments before final approval by Chairperson.
- The minutes of the IEC meeting will be approved and signed by Chairperson/Member Secretary, IEC
- The minutes of the IEC meeting will be ratified in the subsequent IEC meeting
- The IEC decisions will be communicated to the PIs

Filing of the minutes of the meeting

- Place the original version of the minutes in the minutes file and copy of the minutes are filed only in the corresponding initial review research protocol file

Communicating Decision

The decision will be communicated in writing to the PI and relevant stakeholders, preferably within a period of 15 working days of the IEC meeting at which the decision was made.

The communication of the decision will include, but is not limited to, the following

- Project No. and title of the research proposal reviewed
- The clear identification of the protocol of the proposed research or amendment, date and version number (if applicable)
- The names and specific identification number version numbers/dates of the documents reviewed, including the potential research participant information sheet/material and informed consent form
- The name and title of the Principal Investigator
- The name of the site(s)
- The date and place of the decision
- A clear statement of the decision reached
- Validity of approval will be for the complete duration of the study. This approval is subject to annual review. However failure to submit completed status report by the late due date may result in the expiration of approval.
- Calculation of Approval and Expiration Dates

The IEC calculates the date of initial IEC approval in the following manner:

- When a research study is approved at a convened full board/expedited review meeting, the date of the approval letter is the date of issue of letter

5.4.6 AFTER THE SRC/IEC MEETING

5.4.6 (A) preparing the minutes and the decision letters

For SRC

- The Chairperson/Vice-Chairperson of SRC with the help of IRB staffs will compile the proceedings of SRC meeting in a concise and easy-to-read style and will e-check, grammar and context of the written minutes.
- The minutes of the meeting will be compiled within a week.

***For IEC* Preparing the minutes and the decision letters**

- The IRB Administrators will 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.
- The minutes of the meeting will then be finalized by the Member Secretary preferably within 15 working days

- The minutes will record whether the decision was unanimous, or whether a vote was taken for the decision. 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 basis for requiring changes in or disapproving research; and a written summary of the discussion of controversial issues and their resolution must be recorded.

5.4.6 (B) Approval of the minutes and the decision

For SRC

- The minutes of the SRC meeting will be signed by all the members who attended that particular meeting and finally the Chairperson will sign it.
- The minutes of the SRC meeting will be ratified electronically before final signature by the Chairperson.
- The SRC decisions will be communicated to the PIs by e-mail initially.

For IEC

- The minutes of the IEC meeting will be signed by Member Secretary, IEC and Chairperson, IEC.
- The minutes of the IEC meeting will be ratified in the subsequent IEC meeting.
- The IEC decisions will be communicated to the PIs by e-mail initially.

5.4.6 (C) Filing of the minutes of the meeting

- Place the original version of the minutes in the meeting file and copy of the minutes are filed in the corresponding research protocol file.

5.4.7 COMMUNICATING DECISION

The decision will be communicated in writing to the PI and relevant stakeholders, preferably within a period of 15 working days of the IRB meeting at which the decision was made.

The communication of the decision will include, but is not limited to, the following

- Project No. and title of the research proposal reviewed
- The clear identification of the protocol of the proposed research or amendment, date and version number (if applicable)
- The names and specific identification number version numbers/dates of the documents reviewed, including the potential research participant information sheet/material and informed consent form
- The name and title of the Principal Investigator
- The name of the site(s)
- The date and place of the decision
- A clear statement of the decision reached

- Validity of approval will be for the complete duration of the study. This approval is subject to annual review. However failure to submit completed status report by the late due date may result in the expiration of approval.
- Calculation of Approval and Expiration Dates

The IEC calculates the date of initial IEC approval in the following manner:

- When a research study is approved at a convened full board/expedited review meeting, the date of the approval letter is the date of issue of the IEC approval letter.

Calculation of Validity period of the IEC approval Initial Approval

The expiration date is the last date that the protocol is approved

The IEC calculates the date of expiration in the following manner:

- Based on the proposed duration of the project– the date of expiration is calculated by the following means-

  Date of IEC approval +364 days= Date of expiry

  01/05/2016 + 364 days =) Valid till 30/04/2017

  01/05/2016 + 179 days = Valid till 31/10/2016

- Location of study conduct
- Number of participants to be accrued
- To submit the continuing review application/annual status report
- To register the study in the Clinical Trials Registry
- Any suggestions by the IEC
- The date of approval of a study is the date of issuance of the IEC approval letter.
- In the case of a positive decision, the PI is notified of the following requirements through an approval letter(ANX2-VER2/SOP05/VER2)
  - Responsibilities of the PI
  - Submission of annual status reports/progress report(s) is decided on a case to case basis, usually yearly.
  - The need to notify the IEC in the case of amendments to the recruitment material like the potential research participant information, or the informed consent form
  - The need to report serious and unexpected adverse events related to the conduct of the study
  - The need to report unforeseen circumstances, the termination of the study, or significant decisions by other IECs or DSMBs
  - The information the IEC expects to receive in order to perform ongoing review
  - The final summary or final report
  - The schedule/plan of ongoing review by the DSMB of sponsored trials
  - Recruitment to start only after submitting the CTRI registration details to the IEC, in writing.

- Academic Clinical Trials: In the event of a possible overlap between the academic clinical trial and clinical trial or a doubt on the nature of study, the Ethics Committee concerned shall inform the Central Licensing Authority in writing indicating its views within thirty working days from the receipt of application to that effect. In case the Central Licensing Authority does not send the required communication to institutional Ethics Committee within thirty working days from the date of receipt of communication from the Institutional Ethics Committee, it shall be presumed that no permission from the Central Licensing Authority is required. The final approval letter will be issued by the IEC.
- An IEC may decide to reverse its positive decision on a study if it receives information that may adversely affect the risk/ benefit ratio
- In the case of a negative decision, the reasons will be stated in the communication to the PI
- The PI will also be notified of the cap for accrual of number of participants
- All decision and approval letters will be signed by the Member Secretary, IEC or the nominated Secretary for that meeting. In case Member Secretary IEC is Principal Investigator, the decision letters will be signed by Acting Member Secretary / Chairperson / IEC.
- The decisions letters will be communicated to the Principal Investigator and wherever required to the organizational offices and officials and other concerned authorities.
- Member Secretary, IEC/Chairperson IEC, will sign and date the approval certificate in the original research protocol.
- The letter will mention whether the decision has been arrived at by consensus unanimous or majority opinion amongst the voting members of IEC, or by voting.
- If the decision has been arrived by voting, the letter will state the number of votes for and against approval of the project.

Procedures for Appealing the IEC Decision to Disapprove or Terminate a Study

- If an investigator disagrees with the IEC decision to disapprove or terminate a study, the Investigator may submit a written appeal of the decision to disapprove of the IEC decision within 21 working days of being notified of the decision. The appeal should address the specific concerns of the PI for the basis for disapproval.
- The appeal will be reviewed by the full board. The Investigator may request to be in attendance at or 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 (Decision making process-Voting). The Principal Investigator will be notified in writing of the decision.
- If the appeal to the decision on disapproving a study is accepted, the Investigator is invited to submit a new study application to the IEC for review and approval, according to the conditions set forth by the IEC in accepting the appeal.
- If the appeal is denied, the IEC decision is final and the study may not be approved or resumed.

ANX1 –VER2/SOP05/VER2

Agenda/Minutes format

1. Minutes-IEC & DSMU
2. SAEs
3. Deviations
4. Projects for Initial Review
5. Resubmission of projects after initial review
6. Post approval amendments a)Protocol b) ICF c)IB d)CRF
7. Status Reports
8. Monitoring Reports
9. Letters
10. Any other

ANX2 –VER2/SOP05/VER2

FORMAT FOR APPROVAL LETTER OF IEC

Approval Letter Format

To,
Dr. _____
Principal Investigator,
MalabarCancerCentre.

Ref: Project No.

Dear Dr.

Institutional Ethics Committee reviewed and discussed your application (dated) to conduct the research study entitled " ven _____ " during the IEC meeting held on ((date) (time)

The following documents were reviewed and approved:

1. Project Submission form.
2. Study protocol (including protocol amendments), dated_____, version o(s).
3. Patient information sheet and informed consent form (including updates if any) in English and/Vernacular language.
4. Investigator's Brochure, dated_____, version no._____
5. Case Record Form
6. Proposed methods for patient accrual including advertisement(s)etc. proposed to be used for the purpose.
7. Current CVs of Principal investigator, Co-investigators
8. Package inserts
9. Insurance policy/compensation for participation and for serious adverse events occurring during the study participation.
10. Investigator's Agreement with the sponsor.
11. Investigator's undertaking.
12. DCGI/DGFT approval
13. Clinical Trial Agreement (CTA)/Memorandum of Understanding (MOU)/Material Transfer Agreement(MTA) if applicable

The following members of the Institutional Ethics Committee (IEC) were present at the meeting held on Date_____Place _____

Name of member/Position on IEC/Affiliation/Gender/Expertise

_____Chairman of the Institutional Ethics Committee

_____Member secretary of the Institutional Ethics Committee

_____Name of each member with designation

The study is approved in its present form for a period of_____till(date)_____.The Principal Investigator should submit continuing review application/annual status report on or before (date). You may request for extension of validity in the submission of continuing review application/annual status report. In order ensure that there is no lapse in the IEC approval period, it is mandatory to submit study status report prior to lapse of study validity.

- **The waiver of consent was granted since_____**
- **PI should intimate IEC on any funding obtained as part of educational/unconditional support and/or other sources. Agreement/MoU as per IEC approved template with the funding bodies should be submitted to the IEC, prior to starting accrual on the study.**
- **It is mandatory that the source documentation should be done in the electronic medical record and case file.**
- **PI should ensure linking of project account to the online cashless payment system prior to initiation of the study.**
- **PI should maintain an itemized reimbursement sheet per patient. It is mandatory that all patients are reimbursed for every investigation/treatment/day care charges as budgeted.**
- **If the study requires institutional insurance coverage, please confirm this with TRAC**

administrator after IEC approval and before commencing the study.

The study should be initiated only after -

- **Registration of the study with Clinical Trials Registry India (CTRI) .**
- **Submission of Finalized and signed Clinical Trial Agreement /Memorandum of Understanding Agreement/Material Transfer Agreement/DataSharing Agreement**
- **Submission of DCGI approval to IEC (if applicable)**
- **Submission of HMSC approval to IEC (if applicable)**

Following points must be noted:

1. **IEC has approved recruitment/review of_____participants/samples on this study.**
2. **IEC has approved the conduct of the study at Malabar Cancer Centre**
3. Principal Investigator and study team should be GCP trained
4. PI and other investigators should notify initiation of the study. Principal Investigator should intimate the IEC after accrual of first 10 participants in the study or after 6 months of initiation of study whichever is earlier.
5. PI and other investigators should co-operate fully with Monitoring team of the IEC , who will monitor the study from time to time.
6. The decision was arrived at through consensus/unanimous or majority opinion amongst the voting members of IEC. Member(s) of the committee who is/are listed as investigator(s) on a research proposal opted out from all deliberations on the proposal and did not participate in decision making. Neither PI nor any of proposed study team members participated during the decision making of the IEC.
7. At the time of PI's retirement/intention to leave the institute, study responsibility should be transferred to colleague after obtaining clearance from HOD and/or convener of the PI's Disease Management Group (DMG) and IEC. Status report, including accounts details should be submitted to HOD and extra mural sponsors.
8. The IEC functions in accordance with its SOP and is compliant with the New Drug Clinical Trial Rules, ICMR guidelines and Indian/ICHGCP
9. In the events of any protocol amendments, IEC must be informed and the amendments should be highlighted in clear terms as follows:
   a) The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc…)
   b) Alteration in the budgetary status should be clearly indicated and the revised budget form should be submitted
   c) If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Institutional Ethics Committee for approval.
   d) If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
   e) If there are any amendments in the study design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the

IEC, only then can they be implemented.

f) Approval for amendment changes must be obtained prior to implementation of changes. Without including all the above points, the amendment is unlikely to be approved by the IEC.

10. Any Serious Adverse Events (SAEs) occurring on the study should be reported to IEC within 24 hours of its occurrence or it comes to the knowledge of the PI.

11. Any deviation/violation/waiver in the protocol must be informed to the IEC.

12. Principal Investigator should conduct the study in accordance to the IEC approved protocol

13. The PI should submit a report to the IEC at the time of study completion or Premature Termination / Suspension / Discontinuation Report as is applicable

14. PrincipalInvestigatorshouldcomplywithregulationsandguidelinesasapplicable

Thanking You,

Yours Sincerely,

Member secretary, IEC

ANX3 –VER2/SOP05/VER2

Letter Format for Amendments

Dr…
Principal Investigator,

Ref: Project No. Title Dear

Dr…

The following documents of the above referenced project was reviewed and discussed during the IEC meeting held on date/time/place

The following members of the IEC were present:

IEC comments were as follows- a.
b.
c.

Status-

i. **Approved**
ii. **Revision with minor modifications/amendment, Revision with major modifications for resubmission. Kindly comply with the above suggestions of the IEC and submit the one copy of revised proposal or documents within six months for review. If you fail to submit within six months, this project will be closed by IEC and you will have to submit a new project.**
iii. **Not Approved.**

This decision was taken by consensus.

Neither PI nor any of proposed study team members participated during the decision making of the IEC.

Thanking you,
Yours sincerely,
Member Secretary, IEC

ANX4 –VER2/SOP05/VER2

FORMAT FOR APPROVAL LETTER OF SRC
(In case of Exemption from review/Expedited review Study Proposals)

SRC File No. Date: Month Day-Year (e.g. January 1st -2021)

To
Dr./Mr./ Mrs _____
Principal Investigator,
Malabar Cancer Centre, Thalassery.

Sub.: Decision Forwarding-SRC Meeting-MCC-Reg.

Ref: Project No./Title

Dear Dr./Mr./Mrs. ..... ,

The Scientific Review Committee of Malabar Cancer Centre reviewed and discussed your application (dated) to conduct the research study entitled "_____" during the SRC meeting held on (date) at the Malabar Cancer Centre, Thalassery

The following documents were reviewed and approved:

1. Project Submission form.
2. Study protocol (including protocol amendments), dated_____, version no(s).
3. Investigator's brochure, dated_____, version no._____
4. Proposed methods for patient accrual including advertisement(s) etc. proposed to be used for the purpose.
5. Current CVs of Principal investigator, Co-investigators
6. Package inserts, if applicable
7. Investigator's undertaking
8. MoU/CTA if any
9. Status of funding , insurance coverage details if any

The Research Proposal is approved by SRC in its presented form and forwarded to IEC, MCC for ethical review.

Following points must be noted:

1. No clinical intervention for the purpose of the study is allowed in the proposed study site.
1. You are requested not to start the study until the IEC/ERC clearance is obtained
2. Please keep in touch with the Office of IRB for the IEC status of your study proposal
3. A study Completion Report must be submitted to the Office of IRB after completion of the study

Thanking You,

Yours Sincerely,

Chairperson*
Scientific Review Committee ***IRB OFFICE ROUND SEAL***
OFFICE SEAL

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*NOTE:
In case the Chairperson is a PI, the Vice-Chairperson of SRC will sign the letter.

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CHAPTER 6

Review of post approval amended protocol / Protocol related documents

6.1 PURPOSE

The purpose of this procedure is to describe how protocol amendments (post approval modifications) or any other amendments/letters are reviewed by the IEC.

6.2 SCOPE

This SOP applies to amended study protocols/ documents and letters that are modified after 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.

6.3 RESPONSIBILITY

PIs are responsible for obtaining IEC approval of proposed amendments to an IEC approved protocol before implementing them. Amendment is a revision, modification, addition to or deletion from an approved research protocol. It is the responsibility of the IEC secretariat to manage protocol amendments/ documents and letters. Receipt of the Amendment Package

- The amendment /documents along with the appropriate soft copy forwarded by the PI is received by the secretariat. The amendment /documents along with the covering letter should be accompanied by Amendment Reporting Form (ANX2 –VER2 -SOP06/VER2)
- Separate document with summary of changes to be provided. Additionally the study team should submit soft copies of amended documents in track changes and highlighted texts.
- The secretariat will confirm that the: changes or modifications in the amended version are underlined or color highlighted along with detailed summary of changes
- The Secretariat will check for completeness of the submission and inform the Principal Investigator to submit the required documents at the earliest, if any of the documents are missing/ incomplete.
- The secretariat of the IEC should follow the procedures as in SOP03/VER2 (Procedures for Management of protocol submission)

The Member Secretary, IEC, classifies the amendments into minor or major and tables the major amendments on the agenda of the subsequent scheduled meeting (for major amendment refer 6.4.1 and for Minor amendments refer to 6.4.2). The amendments and other documents which need full board review are processed as per the SOP 04a/VER2

6.4 REVIEW AMENDED PROTOCOLS/DOCUMENTS/LETTERS: Review as per Section 4a.3 SOP 04a/VER2

6.4.1 Review process for major protocol amendment:

The protocol amendment and other related documents will be reviewed by primary reviewers and will be discussed in the scheduled full board meeting. The reviewer will present a brief summary list of amendment and the comments on the amendment in the IEC Full Board meeting.

The primary reviewers will review the amended documents and assess the change in risk benefit ratio and impact of the amendment (modifications in the ICD, re-consent of research participants, untoward effects likely to occur because of the amendment or any other)

Following aspects of the Protocol amendment which may include but is not limited to:

a) Change in study design

b) Additional treatments or the deletion of treatments

c) Changes in inclusion/exclusion criteria.

d) Change in method of dosage formulation, such as, oral changed to intravenous

e) A significant change in the number of research participants (if the decrease/increase in the number of research participants alters the fundamental characteristics of the study, it is significant) f) A significant decrease or increase in dosage amount

g) Change in risk/benefit ratio

6.4.2 Minor amendments and notifications:

Minor amendments (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: Where the research is permanently closed to the enrolment of new subjects; all subjects have completed all research-related interventions may be reviewed in the expedited review subcommittee meeting (Refer SOP No. 04b/VER2.)

Minor notifications may be noted by the Member Secretary, IEC and not tabled in IEC meeting.

This may include but may not restrict to:

- Renewed insurance policy
- DCGI approvals
- Administrative notes
- Documents of administrative nature

6.5 Decision

- If the IEC approves the amendments, the decision is communicated to the PI.
- If the IEC does not approve the amendments, the secretary should immediately notify the investigator in writing of the decision and the reason for not approving the amendment.
- 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.
- Member Secretary will issue an approval letter to the Principal Investigator, if response from the PI found to be satisfactory

6.6 Storage of Documents:

File the amendments in the corresponding research protocol file, as per the SOP 10/01 on documentation and archival.

ANX1/VER2/SOP06/VER2

Amendment /Document Amendment Decision letter

Format for Decision for amendment documents

Date:

Dr. ,

Principal Investigator,

Malabar Cancer Centre

Ref: Project No. Title

Dear Dr.

The following documents for the above referenced project were tabled and discussed during the IEC meeting held on (date) (time) (place)

The following members of the IEC were present:

Status: Approved / Revision with major modification for resubmission / Revision with minor modification/amendments / Not approved / Deferred

This decision was taken by consensus.

Neither Principal Investigator nor any of the study team members participated during the decision making of the IEC.

Thanking you,

Yours truly,

Member-Secretary,

Institutional Ethics Committee

ANX2-VER2/SOP06/VER2

Post approval Amendment Reporting Form

(Kindly tick in the boxes provided)

Project No. :	
Title :	
Principal Investigator :	
Date of IEC Approval:	
Start Date of Study : Status of Study : Validity of IEC approval :	
No. of amendment: Have the changes modifications in the amended versions been highlighted/ underlined? …Yes …No Nature of amendment …Major …Minor	
Does this amendment entail any changes in Informed Consent Form (ICF)	…Yes …No
If yes, whether amended ICFs are submitted pl. specify ICF Version No. & Date and its IEC approval	
Please mention version no. and date of amended Protocol / Investigators Brochure / ICF Addendum/ Case Record Form /Any other documents	
• Does the revision entail any change in the Risk vs Benefit Analysis	…Yes …No
• Target accrual of trial (entire study) _____ • Total patients to be recruited at MCC (IEC ceiling)_____ • Screened: _____ • Screen failures: _____ • Enrolled: _____ • Consent Withdrawn: _____Reason: (Attach in format below) • Withdrawn by PI: _____Reason: (Attach in format below) • Active on treatment: _____ • Completed treatment : _____ • Patients on Follow-up: _____ • Patients lost to follow up: _____ • Any other: _____ • Any Impaired participants • None_____ • Physically _____ • Cognitively _____ • Both _____	

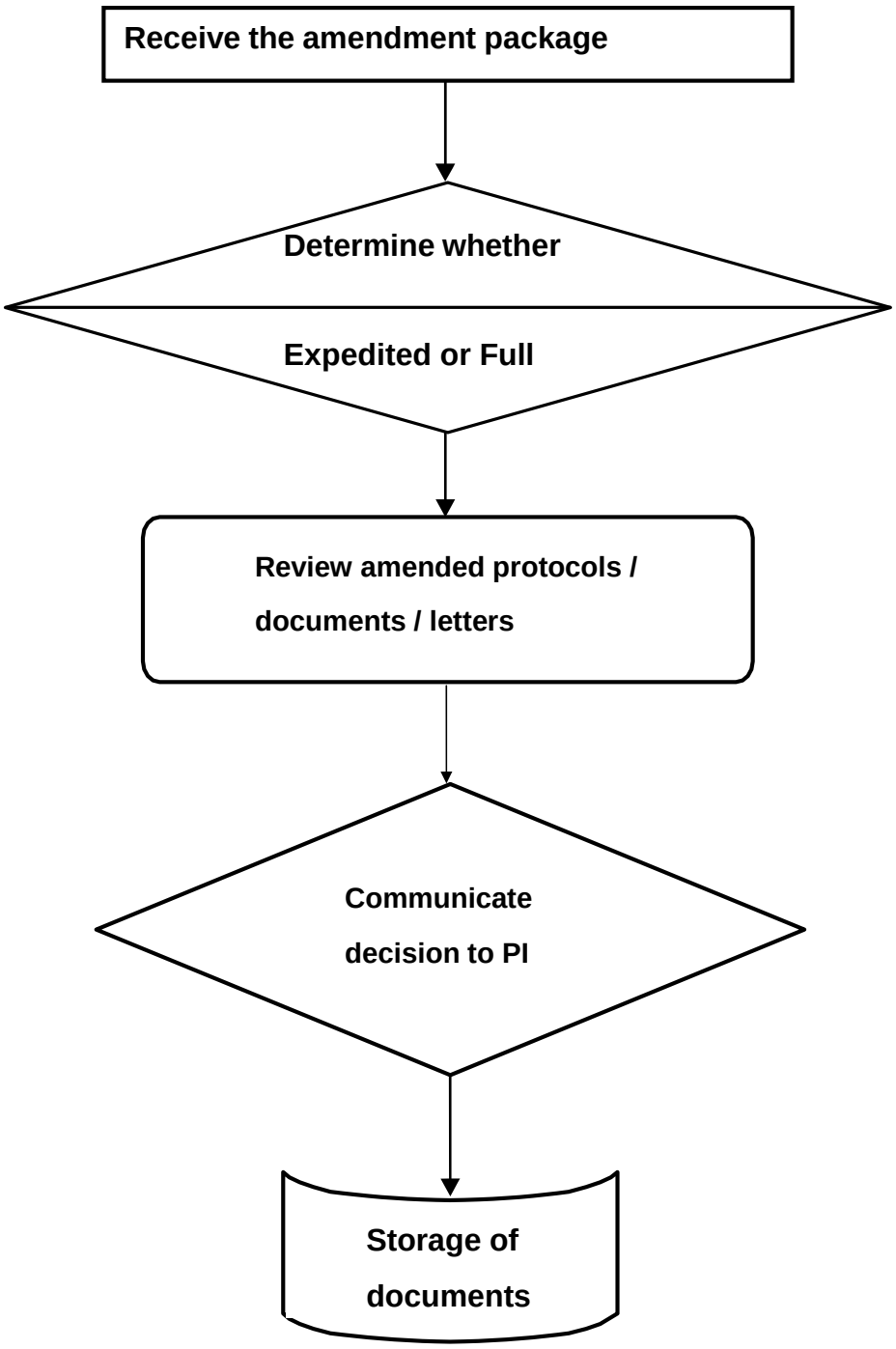
(**Important note**: Please submit summary list of changes should include document/Revised version no Section, page no, change(s) and risk/benefit or justification.

Table 1: Summary List of Changes (Comparison Chart)

Name of document	Revised version/Date	Section	Page No	Previous/ Old text	New text	Risk/Benefit Assessment/Justification

Signature of the Principal Investigator & Date:

FLOW CHART



CHAPTER 7

Continuous Protocol Review

7.1 PURPOSE

The purpose of continuous protocol review is to monitor the progress of the study which was previously approved; not only for the changes but to ensure continued protection of the rights and welfare of research subjects.
Continuing review of the study may not be conducted through an expedited review procedure, unless

1) the study was eligible for, and initially reviewed by, an expedited review procedure; Or
2) The study has changed such that the only activities remaining are eligible for expedited review.
3) Continuing review of research previously approved by the convened IRB (e.g., not originally subject to expedited review) may be eligible for expedited review:

(a) Where

- the research is permanently closed to the enrollment of new subjects;
- all subjects have completed all research-related interventions; and
- the research remains active only for long-term follow-up of subjects;

Or

(b) Where no subjects have been enrolled and no additional risks have been identified;
Or
(c) Where the remaining research activities are limited to data analysis.

4) Minor changes in previously approved research during the period covered by the original approval: Where the research is permanently closed to the enrolment of new subjects; all subjects have completed all research-related interventions.

7.2 SCOPE

This SOP 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, IRB may choose to review the study more frequently.

7.3 RESPONSIBILITY

It is the responsibility of the IRB, MCC, to send reminders to PIs regarding the submission of Continuing Review Application/Annual Status Report.
All the approved studies will be reviewed annually. The Chairperson, IRB-IEC, is responsible for determining the date of continuing review if the project will be reviewed more frequently in the year. This decision is taken during the IRB-IEC meeting wherein the project is finally approved.

IRB 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. The IRB has delegated this responsibility of initial detailed review of Continuing Review Application to Data Security and Monitoring Board (DSMB).The IRB has the same options for decision making on a continuing review application as for an initial review application. The decision is made as, approval to continue the study; approval with conditions; or disapproval.

7.4 DETAILED INSTRUCTIONS

7.4.1 Determination the date of Continuous Review:

a) The Office of IRB will look through the master file of projects approved by the IRB for the due date of continuous review
b) The Office of IRB should receive the continuous review application well in advance i.e., 10 months after final IRB approval

7.4.2 Notify the Principal Investigator or the study team

- Reminder emails are sent from the IRB secretariat to the Principal Investigators for submission of continuing review applications for projects, 3 months prior to the expiry of study approval/CRA approval validity date. Principal Investigators are required to submit one signed hard copy of the CRA to the ethics committee.
- First reminder will be sent 3 months in advance to the lapse in validity/annual review
- Failure to submit the CRA within the due date after the 1st reminder will result in issuance of warning letter and necessary action.
- IRB may close/suspend the study if PI fails to submit CRA on time and consider appropriate decision on publication and presentation of study data.

7.4.3 Management of Continuous Review Application (CRA) upon receipt

- The Office of IRB will receive the Continuous Review Application submitted by the Principal Investigator for each approved study.
- Upon receipt of the Continuing Review Application, the Office of IRB of the IRB will perform the following (as per instructions in SOP03/VER2)

7.4.4 Verify the contents of the package

I. Continuing review applications will be checked for completeness before submission to DSMB
II. The Office of IRB will check for duly complete and signed application by Principal Investigator.
III. An original copy with 2 photo copies and a soft copy will be submitted

7.4.5 Review of Continuous Review Application (CRA)

- The DSMB secretary will review the Continuing review Application and will record his/her comments on the application and the same will be forwarded to the IRB Secretary
- In case any clarifications or queries are raised by the Secretary, DSMB, the same will be intimated to PI and reply will be awaited.
- The IRB Secretary will decide whether to table the application along with the comments of the DSMB and Principal Investigator's response in the next full board meeting or expedited review meeting.

7.4.6 Prepare meeting agenda

The Office of IRB will follow procedures on the preparation of meeting agenda and place the forwarded Annual Progress Report/Continuing Review Application on the agenda for the full board/expedited review meeting of the IRB

7.4.7 Review Process

- The IRB-IEC Chairperson/ Member Secretary/ members will use the Continuing Review Application Form (*ANX1-VER2/SOP07/VER2)* to guide the review and deliberation process.
- The IRB members could arrive at any one of the following decisions at the IRB meeting:

1. Approval to continue the study
2. Revision with minor modifications- - Studies for which modifications have been suggested by the IRB may not proceed until the conditions set by the IEC have been met. Studies should be amended and submitted to the IRB within one month for re- review.
3. Query – The IRB and/or DSMB has raised queries against the continuing review application submitted. PI should respond to the IEC/DSMU queries at the earliest to maintain the study approval validity.
4. Deferred/On-hold-The IRB has postponed the decision on approval of continuing the study due to reasons such as awaiting expert opinion, awaiting site monitoring reports from the DSMB etc.
5. Not approved-The IRB feels that there are major concerns related to participant safety &/or data credibility in the conduct of the study.
6. The decision will also include any significant findings that have arisen during review process and this will be communicated to Principal Investigator. It is the responsibility of Principal Investigator to provide this information to the participants and once done submit the report to IRB.

7. The decision regarding the approval/recommended modifications/disapproval will be noted and documented in the minutes of the meeting is recorded by the Member-Secretary of IRB-IEC, MCC.
8. The IRB Office of IRB will maintain minutes of the meeting relevant to the continuous review as part of the official record of the review process.

- Continuing review of the study may not be conducted through an expedited review procedure, unless

1. The study was eligible for, and initially reviewed by, an expedited review procedure; or
2. The study has changed such that the only activities remaining are eligible for expedited review.
3. Continuing review of research previously approved by the convened IRB (e.g., not originally subject to expedited review) may be eligible for expedited review:
   a. Where
      i. the research is permanently closed to the enrollment of new subjects;
      ii. all subjects have completed all research-related interventions; and
      iii. the research remains active only for long-term follow-up of subjects; or
   b. Where no subjects have been enrolled and no additional risks have been identified; or
   c. Where the remaining research activities are limited to data analysis.

7.4.8 Store original documents

The Office of IRB will file the continuous review in master file of the research study.

7.4.9 Communicate the IRB decision to the Principal Investigator

The Secretariat will notify the Principal Investigator of the decision of the IRB. If IRB has recommended modifications, the decision will be notified to the Principal Investigator and he/she will be requested to comply to IRB recommendations/ respond to IRB queries within 1 week of receipt of the IRB decision letter. If the PI requires additional time to respond to queries raised against the CRA, he/she has to inform the IRB about the same and provide an approximate time frame for submission of data or information asked by IRB. In case the IRB decision is to put the study on-hold, then the subject recruitment or enrollment is suspended, however in case of safety concerns the project is completely suspended.

7.4.10 Lapse in IRB Approval

Investigators must plan ahead to meet IRB determined dates of submission of continuing review application. If an investigator fails to submit continuing review application to the IRB or the IRB does not approve continuation of the research, the research must stop. All of the following

research procedures must stop:

- Subject recruitment or enrollment
- Collection of data/information
- All research-related interventions or interactions with currently enrolled subjects*
- Data analyses involving subject identifiable data

*Exception: Research-related interventions or interactions with currently enrolled subjects can continue only if stopping the research would jeopardize the rights or welfare of current subjects or affect data credibility/accuracy. The IRB must make this determination and decide which subjects should continue with the intervention during the lapse. A request for such an exception must be made in the writing to the IRB by the PI.

AX1-V6/SOP 07/V6

Form A

Continuing Review Application

SECTION A

1) MCC Study No:
2) CTRI No (if applicable):
3) Date of Registration:
4) Protocol title:
5) Principal Investigator:
6) Phone No:
7) Email Id:
8) Institute:
9) Source of funding: Please tick
   - ☐ Intramural
   - ☐ Extramural – Please specify and provide relevant documents (CTA/MoU/sanction letters from funding agencies)_____
   - ☐ Pharma – Please specify_____
   - ☐ Others- Please specify_____
   - ☐ Not applicable
10) Account No (If Applicable):
11) Date of IEC approval:
12) Date of Validity of IEC approval (for the full duration of the study):
13) Mention overall duration of study (in years/months) approved by IEC at the time of study approval:
14) Start Date of study:
15) If the start date is > 6 months from the IEC approval date kindly provide the reasons for the same
16) Date of approval of last CRA (if applicable):

17) CRA approval valid till date:
18) Period of report of the current CRA :___/___/_____to___/___/_____
19) Study was initially reviewed by expedited review (Please tick) □Yes □No
20) Is the study expected to extend beyond the projected duration □Yes □No
21) If Yes- provide reasons for not being able to complete the work in stipulated time
22) Are you applying for extension for the same: □Yes □No
23) If yes- period of extension requested?_____
24) How many prior extensions sought? (in number) _____

SECTION B

If the study pertains to retrospective case series / paraffin blocks / MRI or other radiological studies, etc. Please provide information on the status/progress of the study so far with regards to the final accrual/objective. Please mark what is not relevant as not applicable.

1. No of study arms (If Applicable):

2. Project Status (In case of studies on blocks/samples/retrospective case series pleasegive the following information with respect to amount of work completed)

   a. Active enrollment ongoing
   b. Active accrual and intervention ongoing
   c. Accrual completed and intervention ongoing
   d. Accrual completed and follow-up ongoing
   e. Case review/sample review ongoing (audit studies)
   f. Data Analysis ongoing
   g. Publication activities ongoing
   h. Not started/Not initiated

If 'Not started' state reasons

The research is permanently closed to the enrollment of new subjects (Tick)

i. Yes ☐No ☐NA

All subjects have completed all research-related interventions; and the research remains active only for long-term follow-up of subjects; (Please tick)

ii. Yes ☐No ☐NA

The remaining research activities are limited to data analysis (Please tick)

iii. Yes ☐No ☐NA

3. Provide the date of last status review report submitted to IRB for this project

_____(State NA if this is the first status report)

4. Summary of Protocol participants: (If the study does not deal with patient accrual,please provide a summary of the progress on the study so far)
   a) Target accrual of trial (entire study) including healthy volunteers, patients and biomedical samples/blocks) _____
   b) Total patients/samples to be recruited at MCC (IRB ceiling)_____Screened:
   c) Screen failures: _____
   d) Total participants/samples accrued since protocol began (should be equal to sum of it on)
   e) Date of accrual of first subject/sample:
   f) New participants accrued since last review _____
   g) Date of accrual of last participant: _____
   h) Active on intervention:- (exclude subjects who have completed intervention)05
   i) No of participants who have completed intervention and are onfollow-up:02
   j) Patients lost to follow up:- (includes subjects who have completed intervention)
   k) Consent Withdrawn:- Reason and state at which phase of the study– before/during/after completion of intervention (Specify MCC case number/Sub Id)
   l) Withdrawn by PI: Reason and state at which phase of the study –before /during/after completion of intervention (Specify MCC case number/Sub Id)
   m) Deaths: State at which phase of the study – before/during/after completion of intervention (Specify MCC case number/Sub Id)

Sub ID	**Phase –Before/during/ after completion of intervention**	**Whether notified to IEC- Yes/No If No- Provide reasons**

   n) Any other:_____

o) Any Impaired participants

- <None_____
- Physically_____
- Cognitively_____
- Both _____

5. a) Have any SAEs been noted since the last status report?

□Yes □ No □ NA If 'Yes', attach in format below

MCC Case No/Sub Id	SAE Event	Report type	Arm	Date submitted to DSMB

b)In case of multi centre trials state whether reports of offsite SAEs have been submitted to the IEC–

ϒ Yes □ No □ NA

6. Have any Deviations/Violations/Waivers been noted since the last status report?

□Yes □ No □ NA If 'Yes', attach in format below

MCC Case No/Sub Id	Type of Deviation	Study Arm	Date of submission

7. Have any unanticipated problems involving risks to participants or others(including but not limited to adverse events) been noted?

ϒ Yes □ No □ NA If Yes please provide a summary-

8. Were there any Complaints about their search?

ϒ Yes □ No

If yes please provide a summary-

If this is your first CRA kindly mention about the changes which has been done in the period after final approval till the submission of this CRA.

9. Have there been any Protocol amendments since last status report

ϒ Yes □ No □ NA

If 'YES', please provide in format below

Amendment No. Version Dated	Date of submission	Date of IRB Approval

1. Were any changes initiated in approved research without IRB approval to eliminate apparent immediate hazards to the participants:

□ Yes □ No □ NA If yes please provide in format below

Date Reported to the IEC.	Description of change	Date of IRB Approval

2. Have any Informed Consent documents been amended since the last status report? ☐ Yes ☐ No ☐ NA

If 'YES', fill in format below

Amendment No. Version Dated	Date of submission	Date of IRB Approval

3. If the amendments were approved by IRB then please state whether all the patients were re consented on the amended ICF on the next scheduled visit

☐ Yes ☐ No ☐ NA

Amendment No. Version Dated	Date of submission	Date of Approval

4. Is the recruitment on schedule?

ϒ Yes □ No □NA

(If 'NO', please attach a sheet giving reasons and your plans to improve accrual)

5. Have there been any changes in the participant population, recruitment or selection criteria since the last status report was submitted to IRB?

ϒ Yes □ No □NA

If 'YES', kindly attach a sheet explaining the changes)

10. Have any participating investigators been added or deleted since the last statusreport was submitted to IRB?

ϒ Yes □ No □NA (If 'YES', kindly attach a sheet with details regarding the changes)

11. Have any new collaborating sites (institutions) been added or deleted since the last statusreport was submitted to IRB?

 Yes ☐No ☐NA

(If 'YES', kindly give details in the attached sheet)

If 'YES', kindly confirm if MOU/CTA has been submitted to the IEC: ☐ Yes ☐ No ☐ NA

12. Does the protocol have an inbuilt monitoring plan?

 Yes ☐No ☐NA

(Kindly mark the above as 'No' in case of an Investigator initiated study wherein there is no external DSMB to monitor the data generated. The study will be then monitored by DSMB, MCC)

13. Has the study been monitored?

 Yes ☐No ☐NA

(If 'YES', submit the monitoring report only in case of pharma -sponsored)

Date of monitoring _____

Monitored by _____

Number of subjects monitored _____

14. Is the Data Safety and Monitoring Board report available?

 Yes ☐No ☐NA

(If 'YES', submit as an attachment)

15. Did the monitoring team have any adverse comments regarding the study?

 Yes ☐No ☐NA

(If, 'YES', please attach a copy of their comments)

16. Is the report on interim data analysis available?

 Yes ☐No ☐NA

(If 'YES', kindly submit as an attachment)

17. Has any information appeared in the literature, OR evolved from this OR similar research that might affect the IEC evaluation of the risk/benefit analysis of human subjects involved in this protocol?

 Yes ☐No ☐NA

(If 'YES' kindly attach a sheet providing the details)

18. Has there been any presentation/publication related to the data generated in this trial?

    ☐ Yes ☐No ☐NA

    (If, 'YES', kindly attach a sheet enclosing the details)

    If 'YES' then has this been intimated to the CRB office?

    ☐ Yes ☐No ☐NA

    Please provide summary of current risk-potential benefit assessment based on study results if any?

19. Details regarding the budget- : (kindly attach consolidated account summary dulysigned by Accounts Officer)

    Total budget proposed for the project_____Total budget

    sanctioned for the project _____

    Total budget utilized for the project (entire budget utilized)

    _____

20. Total Budget utilized for patient reimbursement (entirebudget) (kindly attach details of reimbursement to participants e.g. investigations/scans/travel as per IEC approved budget)

21. Have any investigators developed an equity or consultative relationship with a source related to this protocol which might be considered as conflict of interest?

    ☐ Yes ☐No ☐NA

    (If YES, kindly append a statement of disclosure for the same)

22. Any other information: _____

SIGNATURES:

Principal Investigator:

Date:

ANX1/VER2/SOP/VER

Form B

Continuing Review Application Form/Annual Status Report Form (Basic Human study)

MCC Project No:

PROTOCOL TITLE:

Principal Investigator:

Co- Investigator (s) :

Phone no:

Email Id:

Institute: MCC

Date of MCC IRB **approval:_____Approval valid up to: _____**

Mention overall duration of study (in years/months) approved by IRB **at the time of study approval:**

Start Date of study:
If the start date is > 6 months from the IEC approval date kindly provide the reasons for the same

Duration of study:

Period of Report of the current CRA:_____/_____/_____to _____/_____/_____

Funding Source:Account no :

1) Project Status

□ Ongoing

- Active accrual on going
- Accrual completed/Follow-up
- Analysis ongoing

□ Not started/Not initiated

If 'Not started' state reasons

2) Provide the date of last status review report submitted to MCC- IRB for this project : _ _ /_ _/_____ □NA

3) Have there been any Protocol amendments since the last status report?

 Yes ☐No

If '**YES**', Were these Protocol Amendments approved by **MCC- IRB**?

- YES If '**YES**', please provide date of approval _____
- NO

Note: Kindly attach a sheet with the list of amendments to be approved/approved by the **MCC- IRB** in a tabular column with details of amendment no. with date, date of submission to **MCC- IRB** and date of approval by **MCC- IRB**.

4) Have there been any Informed Consent document amendments since the last status report?

 Yes ☐No ☐NA

If '**Yes**', were these informed consent document amendments approved by

MCC- IRB?

- YES If '**YES**', Please provide date of approval _____
- NO

Note: Kindly attach a sheet with the list of amendments to be approved/approved by the **MCC- IRB** in the tabular column with details of Amendment no. with date, Date of submission to **MCC- IRB** and Date of approval by **MCC- IRB**.

5) Summary of Protocol participants:

- Total patients/samples to be recruited at MCC (IRB ceiling)_____
- Total number of samples screened since protocol began:_____
- Total Screen failures since protocol began: _____
- Total participants accrued/samples collected since protocol began_____
- New participants accrued /samples collected since protocol began: _____
- Date of accrual of last participant /Samples:
- Number of active participants/Sample (analysis going on)
- Number of samples analyzed: ____
- Any other:_____

6) Is the recruitment on schedule?

☐ Yes ☐No ☐NA

(If '**NO**', please attach a sheet giving reasons and your plans to improve accrual)

7) Have there been any changes in the participant population, recruitment orselection criteria since the last status report was submitted to MCC-IRB?

☐ Yes **(Kindly attach a sheet explaining the changes)**

☐ No

☐ NA

8) Were any samples not suitable for analysis during the last one year (only thereport period.)**?**

☐ Yes (Kindly attach a sheet stating reasons)

☐ No

☐ NA

9) Have any participating investigators been added or deleted since the last statusreport was submitted to MCC-IRB?

☐ Yes (Kindly attach a sheet with details)

☐ No ☐ NA
10) Have any new collaborating sites (institutions) been added or deleted since the last status report was submitted to MCC- IRB? ☐ Yes (Kindly attach a sheet with details) ☐ No ☐ NA
11) Were there any protocol deviations/violations in the study? ☐ Yes (Kindly attach a sheet with details) ☐ No ☐ NA
12) Is interim data analysis report available? _____ ☐ Yes (If '**YES**', kindly submit as an attachment) _____ ☐ No ☐ NA
13) Has there been any presentation/publication related to the data generated in this study? ☐ Yes (Kindly attach a sheet enclosing the details) ☐ No If '**YES**' then has this been intimated to the TRAC office? ☐ Yes ☐No ☐NA
14) Has any information appeared in the literature, OR evolved from this OR similar research that might affect the MCC- IRB evaluation of the risk/benefit analysis of human subjects involved in this protocol? ☐ Yes (If '**YES**' kindly attach a sheet providing the details) ☐ No ☐ NA

15) Was the study Monitored by Data Monitoring Committee (DMC)?

- Yes (If '**YES**' kindly attach a sheet providing the details)
- No
- NA

If Yes, When was study last monitored?

Date of monitoring _____

Monitored by_____

Number of subjects monitored _____

16) Is the DMC report available?

- ☐ Yes (If '**YES**', submit as an attachment)
- ☐ No
- ☐ NA

17) Did the Data monitoring team have any adverse comments regarding the study?

- ☐ Yes (If, '**YES**', please attach a copy of their comments)
- ☐ No
- ☐ NA

18) <u>Scientific and Technical Progress</u>

a) Progress made against the Approved Objectives, Targets & Timelines during the Reporting Period.(Attach a separate sheet of detailed work progress report till date, including tables/figures and experimental data generated last one year and future objectives)

b) Summary and Conclusions of the Progress made so far (minimum 100 words, maximum 200words)

c) Details of New Leads Obtained, if any:

Is the project likely to finish in the stipulated time? If no please mention reason for not being able to complete the work in stipulated time, what percent of work is pending and the period of extension (months/year(s)) is required to complete the project. How many prior extensions sought? (in numbers)

20) Have any investigators developed an equity or consultative relationship with a source related to this protocol which might be considered as conflict of interest?

- ☐ Yes (If YES, kindly append a statement of disclosure for the same)
- ☐ No
- ☐ NA

21). Details regarding the budget: (kindly attach account statement sheet duly signed by Accounts Officer)

Total budget proposed for the project: Rs. _____

Total budget sanctioned for the project: Rs. _____

Total amount utilized for the Project: Rs _____

If extramural funding was sought, name the funding source and amount.

Funding Source:_____Amount : Rs. _____

SIGNATURE
Principal Investigator

Date :

ANX2-VER2/SOP 07/VER2

Reminder letter to investigator

Name of Principal Investigator:-
Address of Principal Investigator:-
Ref: - Project Title: XXXXXX

The above referenced project was approved by the IEC on (date) and CRA validity is up to (date) and is due for continuing annual review by the IEC.

Kindly submit the continuing review application on or before_____. In case the project have been completed / terminated, kindly complete the appropriate form and submit to IEC/DSMU on or before(date).

Thanking you for your co-operation,

Yours truly,

Signature with date
Secretary, DSMU

ANX3-VER2/SOP 07/VER2

Format for Continuing review Approval Letter

Date

To
Dr._____
Principal Investigator,
Malabar Cancer Centre

Sir,

Subject: Continuing Review Approval-reg.
Ref.: Project No./ Title

The Continuing Review Application for the above referenced project was tabled and discussed during the IRB Institutional Ethics Committee (IRB-IEC) meeting held on date (place)(time)

The following members of the IRB-IEC were present:

IRB-IEC comments were as follows:

Status: IRB approved the continuation of the study /approved with modifications/Not approved

This decision was taken by consensus. Neither Principal Investigator nor any of study team members participated during the decision making of the IRB-IEC of Malabar Cancer Centre.

Thanking you,

Yours faithfully,

Member-Secretary,
Institutional Ethics Committee (IEC)
Institutional Review Board (IRB)
Malabar Cancer Centre, Thalassery

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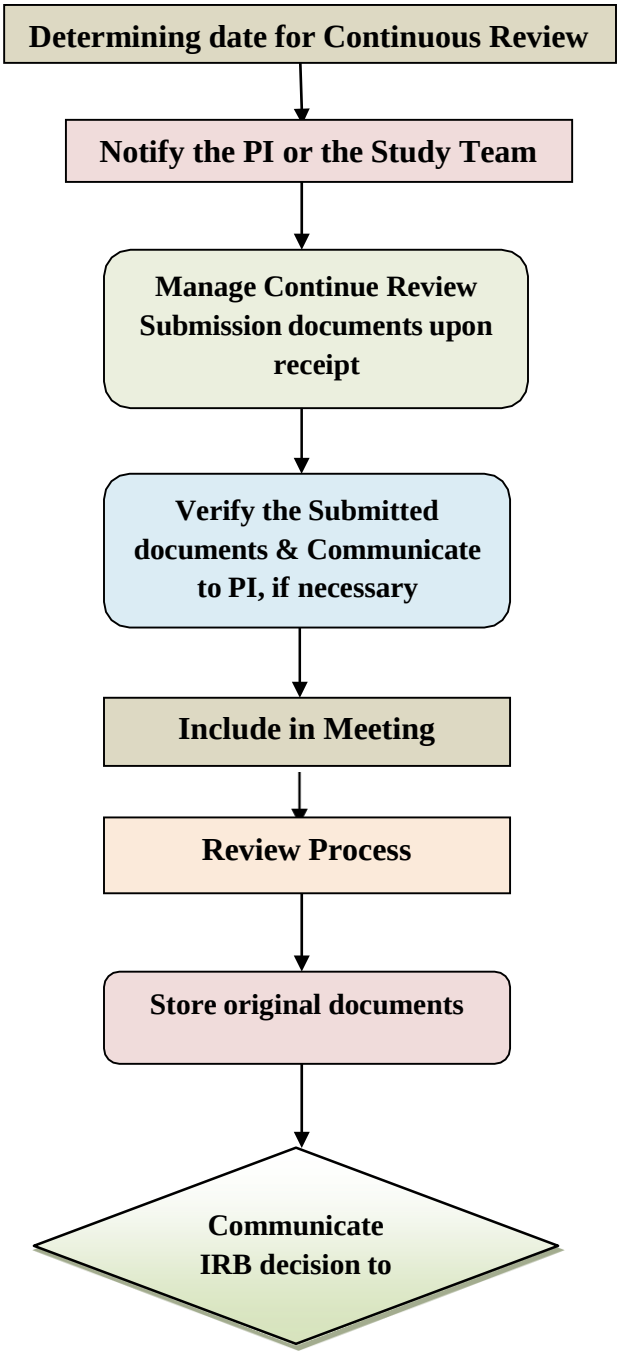
Determining date for Continuous Review
Notify the PI or the Study Team
Manage Continue Review Submission documents upon receipt
Verify the Submitted documents & Communicate to PI, if necessary
Include in Meeting
Review Process
Store original documents
Communicate IRB decision to

CHAPTER 8

Review of Protocol Deviation/Violation/ Waiver/ Non-Compliance

8.1 PURPOSE

To provide instructions for taking action and maintaining records, when investigators/ trial sites, fail to –

- follow the procedures written in the approved protocol
- comply with national / international guidelines for the conduct of human research, including those who fail to respond to the IRB, MCC requests

8.2 SCOPE

This SOP applies to all IRB, MCC approved research protocols involving human subjects.

8.3 RESPONSIBILITY

1. Office of IRB is responsible for receiving deviations /violations/waiver reports as per (*ANX1–VER2/SOP08/VER2*) submitted by the PI and placing it on agenda of the meeting. Reporting of deviation/ non-compliance/violation/waiver in any other reporting format will not be accepted.
2. IRB members should review and take action on such reports.

8.4 DETAILED INSTRUCTIONS

a) Protocol violation/s

Definition: Divergence or departure from the expected conduct of an approved study not consistent with the current Institutional Ethics Committee approved version of the research protocol, consent document or addenda

This usually

- Constitutes a change in the conduct of the research that should have received prospective IEC review and approval prior to implementing the change; or
- Has harmed or posed a significant risk of harm to a research participant or others; or
- Has damaged the scientific integrity of the data collected or confounded the scientific analysis of the study results; or
- Has resulted from willful or voluntary misconduct on the part of a Principal Investigator or a member of the research team.

Examples:

- Improper consent.
- Participant was enrolled but did not meet the protocol's eligibility criteria.
- Participant received the wrong treatment or incorrect dose.
- Participant being consented after the screening procedures are completed
- Participant being consented after the first dose of the drug has been given
- Wrong version of the informed consent form being used.
- Consenting lapse e.g. LAR signing as impartial witness.
- Delays or non-reporting of SAEs.
- Missed investigations which comprise participant safety.

b) Protocol deviation/s

Definition: Divergence or departure from the expected conduct of an approved study not consistent with the current Institutional Ethics Committee approved version of the research protocol, consent document or addenda is a protocol deviation if it:

- Has no substantive effect on the risk posed to a research participant or others;
- Will not affect the participants' willingness to participate in the study;
- Has no substantive effect on the value of the data collected;
- Does not confound the scientific analysis of the study results and
- Did not result from willful or voluntary misconduct on the part of an Investigator or a member of the Investigator's study team.

Examples:

- Sample collections at different time points than specified in the protocol.
- Participant following up on days not specified in the protocol.
- Out of visit window periods
- Deviations in visit timelines, missed labs due to COVID pandemic

c) Protocol Waiver

It is a prospective deliberate decision to deviate from the protocol that has been approved by the sponsor. Such waivers must be notified to and approved by IEC Member Secretary/Chairperson.

e.g. Protocol Waiver means a prospective decision by a sponsor or investigator to permit accrual of a participant who does not satisfy the approved inclusion/exclusion criteria for enrollment (age, concurrent medication).

When a deviation occurs it should be reported to the sponsor as well as the IEC. In some instances, a sponsor will issue a waiver related to a specific participant, to continue the participant in the study

Examples of waivers are:

- It is in the participant's best medical interest to remain on study
- Exception to inclusion/exclusion criteria (age, concurrent medication)
- Visits out of sequence or out of protocol" window"
- Injection of study drug in left arm rather than right arm

d) Non-compliance

Noncompliance is defined as failure to comply with national regulations, IEC policy or the determinations or requirements of the IEC.

i. Non-serious and Non-continuing noncompliance involves isolated incidents,

e.g. an unintentional mistake, an oversight or a misunderstanding. The issue is not serious or continuing in nature.

ii. Serious Non-compliance: An action or omission, non-compliant with national regulations or IEC policy, taken by an investigator that any other reasonable investigator would have foreseen as increasing risks or compromising the rights and welfare of a participant or other person.

iii. Continuing non-compliance: A pattern of repeated actions or omissions taken by an investigator that indicates a deficiency in the ability or willingness of an investigator to comply with protocol, SOPs, national regulations and guidelines, IEC policy or determinations or requirements of the IEC.

iv. Research Misconduct noncompliance that involves disregard for the protection of human participants or for the integrity of research may meet the definition of research misconduct. Any fabrication, falsification, or plagiarism in proposing, performing, or reviewing research or reporting research results.

8.4.1 Detection of Protocol deviation/ non-compliance/ violation/waiver

8.4.1.(a) The IRB members performing monitoring of the project at trial site can detect protocol deviation/non-compliance / violation, if the project is –

- not conducted as per protocol / national / international regulations
- when scrutinizing annual / periodic reports / SAE reports
- any other communication received from the Investigator / trial site / sponsor /study monitor / CRO

8.4.1.(b) The Office of IRB can detect protocol deviation / non-compliance / violation from failure to

- comply with statutory requirements
- respond to requests from IRB within reasonable time limit
- respond to communication made by IRB office, MCC

8.4.1.(c) The PI himself / herself may forward protocol deviation / non- compliance/violation / waiver reports to inform the IRB.
Protocol Waiver is analogous to a Protocol Deviation, except that prior IRB approval must be obtained before implementing the necessary departures from the protocol. Therefore, Protocol Waivers are anticipatory, while Protocol Deviations are not. e.g., Protocol Waiver means a prospective decision by a sponsor or investigator to permit accrual of a subject who does not satisfy the approved inclusion /exclusion criteria for enrollment.

8.4.1.(d) Communication /complaint/information received from research participant who has been enrolled or any individual who has been approached for enrollment

8.4.1.(e) Any report / communication brought to the notice of Member-Secretary / Chairperson of IRB-IEC. Communication received from the Director, MCC informing IRB-IEC about an alleged protocol violation / non-compliance / protocol deviation.

8.4.2 Noting protocol deviation / non-compliance / violation / waiver by the office of IRB

- The IRB members who have performed monitoring of a particular trial site and detect protocol deviation / non-compliance / violation will inform the Secretariat in writing within 24 hours [one working day].
- Whenever protocol deviation / non-compliance / violation has been observed, the Secretariat will ensure that the issues as well as the details of non-compliance involving research investigators are included in the agenda of the IRB-IEC meeting.

The deviations / violations will be scrutinized for gravity and implications in the formal IRB-IEC meeting. The IRB decision will be communicated to PI.

8.4.3 Board discussion, Decision and Action

- If the protocol deviation / non-compliance / violation is detected by IRB member during monitoring visit, he/she will present the protocol deviation / noncompliance /violation information.
- If detected by Office of IRB / forwarded by PI, the in charge of IRB office will present the protocol deviation / non-compliance / violation / waiver information.
- The Chairperson / IRB-IEC members will review the information available and take a decision depending on the seriousness of the violation.
- The decision will be taken to ensure that the safety and rights of the research participants

are safeguarded. The decision will be taken by consensus and if no consensus is arrived at, voting may be conducted.

The actions taken by IRB could include one or more of the following:

i. Inform the PI that IRB-IEC has noted the violation/noncompliance/ deviation and inform the PI to ensure that deviations/noncompliance /violations do not occur in future and follow IRB-IEC recommendations.
ii. Enlist measures that the PI would undertake to ensure that deviations/ noncompliance /violations do not occur in future.
iii. Reprimand the PI
iv. Call for additional information
v. Suspend the study till additional information is made available and is scrutinized
vi. Suspend the study till recommendations made by the IRB-IEC, MCC are implemented by the PI and found to be satisfactory by the IEC
vii. Suspend the study for a fixed duration of time
viii. Inform the Director, MCC
ix. Revoke approval of the current study
x. Inform DCGI / Other relevant regulatory authorities
xi. Keep other research proposals from the PI/ Co-PI under abeyance
xii. Review and / or inspect other studies undertaken by PI/Co-PI

8.4.4 Notify the investigator

- The Office of IRB records the IRB-IEC decision drafts and types a notification letter.
- The Chairperson / Member-Secretary of IRB-IEC signs and dates the letter.
- The Office of IRB makes four copies of the notification letter.
- The Office of IRB sends the original copy of the notification to the investigator.
- The Office of IRB sends a copy of the notification to the relevant national authorities and other trial sites, in case of multi-centric trial.
- The Office of IRB sends the fourth copy to the sponsor or the CRO of the study.

8.4.5 Records and follow up to be kept by IRB Secretariat

- Keeps the last copy of the notification letter in the "non-compliance' file.
- Stores the file on the shelf with an appropriate label.
- Follows up the action after a reasonable time.

ANX1-VER2/SOP08/VER2

WAIVER(W)/VIOLATION(V)/DEVIATION(D): Reporting Form
Institutional Review Board (IRB)
Malabar Cancer Centre (MCC), Thalassery- 670 103, India

Specify if W/V/D :

Nature:

☐ or Major Other(T ☐ whichever applicabl ☐

If other, please specify:……..

Date of Occurrence (DD/MM/YYYY) [***Not applicable in case of waiver***]

No. of similar W/V/D occurred during the same trial:

Patient ID no.

MCC Project No.:

Project Title:

Details of W/V/D:

Action taken by PI/Co-PI/Co-I : (***Not applicable in case of Waiver***)

Impact on trial subjects: (***Not applicable in case of Waiver***)

Signature of the PI with date:

Name of the PI:

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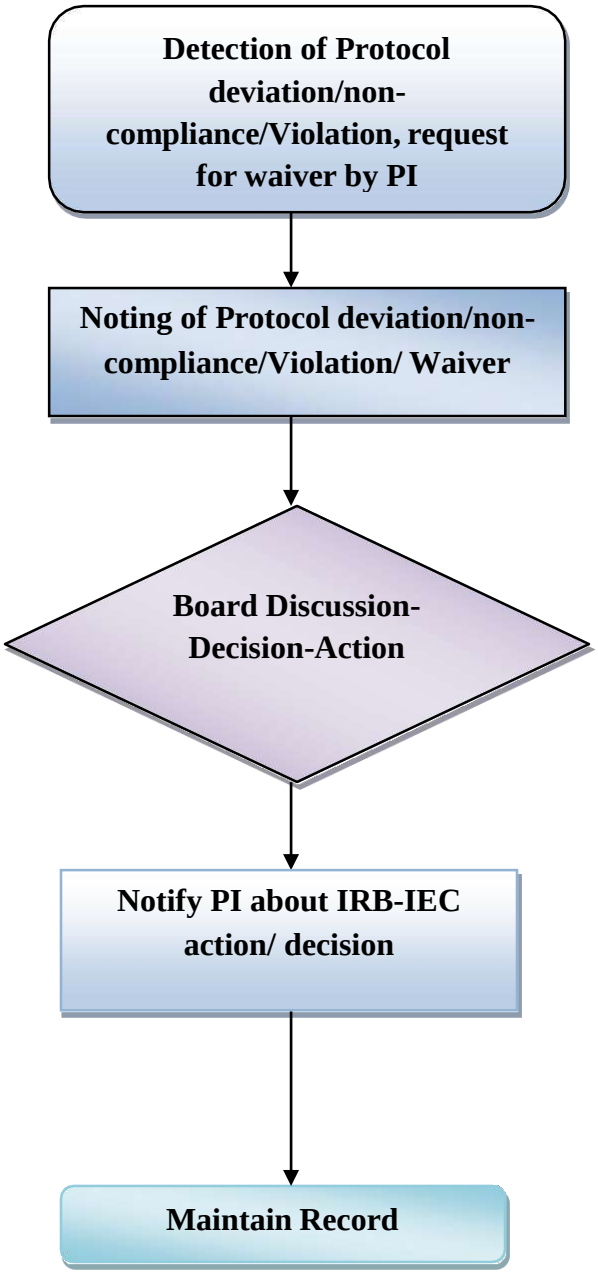
Detection of Protocol deviation/non-compliance/Violation, request for waiver by PI
Noting of Protocol deviation/non-compliance/Violation/ Waiver
Board Discussion-Decision-Action
Notify PI about IRB-IEC action/ decision
Maintain Record

CHAPTER 9

Review of Reports on Serious Adverse Events (SAEs)

9.1 PURPOSE

The purpose of this SOP is to provide instructions on the submission of Serious Adverse Events **(**SAEs) and unexpected events and review of SAEs and unexpected events for any active Research Study approved by the IRB, MCC.
In course of studies, there are sometimes unanticipated risks. Information that may throw impact on the risk/benefit ratio should be promptly reported to and reviewed by the IRB to ensure adequate & extra protection of the welfare of the study participants. The unanticipated risks may as well include any event that in the investigator's / researcher's opinion, may adversely affect the rights, welfare and/or safety of subjects included in the study.

9.2 SCOPE

This SOP applies to the Data Safety Monitoring Board (DSMB, if applicable) and IEC review of SAEs and unexpected events reports, both onsite and offsite, including follow up reports submitted by investigators.
Investigators, IEC/DSMB members must follow the procedure as per current regulations. This prescribes procedures for reporting of SAEs and the provision of compensation in case of injury or death during clinical trial. The IEC may also consider appointing a sub-committee to review all the safety data that gets submitted, including SAE reports, CIOMS, SUSARs etc.

9.3 RESPONSIBILITY

The primary responsibility of the Data Safety and Monitoring Board (DSMB)/IRB is to review and address SAEs and unexpected events involving risks to research participants. Moreover, the board is well authorized, in addition, to offer mediation under appropriate circumstances.

IRB should also make sure that researchers are made aware of the policies and procedures concerning reporting and continuing review requirements.

The Office of IRB is responsible for receiving the complete SAEs / unexpected events reports and directing them to DSMB for detailed review. Following the DSMB meeting, the Secretary, DSMB will then forward the minutes of the DSMB meeting to the IRB. DSMB minutes are discussed in the subsequent IRB meeting.

Notifying the IRB/DSMB does not relieve the PI from his/her responsibility to notify the sponsor and regulatory authorities, if any.

9.4. DETAILED INSTRUCTIONS

(A) On site SAEs

9.4.1 Instructions for PI

- The initial reports of all serious adverse event of Death/ other than death should be reported by the PI along with the justification for the causality assessment within 24 hours of the occurrence to-
    - IEC
    - Sponsor or its representative
    - CDSCO (in case of studies that require approval of the CDSCO)ifthe investigator fails to report any serious adverse event within the stipulated period, he shall have to furnish the reasons for delay to the satisfaction to IEC and CDSCO along with the report of the serious adverseevent.
- The follow up report of the serious adverse event of Death/ other than death along with the due analysis including the Principal Investigator's causality assessment shall be forwarded by the Investigator within fourteen calendar days of the occurrence of the serious adverse event of death to-
    - IEC
    - Sponsor or its representative
    - CDSCO (In case of studies that require approval of the CDSCO)
    - Head of the institution (In case of studies that require approval of the CDSCO)
- In case the event is Death due to disease progression, the event should be notified in the SAE reporting format unless it is specified in the IEC approved protocol that such events will not be reported. E.g. – death due to disease progression.
- If the patient is out of trial and on survival, follow up the event should be notified unless it is specified in the IEC approved protocol that such events will not be reported
- SAE reports are received at IRB as one original + 2 photo copies+ soft copy.
- Serious Adverse Event should be graded as per "***Common Terminology Criteria for Adverse Events***" (***CTCAE Version 3.0/CTCAE Version 4.02*****).**

- Follow-up reports on the SAEs should be submitted within 15 days of the initial report or when any additional information regarding the event is available, whichever is earlier.

9.4.2 SAE related activities before conducting IEC meeting

- One signed hard copy and a soft copy of the SAE report must be submitted to the IEC/DSMB Office.
- The IEC Secretariat will verify if the reports are complete, signed and dated by the PI/Co-PI/Co-I and will check for dates and typo errors in the SAE report such as SAE description, SAE term and CTCAE grading
- In case the IRB Secretariat notes that the report is incomplete or incorrect, the report will be returned to the PI with the consent of IEC Secretary/DSMB
- The IRB secretariat should receive the reports of all SAEs including deaths for IEC approved studies within 24 hours of the occurrence of the SAE.
- In case of public holidays or weekends or any other justified reasons, SAEs may be reported as email notifications or soft copy attachment of SAE form in order to meet SAE reporting timelines. Email notifications should include patient trial id, patient case number, SAE event and a brief description of the SAE. However dulysigned hard copies of the SAEs along with the email notification (hard copy) shouldbe submitted to IEC/DSMB office on the next working day.
- SAE reported for death will be stamped "Death" on the right corner of the 1st page of SAE form for easy / immediate identification.

9.4.3 Actions to be taken by Member Secretary, IEC

- The Member Secretary/DSMB will review the SAE report and will write the comments if any
- 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 discussion, necessary action may be taken by the DSMB Secretary/IEC Member Secretary
- SAE's received will be discussed in subsequent IEC/DSMB Meeting
- Regulatory SAEs may be taken on table for IEC/DSMB review
- Two lead discussants are assigned by Secretary IEC/DSMB for SAE review. It is ensured that the lead discussant is not a part of the study team and has no conflict of interest.
- Agenda is sent to Secretary IEC/ DSMB for finalization and signature
- The original signed hard copy of agenda is filed. The soft copies of meeting agenda and SAE reports are sent to IEC/DSMU members via email for review.

9.4.4 After the DSMB review of SAE

- After the meeting, the Minutes are finalized by the Secretary IEC/DSMB.
- The IEC secretariat will send a formal letter signed by the Secretary to the investigator/s with instructions for specific actions as per the decision.
- In case a PI fails to respond to the letter, the matter will be discussed at the next full board IEC meeting and a decision will be taken for specification
- The IEC secretariat will send the letter to the PI and file a copy of the letter in the master file of the research protocol.
- The original signed hard copy of Minutes of meeting is filed in the Agenda and Minutes file'
- Minutes are ratified in the next meeting.
- PI should respond to queries within 07 working days from the receipt of the query letter. The PI response to queries are reviewed by Secretary. These replies if required will get discussed in the next scheduled meeting in case further opinion is required.
- The Member Secretary will table the SAEs and the minutes in the next earliest full board meeting of respective IEC.
- Responsibilities of the IEC in case of studies that are approved by licensing authority(DCGI):

  In case of SAE (any) report, IEC after due analysis will send its opinion on compensation to the licensing authority within 30 calendar days of the occurrence of the serious adverse event as per the prevailing regulatory guidelines/procedures.

9.4.5 During the IRB meeting

On site SAEs

The Secretary will discuss the SAEs and actions taken in the IEC meeting. . If appropriate, specific action or combination of actions will be taken, based on the consensus decisionof the IEC. Some of which are listed below:

- Note the SAE report in the IEC records if information submitted is found to be adequate
- 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
- Direct the PI to re-evaluate the event as to whether it is AE/SAE and report to IEC.
- 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.
- Request further follow up information
- Request additional details
- Recommend an amendment to the protocol, the ICD, Participant information sheet, investigator brochure and/ or any other document.

- Recommend whether or not compensation should be paid to the patient /hisnominee for trial related injury / death as per institutional policy.
- 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
- Suspend the study for a fixed duration of time;
- Suspend the study till additional information is obtained;
- Suspend the study till review is completed;
- Terminate the study;
- Any other action

9.4.6 Actions to be taken by Chairperson, IEC

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

- Calling for an Emergency Review by full board

  - This review should be initiated within 48 working hours (2 working days) of receipt of information.
  - This review could be done through a meeting, teleconference, email or telephonic conversation.
  - The IRB Secretariat will take appropriate steps to ensure that IRB members are informed about this full board meeting.
  - Depending upon the complexity of the issue(s) involved, the chairperson could direct the Member Secretary, IEC, to invite one or more experts whose opinion would be valuable. These experts could participate after they agree to the confidentiality clause and abide by the rules and regulations of IRB.

- Suspend trial-related procedures as listed by the secretariat suspending all trial related procedures (except those intended for safety and well-being of the participant) till further review by the IRB
- Suspending enrolment of new research participants till further review by the IRB

(B)Off Site SAEs

Off Site SAEs where adverse event reports that are serious, unexpected and related (definitely, probably and possibly) to the drug need prompt reporting to the IRB, MCC.
The SAEs that are expected (if listed in the informed consent) or unexpected but unrelated to the drug (classified as per the Offsite SAE Classification form – *ANX2-VER2/SOP09/VER2*) have to be logged by the PI and to be submitted timely The following log has to be maintained continuously until the end of the study.
Those off site SAEs which qualify for prompt reporting, (classified as per the Offsite SAE Classification form – *ANX2-VER2/SOP09/VER2*) will be reported to IRB Secretariat, and forwarded to the Member-Secretary, IEC and Secretary, DSMB.

If the IRB and DSMB need to review the offsite SAE reports, the committee will request copies of SAE reports at any time, as and when necessary.

If a trend is observed in SAEs by PI, such a trend will be reported to IRB Secretariat, action on such reports will be taken by the Member Secretary, IEC and Secretary, DSMB, as per 7.3-7.4

The Office of IRB will not accept the complete set of "Offsite SAE reports" and/ or the log. However, the IRB will accept the log of the SAEs every 3 months and/or at the time of continuing review/ annual status report.

9.5 Off site SAEs

The Line listings submitted by PI on a monthly/quarterly/annual basis are filed by DSMB as a detailed review of the same is out of the scope of IEC/DSMB.
It is the PI's responsibility to review the listings in detail and report if a trend is observed and communicate the same to DSMB.
The offsite SAEs are received in the format as per SOP and one copy is acknowledged and returned back to PI

- The soft copy is saved
- The same is entered in the Offsite SAE entry book by Office of IRB.
- The SAEs are checked and stamped 'For DSMB/Noted & File' and then forwarded to Member Secretary of IEC for signature/review
- If any queries are raised by the IEC Member- Secretary, they are sent to PI by email or letters as applicable; else the Offsite SAEs are filed in the respective project files.
- Depending on the trend observed by the PI, if appropriate, specific action or combination of actions will be taken. Some of which are listed below:

    - Note the SAE report in the IRB records if information submitted is found to be adequate
    - 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 prescribed in the amendment.

- Direct the PI to inform participants already enrolled in the study about the SAE and obtain their consent regarding continuation in the research trial, if necessary.
- Request further follow up information
- Request additional details
- Recommend an amendment to the protocol, the ICD, Participant information sheet, investigator brochure and/ or any other document.
- 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 IRB are accepted
- Suspend the study for a fixed duration of time;
- Suspend the study till additional information is obtained;
- Suspend the study till review is completed;
- Terminate the study;
- Any other action.

All Off site SAE reports, CIOMS forms, SUSAR reports etc. have to be recorded in the minutes of meeting with the IEC members opinion and action taken (if any) after discussion in the IEC meeting. If no action is required, a statement of no action required should be mentioned clearly in the Minutes of Meeting.

9.6 DCGI Query on Serious Adverse Events

1) DCGI queries on SAEs which were already discussed in DSMB and ratified in previous IEC meetings will be answered based on the opinion and findings of the IEC/DSMB at that time. IEC discussion or opinion at that time will be conveyed to DCGI and Principal Investigator.
2) In potentially contentious issues, Member Secretary, IEC will inform Chairperson. Chairperson may use his/her discretion to bring it to the full board IEC meeting. The reply to DCGI is sent with a copy of same to Principal Investigator.

3) It is the responsibility of the IEC to confirm that the loop of all SAEs reported is completed and the compensation is paid by sponsor and received by participant/nominee wherever applicable

ANX1-VER2/SOP09/VER2

SERIOUS ADVERSE EVENT REPORT

Malabar Cancer Centre, Thalassery
PIN-670 103 ,India

MCC Project No.:_____

As per ICH-GCP:

Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (Serious ADR) is 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,
• results in persistent or significant disability/incapacity,
or
• is a congenital anomaly/birth defect
Investigator(s) shall report all SAE to the Sponsor within 24 hours and to the Ethics Committee within 7 working days of their occurrence. In case of Death the *DSMB* should be notified within 24 hrs of the knowledge of the PI. If a delay is expected kindly notify the same by email.

1.Title of the Project:

2. Name of the PI :

3. Report Date:

Report type □ Initial
□ Follow up_____
If Follow-up report, state Date of Initial report _____

□ Final

4.MCC Case No:	**5a. Age**	**5b. Sex**

6. Mention the total number of SAE (prior) occurred at this site:_____& Other Site(s)_____

7. Mention number of similar SAEs (prior) occurred for same study at this site: _____

Other site(s):_____

8. Does the Principal Investigator feel this SAE is related to participation in the trial

□Yes □ No □ Possibly □ Can't say

9.Tick whichever is applicable for serious adverse event: (Kindly note that this refers to IP/intervention being evaluated and NOT disease process)

A] □ Expected Event □ Unexpected Event

B] □ Hospitalization □ Increased Hospital Stay □ Death □ Others

In case of Death , state probable cause of death :

_____

_____

(If Others, please specify):_____

……..

C] □ No permanent significant functional/ cosmetic impairment
□ Permanent significant functional/ cosmetic impairment
□ Not applicable

10.Cost of treatment/hospitalization for SAE was borne by,

□Patient □ Institute □Sponsor/CRO □ NA

Relevant Drug Information - IP Information

11. Relevant drug/IP(include generic name)/device/intervention:

12. Dose: Dosage Form:	**13**. Route(s) of Administration:
14. a) Therapy Dates(from/to):	**14.b)**Therapy Duration (in days):

15. Did the reaction decline after stopping the drug/procedure (DE challenge &Re-challenge information)

□ YES□ NO □ NA

16.Concomitant drug(s) and date of administration:

Sr. No.	Name of Drug	Dose	Frequency	Route of Administration	Start Date	End Dat	

17. Patient relevant Case history(e.g. diagnosis, allergies, Date of ICF and randomization):

Reaction Information

18. Description of adverse event (indicate if this is follow-up report and if so, include follow-up information only)

19.a) Describe the medical treatment provided (if any) to the research subject: This is an update on treatment given during hospitalization.

b) Lab Investigations/Blood investigations done:

TEST	DATE	RESULT

20.Outcome was

□ resolved □ ongoing □ death

21.Was the research subject continued on the research protocol

□ yes □ no □ NA *Mark 'NA' in case of death

22. In your opinion, does this report require any alteration in trial protocol?

□ yes □ no

If yes then please specify :
……..

Name of Principal investigator :……

Profession (Specialty) :……..

Signature of Principal investigator:……..
Date:
*Upon receipt of this report, the IRB/**DSMB** will decide whether additional information is needed or whether further investigation of the incident is required*

For IRB use only

I_____agree_____
disagree with the assessment of the principal investigator.

DSMB Reviewer_____date:_____

Explanation:

ANX2-VER2/SOP09/VER2

OFF SITE SAFETY REPORTS CLASSIFICATION FORM
INSTITUTIONAL REVIEW BOARD
Malabar Cancer Centre, Thalassery
PIN- 670 103, India

Note to the PI
The following questions will act as a guide for submission of the "Safety Reports". This form is merely providing guidance for reporting / logging of Off-site Safety Reports'.
If the answer to all three questions is "**Yes", prompt reporting is required** and such off site safety reports need to be reported to IRB along with the log.
If any one answer is "**No", it needs to be logged**.
This log should be submitted to the IRB Secretariat every 3 months and/or along with Continuing Review report.

Project No.:

Project Title:

Questions	YES	NO
Is adverse event serious?		

Is adverse event related?		
Is adverse event unexpected?		

Date of reporting:

Signature of PI:

Name of the PI:

ANX3-VER2/SOP09/VER2

Off Site Safety Reports Log

NOTE to PI:

1. Please log in details of Off-Site Safety Reports.
2. The following log has to be maintained continuously until the end of the study.
3. This log should be submitted to the Office of IRB every 3 months and/or along with Continuing Review report.
4. The log must be submitted to the IRB Secretariat, MCC, immediately, if prompt reporting is required and/or if a trend related to the occurrence of SAE is observed.
5. Please note the complete set of Off-site Safety Reports need not be sent to IRB Office, MCC, as and when received. If the IRB needs to review the reports, they can request copies at any time.

Project No.:
Project Title:
Total Sample Size:
Total no. of patients to be enrolled:
Total no. of patients already enrolled:
No. of patients active on treatment :
No. of patients lost to follow up :
No. of consent withdrawn :
No. of patients withdrawn by the PI :
No. of patients Completed treatment :

Sr. No	Country	Date of Onset	Adverse Event	Outcome	Observation/ Remarks

Assessment of PI:

Do you observe a trend? ☐Yes ☐No

……

Name and Signature of Principal Investigator Date

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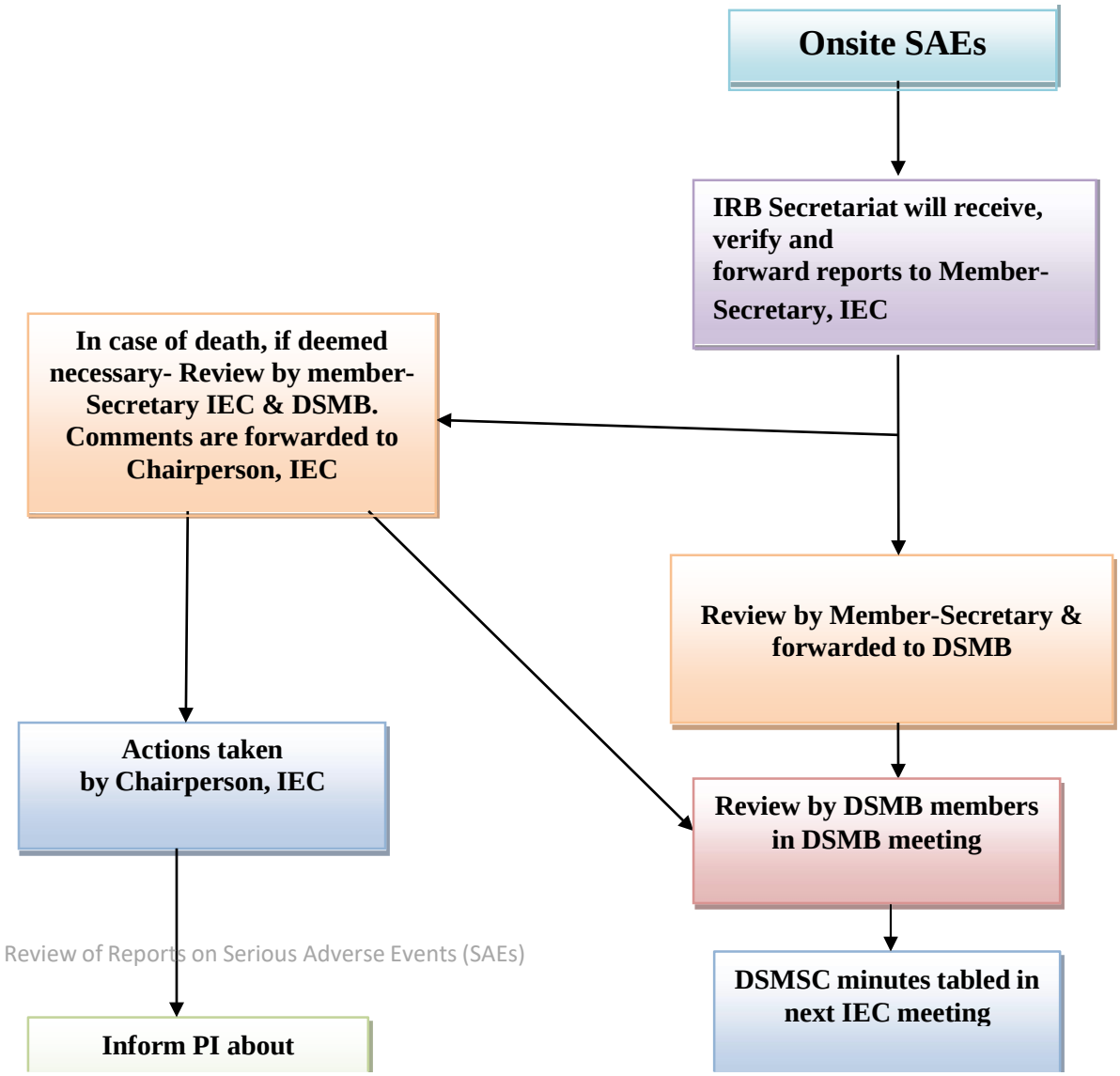

Onsite SAEs
IRB Secretariat will receive, verify and forward reports to Member-Secretary, IEC
In case of death, if deemed necessary- Review by member-Secretary IEC & DSMB. Comments are forwarded to Chairperson, IEC
Review by Member-Secretary & forwarded to DSMB
Actions taken by Chairperson, IEC
Review by DSMB members in DSMB meeting
Review of Reports on Serious Adverse Events (SAEs)
DSMSC minutes tabled in next IEC meeting
Inform PI about

CHAPTER 10

Maintenance of Active Project files, Disposal/ Archival of Closed Projects, Documents Retrieval

10.1 PURPOSE

To provide instructions for preparation and maintenance of active study files and other related documents approved by the IRB, MCC, and storage/archival of closed files and retrieval of documents.

10.2 SCOPE

This SOP applies to all active protocol/study files, closed files and their related documents that are maintained in the IRB office and archival site.

10.3 RESPONSIBILITY

It is the responsibility of IRB staffs to ensure that all study files are prepared, maintained, and kept securely for a period of three years after the closure of the project (under a proper system that ensures confidentiality and facilitates retrieval at any time).

10.4 MAINTENACE OF ACTIVE STUDY FILES &CLOSED STUDY FILES ARCHIVAL

A Study Master File is the file comprising all essential documents and correspondence related to the study/protocol.

Study master files should be established at the time of initial submission in the IRB office.

- The study files are assigned unique identifiers (project serial no.)
- All documents related to the study file are gathered, classified and combined together appropriately.

- All active files are kept in a secured file cabinet with controlled access. Only authorized individuals' i.e. IRB Office, will have access to the files. The study files are maintained in an easily accessible and secure place for at least 3 years after the study closure.
- All closed study files are separately archived.
- IRB staff will arrange for the closed project files to be archived once the completion/status reports are reviewed by the IRB. The completed/closed project files will be stored in archive boxes that are clearly labeled with the project number and title, Principal Investigator and disposal date. The archive boxes will be sent to a secure, dry location. The access to the files should be restricted to the IRB and the regulatory authorities. The details of the archiving location should be recordedin a location register stored in the IRB office. This register should record the project number and title, Principal Investigator and the disposal date. This procedure should be carried out in accordance with MCC regulations.

10.5 DISPOSAL OF CLOSED FILES, PROTOCOL COPIES AND DOCUMENTS SUBMITTED FOR IRB REVIEW

The study master file will be maintained in the IRB office for a period of *three years* following closure of the study. After completion of the archival period the closed files will be shredded and disposed off in the central shredding facility. However, all the copies of the research projects and documents submitted for IRB review will be shredded by the authorized IRB personnel after the IRB meeting without any notification to the Principal Investigator. A log book of disposed documents will be maintained.

10.6 ACCESSIBILITY /RETRIEVAL

Master files will be made available for inspection and copying by authorized representatives of regulatory authorities after receiving the request in writing.
In case any investigator needs a copy of any document from the master file, he/she should make a written request, (*ANX1 –VER2/SOP10/VER2*). The IRB staff will furnish a copy of the required document within a week with the consent of In-Charge, IRB office, MCC. The IRB will issue a copy of the following documents on formal written request.
Archived boxes may be retrieved from storage by the IRB as per MCC regulations.
For administrative purposes, the IRB Office can retrieve archived file(s) without requiring the Chairperson's approval. For this purpose the IRB office in-charge can authorize a staff member of the IRB Office to physically retrieve a file.
Whenever an item is retrieved from the archives, the date, item and person retrieving the item should be documented, together with the date returned to the archives.

10.7 DISPOSAL OF MASTER FILES

The master files will be disposed off by the IRB Office after the *archival period of 3 years*. A formal written off register (*ANX2- VER2/SOP 10/VER2*) will be maintained, providing details of the documents being written off / disposed off after notification to the Member-Secretary, IRB, MCC**.**

ANX1 –VER2/SOP10/VER2

DOCUMENT REQUEST FORM
Institutional Review Board (IRB)
Malabar Cancer Centre (MCC), Thalassery- 670 103

Name of the Principal Investigator/Requesting person:	Date:

Documents requested:

Purpose of request:

Principal Investigator / Requesting person's sign & date

(For IRB Office use only)

IRB Office Decision/Remark:

Permission Status: Yes/ No

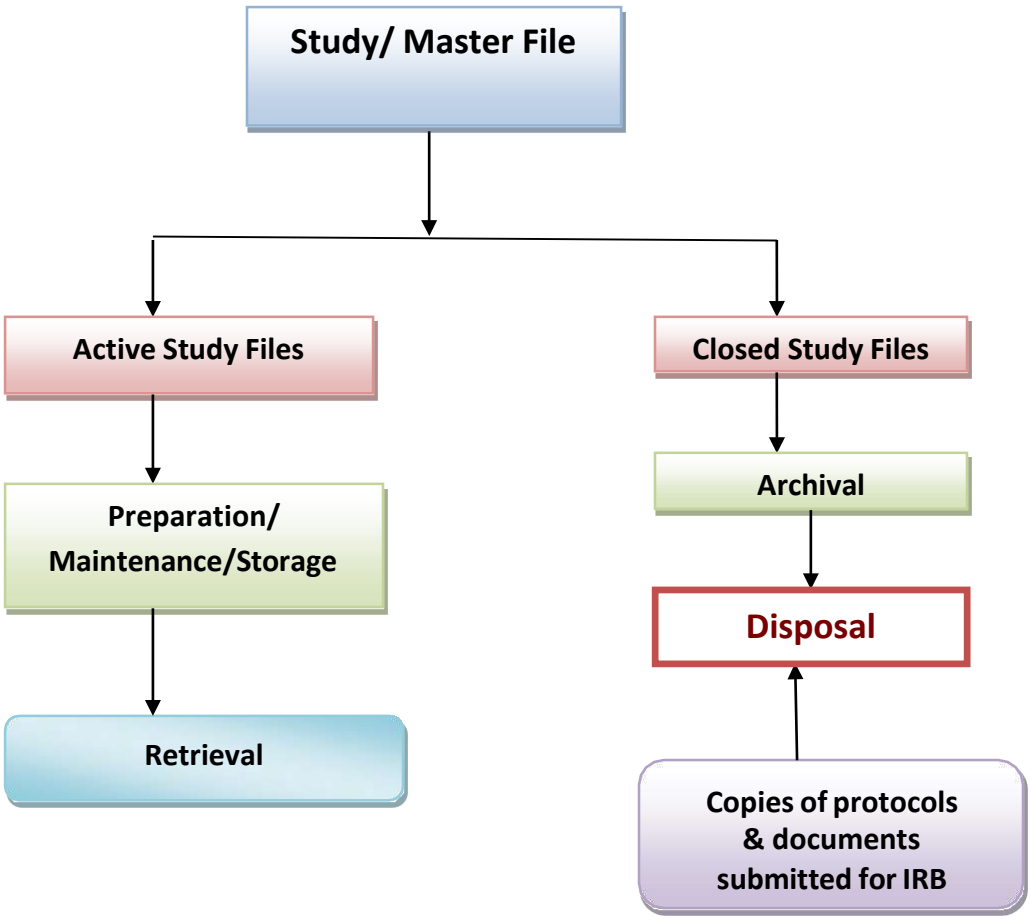
Signature with date of In-Charge, IRB Office

ANX2 –VER2/SOP10/VER2

Format of written off/disposal register

Project No.	Title	PI	No. of Files	IRB Approval Date	Study Initiation Date	Study Closure Date	Name & Sign of Authorized Individual

FLOW CHART


Study/ Master File
Active Study Files
Closed Study Files
Preparation/ Maintenance/Storage
Archival
Disposal
Retrieval
Copies of protocols & documents submitted for IRB

CHAPTER 11

Documentation of IRB Activities

11.1 PURPOSE

To describe the procedures for documenting the IRB activities.

11.2 SCOPE

This SOP will apply to all research activity involving human subjects, irrespective of source and nature of funding.

11.3 RESPONSIBILITY

It is the responsibility of the staff members of IRB office to maintain the IRB files at the IRB office.

11.4 DETAILED PROCEDURES

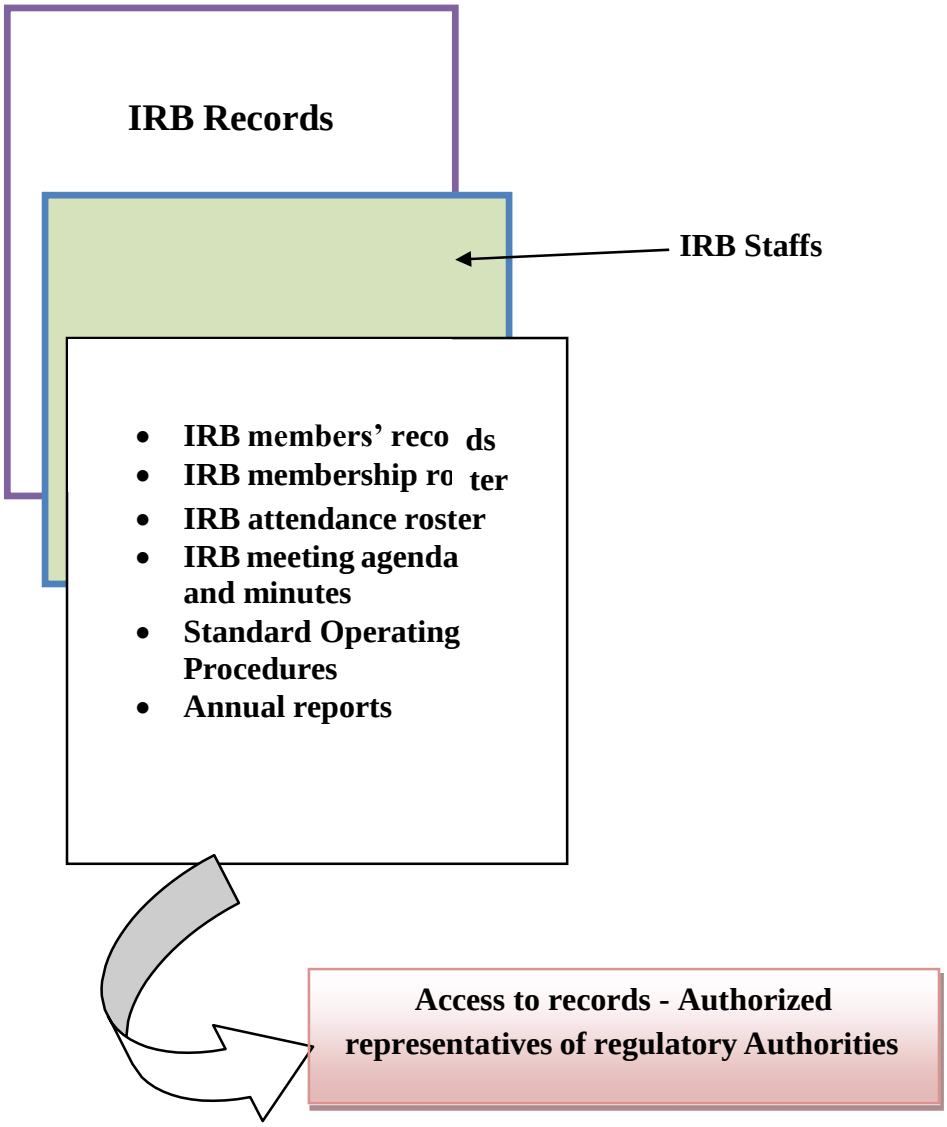
11.4.1 IRB records will include the following

1. IRB members' records
   a. Appointment and Acceptance letters of each member
   b. Signed and dated confidentiality agreements
   c. Updated Curriculum vitae (hard copy or soft copy)
   d. Training records for each IRB member
   e. Documentation of resignations/terminations
2. IRB membership roster/mandate
3. IRB attendance roster
4. IRB meeting agenda and minutes
5. Standard Operating Procedures (SOPs)
6. Annual reports
7. Any other correspondence

11.4.2 Access to IRB records

IRB records will be made available for inspection to authorized representatives of regulatory authorities based on written request.

FLOW CHART


IRB Records
IRB Staffs
IRB members' reco ds
IRB membership ro ter
IRB attendance roster
IRB meeting agenda and minutes
Standard Operating Procedures
Annual reports
Access to records - Authorized representatives of regulatory Authorities

CHAPTER 12

Study Completion Report Review

12.1 PURPOSE

The purpose of this SOP is to provide instructions on the review of Study Completion Report for every study previously approved by the IRB, MCC.

12.2 SCOPE

This SOP applies to the review of the ***Study Completion Report (SCR)***. It is an obligatory review of each investigator's activities presented to the IRB as a written report of study completion.

Although IRB provides a Study Completion Report Form (*ANX1-VER2/SOP12/VER2*) to each investigator whose study is been approved by IRB & the study is initiated and/or ongoing at the proposed site, additional information (letter format, form provided by the Sponsor, etc.) may be submitted to provide adequate and sufficient information.

12.3 RESPONSIBILITY

It is the responsibility of the IRB members to review the SCR and notify it or request for further information, if necessary.

12.4 DETAILED INSTRUCTIONS

12.4.1 Before each board meeting

- The Office of IRB will receive 15 hard copies or 5 hard copies + soft copy of Study Completion Reports from the PI.
- The IRB Office will follow instructions as in *SOP03/VER2* Management of Research study submission) for receiving and checking the report packages.

- It is the responsibility of the IRB Office to review the report for completeness before submission for the Board meeting.
- The Member Secretary, IEC, should keep the study completion reports on the agenda for IRB meeting. (Procedures for Agenda preparation, Meeting procedures and recording of Minutes- *SOP 04/VER2*

12.4.2 Before and during board meeting

- IRB member(s) should review a copy of the completion report.
- The members will discuss the report in the IRB meeting.
- If appropriate to the discussions, the chairperson may call for consensus to accept it or request further information or take any other action.

12.4.3 After the board meeting

- The IRB Office will note the decision in the meeting minutes and the study will be considered as closed if the document is accepted.

- The IRB decision will be communicated to the investigator by e-mail. In case, further information /action is requested, the same should be followed by the PI and communicated to the IRB office within 30 days. This update will be tabled in the full board meeting of IRB.

- IRB Office will file the report in the study master file only after the report is accepted by IRB.

- The IRB Office will archive the entire study as per *SOP 10/VER2* nd the report for a period of 3 years from the date of completion of the project, if the report is accepted.

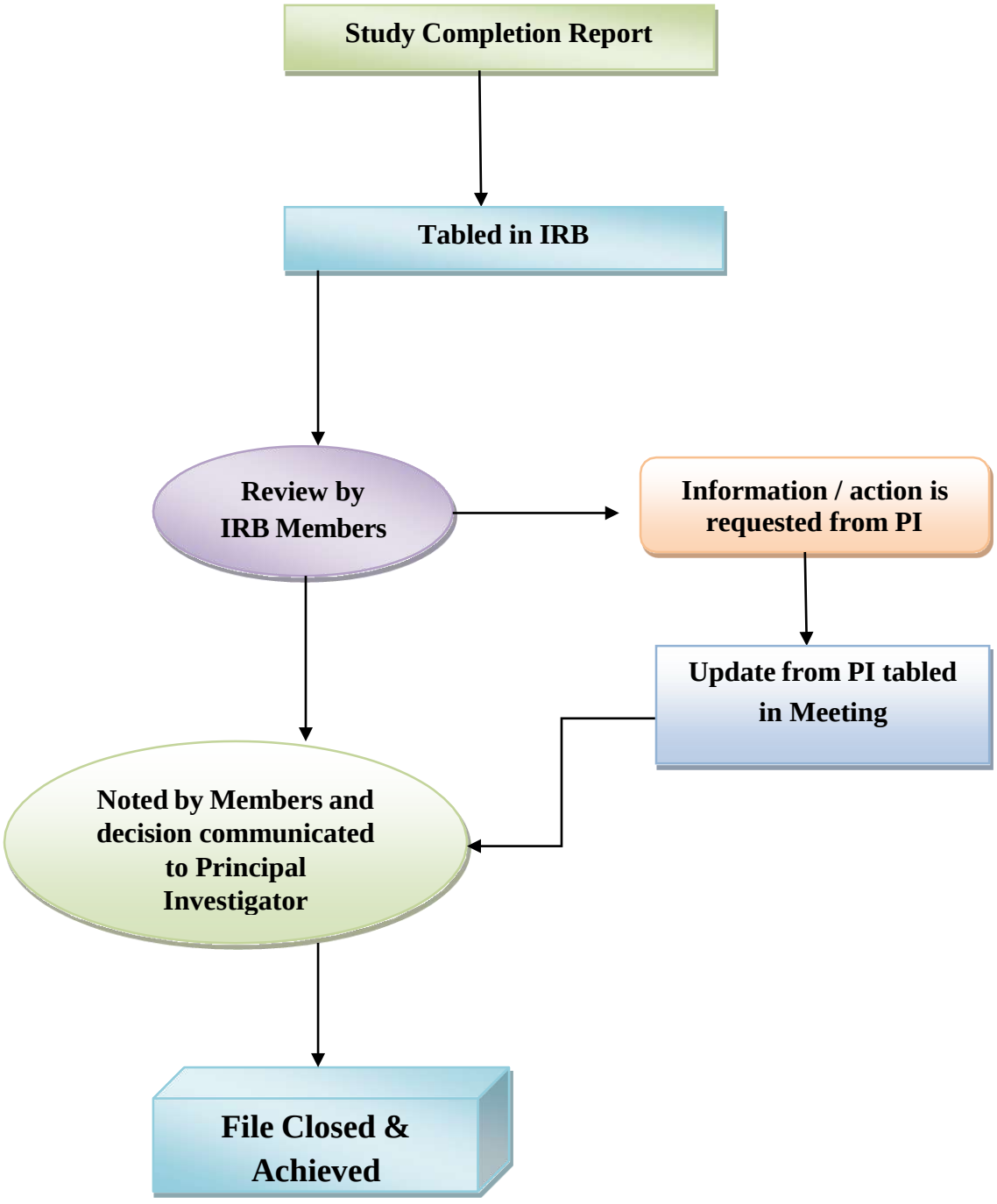
ANX1- VER2/SOP12/VER2

	Study Completion Report (SCR) Form –Retrospective Study Institutional Review Board (IRB)- Malabar Cancer Centre Thalassery, Kerala- 670 103

IRB approval details	:	
Study Title	:	
Name of PI	:	
Name of Co-PI(s)	:	
Name of Co-I(s)	:	
Study initiated on	:	
Study Period	:	
Data Retrieved Period	:	
Number of cases enrolled	:	
Number of cases excluded	:	
Study Objective	:	
Study Result	:	
Study Outcome	:	
Presentation/ Publication details of the study		
Whether Hard copy and Soft copy of the data submitted to the HoD/Department		
Signature of PI: Date:		Recommendation of HoD Signature: Date:

NB:- The PI should ensure the structured abstract in the proper format (Title, Authors information, Introduction, Objectives, Methods, Result and Conclusion) both soft copy and hard copy submitted to Division of Clinical Research & Biostatistics.

FLOW CHART


Study Completion Report
Tabled in IRB
Review by IRB Members
Information / action is requested from PI
Update from PI tabled in Meeting
Noted by Members and decision communicated to Principal Investigator
File Closed & Achieved

CHAPTER 13

Management of Premature Termination/ Discontinuation/ Suspension of the Studies

13.1 PURPOSE

This SOP purposes the management& detailed instructions for the Institutional Review Board in case of premature termination/suspension/discontinuation of a research study.
Research studies are usually terminated as per the recommendation of the IRB and/or DSMB, PI, sponsor or other authorized bodies wherein subject enrollment and subject follow-up are discontinued before the scheduled completion of the study.

13.2 SCOPE

This SOP applies to any study approved by IRB that is being recommended for termination/suspension/discontinuation before its scheduled completion.

13.3 RESPONSIBILITY

The Chairperson and Member Secretary, IEC, has the due responsibility to terminate any study that the IRB has previously approved when the safety or benefit of the study participants is doubtful or at risk, also to review the termination suggested by DSMB, PI, Sponsors or other authorized bodies.
The IRB Office is responsible for management of the premature termination/ suspension/discontinuation process.

13.4 DETAILED INSTRUCTIONS

13.4 A Receive recommendation for study termination/suspension/discontinuation

Detailed instructions

- The IRB secretariat will receive recommendation and comments from PI, Sponsor or other authorized bodies for premature termination/suspension / discontinuation of study.
- **Suspension/Termination/ Discontinuation by IRB**

  The IRB can terminate or suspend previously approved trial in following circumstances but not limited to:

  - When research is not conducted in accordance with IRB policies.
  - When research is associated with unexpected serious harm to participant
  - Failure to submit status report
  - For e.g. - Frequency of SAEs occurring at the institution or other sites in case of multicenter studies may require the study to be prematurely terminated for the safety of the patients.
  - If protocol non-compliance/violation is detected
- **Suspension/Termination/ Discontinuation by Investigator/Sponsor***:*

  An investigator may also put on hold a previously approved research when in the judgment of the investigator this is appropriate to protect the rights or welfare of participants or when new safety information appeared in the literature, or evolved from this or similar research

- Withdrawal of study before site initiation. An investigator may withdraw a study before site initiation due to reasons such as regulatory delays, logistic and budgetary infeasibility etc.
- Reports of Suspension/Termination/ Discontinuation/ by IRB will be tabled in the convened full board meeting.
- The IEC secretariat will receive the study protocol termination/suspension/discontinuation prepared and submitted by the Principal Investigator and verify the contents of the report for inclusion of:
  - Premature Termination Report / suspension / discontinuation / Withdrawal of IRB approved study before site initiation (ANX1- VER6/SOP13/ VER6) signed and dated by the PI and/or other material (letter from Principal Investigator/sponsored)
  - The IRB secretariat will check the completeness of the information
  - The IRB secretariat will receive and acknowledge the reports.

13.4 (B) Review and discuss the Termination /suspension/discontinuation report Review and discuss the Premature Termination / suspension /discontinuation/ report of Withdrawal of IEC approved study

- IRB will review the report of premature termination/ suspension/discontinuation/study withdrawal submitted by Principal Investigator at regular full board meeting or expedited review meeting.
- The Secretary in the meeting will inform of the premature termination/ suspension / discontinuation of the project and the IRB members will review the Premature Termination / Suspension / Discontinuation Report (ANX1- VER2/SOP13/VER2) and Reports of Suspension / Termination / Discontinuation by IRB along with relevant SAE Report / DSMB Reports.
- The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB policies, is not in compliance with the regulations or that has been associated with unexpected serious harm to participants. Suspensions and terminations will be reported to concerned authorities and appropriate institutional officials when applicable.
- The suspension of IRB approval is a decision taken at the convened IRB meeting either to stop temporarily some or all previously approved research activities for a particular study, or to stop permanently some previously approved research activities. Suspended protocols remain open and require continuing review.
- A termination of IRB approval is a decision taken at the convened IRB meeting to stop permanently all activities in a previously approved research protocol.
- Member Secretary IRB, documents in the IRB minutes the reasons for the suspension or termination / withdrawal of IEC approved study by Principal Investigator before site initiation and if applicable, any actions ordered to take place.
- What steps to be taken for on-going patients has to be reviewed by IRB as well.

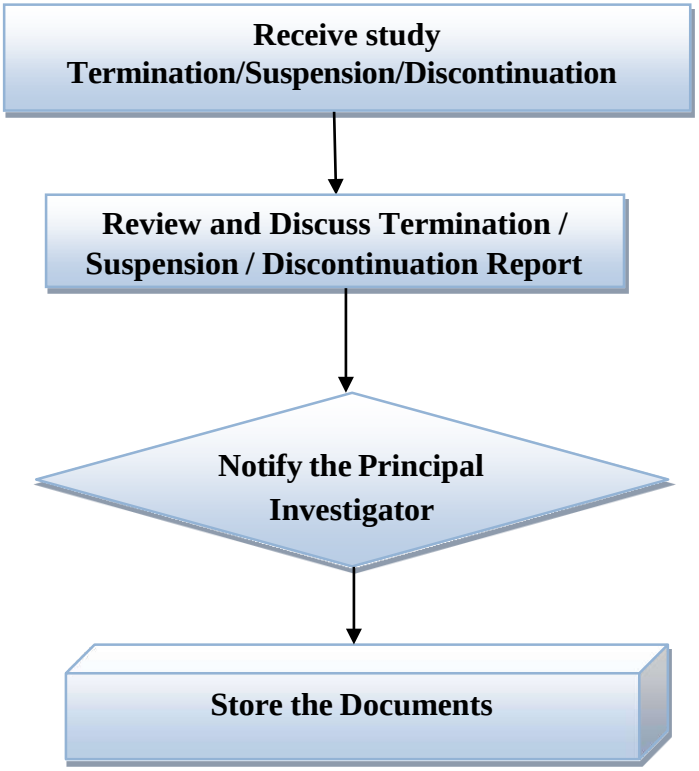
13.4 (C) Notification to PI

- ✓ The IRB Office will prepare a notification letter acknowledging the acceptance of termination /suspension/discontinuation or query letter to request information regarding the premature termination /suspension/discontinuation.
- ✓ The Office will send the notification letter to the PI for their records within 2 weeks after the meeting**.**
- ✓ If a query is sent to PI, on receipt of the reply letter, it will be reviewed in the fourth coming full board meeting /expedited review meeting and steps in **11.4 (B)** will be performed by the IRB secretariat.

13.4 (D) Report Archiving

- ✓ The IRB Office will keep the original version of the Premature Termination/suspension/discontinuation report in the study file and send the file to archive.
- ✓ The study documents will be stored for a period of 3 years from the date of project termination.

FLOW CHART


Receive study Termination/Suspension/Discontinuation
Review and Discuss Termination / Suspension / Discontinuation Report
Notify the Principal Investigator
Store the Documents

ANX1- VER2/SOP13/VER2

Premature Termination/Suspension/Discontinuation Report

Institutional Review Board (IRB)

Malabar Cancer Centre (MCC), Thalassery- 670 103

MCC Project No.:	
Study Title*:	
PI*: Co-PI(s):	
e-mail*:	
Study Site*:	
Sponsor(s):	
IRB Approve Date*	Date of Last Progress Report Submitted to IRB*
Study Start Date*:	

	Termination/ suspension/discontinuation Date:

Study Participants

o Target accrual of study(entire study) _____

o Total patients to be recruited at MCC (IRB ceiling)*_____

o Screened: _____

o Screen failures: _____

o Enrolled: _____

o Consent Withdrawn:_____Reason: (Attach in format below)

o Withdrawn by PI:_____Reason: (Attach in format below)

o Active on treatment: _____

o Completed treatment : _____

o Patients on Follow-up: _____

o Patients lost to follow up: _____

o Any other: _____

Any Impaired participants ▪ None _____ ▪ Physically _____ ▪ Cognitively _____ ▪ Both _____	
SAE (Total No.)*:	SAE Event*:
Reason(s) for Termination/Suspension/Discontinuation*:	
Summary of Results:	
PI Signature	***Date***

***Mandatory fields**

CHAPTER 14

Review of Request for Waiver of Written Informed Consent

14.1 PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to describe the type of research projects for which the IRB may grant waiver for requirement of administering written informed consent and the format of the application form to be used by the investigators for requesting waiver of consent.
The Application Form *ANX1-VER2/SOP14/VER2 is* designed to standardize the process of applying for consent waiver.

14.2 SCOPE

This SOP applies to the all protocols with a request of granting consent waiver submitted for review by the IRB. At the expedited subcommittee meeting or during full board meeting, decision should be taken by IRB members.

14.3 RESPONSIBILITY

It is the responsibility of the Principal Investigator of a study to ask for a request directly to the Member Secretary of IRB, MCC, of Chairperson, SRC, (as the case may be) for tabling the request along with the project proposal for expedited or full board review.

- **14.4 DETAILED INSTRUCTIONS Detailed instructions** The PI can apply to the IRB for a waiver of consent; if the research involves less than minimal risk to the participants and the waiver will not adversely affect the rights and welfare of the participants.
- When a request for waiver of consent is submitted by the Principal Investigator along with the study documents to the IEC secretariat, in the given format ANX1-VER2/SOP14/VER2 stating the reasons for the consent waiver; the following steps are taken:

✓ The IRB Secretariat will check if the concerned documents are filled completely and the required lists of documents are enclosed.
✓ The IRB members will review the request taking into consideration the types of studies

for which waiver of consent may be granted.

- ✓ The IRB will ensure that there are adequate mechanisms described in the protocol for protection of the identity of the research participants and maintaining confidentiality of the study data. This is necessary as the participant cannot be assured directly about confidentiality of health data through a formal informed consent process, when consent waiver is granted.
- ✓ The decision on whether to grant the waiver is taken during expedited or full board review.
- ✓ The IRB will document its findings justifying the waiver or alteration of the consent process.
- ✓ The IRB minutes will document required determinations and protocol-specific findings justifying those determinations for:
    - Waiver or alteration of the consent process.
    - Research involving participants with diminished capacity
- ✓ The decision regarding approval/disapproval of waiver is informed to the Principal Investigator in writing. If the waiver is not granted, the IRB will provide reasons for the same.

14.5 TYPE OF RESEARCH PROJECTS WHICH MAY QUALIFY FOR CONSENT WAIVER:

A request to waive written informed consent must be accompanied by a detailed & logical explanation. The investigator(s) is also required to provide assurance regarding protection of identity of research participants and maintenance of confidentiality about the data of the research participants. The following criteria (*ICMR 2006 guidelines*) must be satisfied for a research project so that it can qualify for granting a waiver of both written and verbal consent.

The researcher can apply to the EC for a waiver of consent if the research involves less than minimal risk to participants and the waiver will not adversely affect the rights and welfare of the participants (5.7-ICMR 2017)

1. The EC may grant consent waiver in the following situations:
    - Research cannot practically be carried out without the waiver and the waiver is scientifically justified;
    - Retrospective studies, where the participants are de-identified or cannot be contacted;
    - Research on anonymized biological samples/data;
    - Certain type of public health studies/surveillance programmes/ programme evaluation studies;
    - Research on data available in the public domain; or
    - Research during humanitarian emergencies and disasters, when the participant may not be in a position to give consent. Attempt should be made to obtain the participant's consent at the earliest.

2. When it is impractical to conduct research since confidentiality of personally

identifiable information has to be maintained throughout research as maybe required by the sensitivity of the research objective.

E.g. conducting interviews with citizens about their religious beliefs/ people with HIV and AIDS/conducting phone interviews with homosexuals.

The only record linking the participant and the research would be the consent document and 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 IRB.

3. 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 following points need to be considered.

   a. The following documents need to be submitted for the IRB review

      - A script for verbal consent - a verbal consent script provides all of the elements of consent in a more informal style. In addition, each subject should be provided with an information sheet that describes the study and gives contact names and numbers.
      - The interview schedule will confirm that the interview is a simple 5 minute call and that no questions are asked that compromise a person's confidentiality or position.

   b. Normally, investigators will be asked to keep a log of those who were approached about the study, and offered verbal consent. A simple chart can indicate the subjects as participant 1, participant 2, and participant 3. A column can indicate that verbal consent was given and a date. Since a specificnumber of study participants are to be recruited. It is important that investigators keep some record to indicate that they are not enrolling more subjects than they originally requested.

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.

5. In emergency situations when no surrogate consents can be taken. (ICMR guidelines) when consent of person/ patient/ responsible relative or custodian/ team of designated doctors for such an event is not possible, the IRB 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.

The points 7-11 DHHS (CFR) criteria may be applicable only when research involving human subjects is conducted, supported or otherwise subject to regulation by any United States Government federal department or agency funded by a U.S. federal agency.

6. An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:
    I. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and
    II. The research could not practicably be carried out without the waiver or alteration

7. An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:
    i. The research involves no more than minimal risk to the subjects;
    ii. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
    iii. The research could not practicably be carried out without the waiver or alteration; and
    iv. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

8. The informed consent requirements in this policy are not intended to preempt any applicable local laws and concerned regulations which require additional information to be disclosed in order for informed consent to be legally effective.

9. Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable local laws and concerned regulations The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:

   (i) public benefit or service programs;

   (ii) (ii) procedures for obtaining benefits or services under those programs;

   (iii) (iii) possible changes in or alternatives to those programs or procedures; or

   (iv) Possible changes in methods or levels of payment for benefits or services under those programs; and the waiver or alteration will not adversely affect the rights and welfare of the subjects; The research could not practicably be carried out without the waiver or alteration; and whenever appropriate, the subjects will be provided with additional pertinent information after participation.

10. An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

    1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.
    2) In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.
    3) An IRB may waive the requirement for the investigator to obtain a signed consent form if an appropriate well documented mechanism is substituted for protecting the children who will participate in the research.
    4) The IRB is allowed to waive parental consent by determining that the

criteria for waivers or alterations are met.

5) The IRB is allowed to waive the requirement for written documentation of the consent process by determining that the criteria for waivers are met.

- **Consent in public health research may be waived:** On routinely collected data under programme conditions, including research involving linkage to large anonymous databases of information that has been routinely collected such as administrative data and through surveillance activities. However, at the time of collection people concerned may have been told that the data would be used for other purposes, including research.
- In circumstances where obtaining consent is impractical, such as for stored anonymous data/ biological samples, surveillance and administrative data or personal non-identifiable data/ material available from public health programmes. For studies performed within the scope of regulatory and public health authorities, such as process and impact evaluations of national policies and programmes, including neonatal screening programmes or diabetes screening as part of national programme activities may be exempt from the requirement for informed consent.
- When the primary purpose is refinement and improvement of the public health programmes;
- For studies using health-related registries that are authorized under national regulations.

ANX1-VER2/SOP 14/VER2

Application form for requesting Waiver of Consent
Institutional Review Board (IRB)
Malabar Cancer Centre (MCC), Thalassery- 670 103

1. Principal Investigator's
Name:_____

2. Department/Affiliation:

1. Project Title:

2. Names of other participating staffs/students:

_____
_
_____
__
_____
__
_____
__

5. Request for waiver of informed consent:
   - Please tick the reason(s) for requesting waiver

a) Research involves 'not more than minimal risk' ☐
b) There is no direct contact between the researcher and participant ☐
c) Emergency situations as described in ICMR Guidelines (ICMR 2017 Guidelines- http://www.icmr.nic.in/ethical_guidelines.pdf) ☐
d) Any other (please specify)

- Statement assuring that the rights of the participants are not violated

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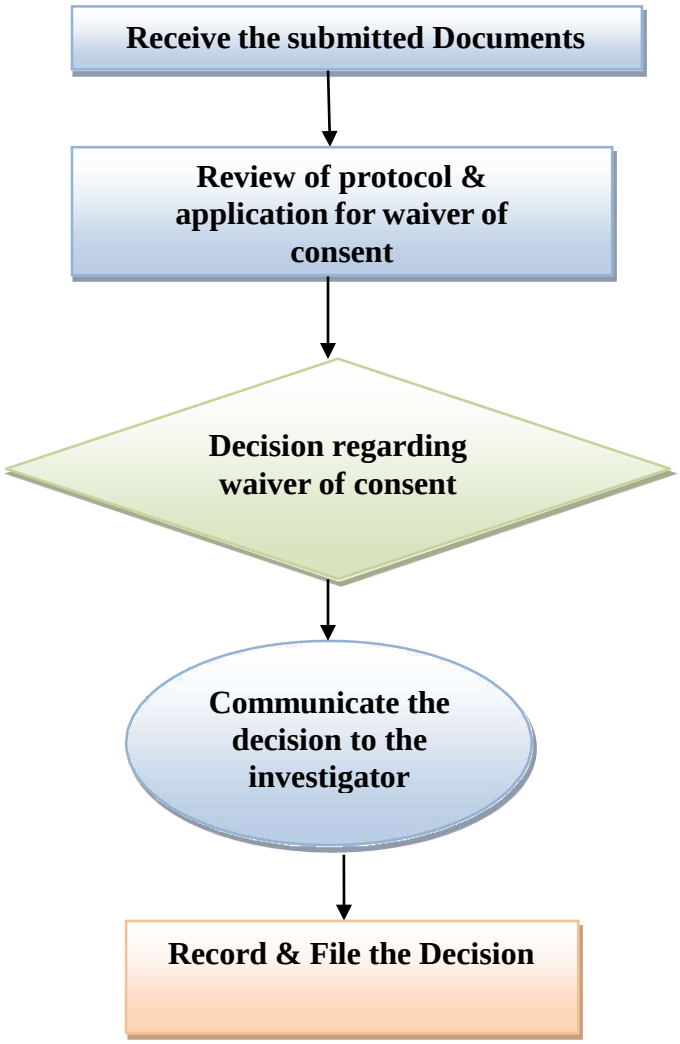
- State the measures described in the Protocol for protecting confidentiality of data and privacy of research participant

Full Signature of Principal Investigator (PI) with Date
…….

FLOW CHART


Receive the submitted Documents
Review of protocol & application for waiver of consent
Decision regarding waiver of consent
Communicate the decision to the investigator
Record & File the Decision

CHAPTER 15

Site Monitoring

15.1 PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to provide the procedures for monitoring any IRB approved study by the IRB member(s) or anyone appointed by IRB.

15.2 SCOPE

This SOP applies to any visit and/or monitoring of IRB approved study protocols. Clinical trials sponsored by external funding sources and industry are continually audited for compliance and monitored for progress by the external monitors. Institutional clinical studies without outside sponsorship are the focus of the monitoring system of this committee. However if any of the aforementioned studies require a "for cause" monitoring, as thought necessary by the IRB, these SOPs will also apply to the same.

15.3 RESPOSIBILITY

Data Safety and Monitoring Board or a subcommittee appointed by the IRB is charged with the mission of developing and enacting quality assurance procedures to monitor the overall progress of institutional clinical trials and for ensuring adherence to clinical trial protocol, SOPs, regulations and guidelines and Institutional procedural requirements.

This includes review of the overall progress of each study to ensure the safety of participants, validity of data, that the projected accrual goals are met on a timely basis, that excess accrual is avoided, that eligibility and evaluability criterias are met, that adverse events are appropriately monitored and reported to the appropriate agencies. Inherent in this process is the goal of enhancing the quality of the research by providing the investigator with constructive criticism.

The DSMB/Sub-committee Secretary assigns the IRB/DSMB/Sub-committee members /independent experts to monitor the trials. The monitoring is conducted by at least 2 members who have expertise and

understanding of the clinical aspects of the disease/ patient population being studied, with an understanding of relevant biostatistics and clinical trial conduct and methodology, including GCP and regulations. External/independent experts from within/outside institution may be approached for monitoring depending upon the nature and complexity of the trial being monitored.

15.4 DETAILED INSTRUCTIONS

15.4.1 Selection of study sites

Sites will be identified for routine monitoring at the time of approval of the project by the full board which will be recorded in the minutes.
For cause monitoring will be performed at sites for reasons identified by any member of IRB, approved by Chairperson, IEC. For cause monitoring could be initiated, in any of the following conditions:

- For high number of protocol violations
- Novel therapy
- Limited existing data
- Interventional studies
- Too many studies carried out by a Principal Investigator
- High number of SAE reports
- High recruitment rate
- High funding requirements
- Multi-disciplinary (e.g. Chemo+ RT)
- Non-compliance or suspicious conduct
- Any complaints related to the research
- Any other cause as decided by IRB

15.4.2 Before the visit

- For cause/routine monitoring of the project, the IRB Chairperson will inform DSMB to perform the task of monitoring during discussion of the study.
- The Secretariat will intimate the PI regarding the scheduled monitoring visit and DSMB and PI will coordinate the monitoring visit.
- A request regarding the monitoring visit will be sent to the monitor along with a copy of the monitoring visit form
- The monitor will also:
  - Notify the site about the scheduled visit.
- A tentative planned agenda for monitoring will be informed to the PI by the monitor

  - The monitor will review the study project files and make appropriate notes.
  - The monitor may carry copy of documents from the IRB approved project files for verification and Site Monitoring Visit Report Form (*ANX1-VER2/SOP15/VER2*).

15.4.3 DURING THE VISIT

- Source files will be a combination of MCC hospital files and Electronic Medical Records. All relevant information regarding consenting, study procedures, documentation of SAE and course of SAE, follow up and outcome assessment should be available either in the hospital file or EMR (if applicable).
- The monitor will–
- Review the informed consent document to make sure that the PI is using the current, approved version
- Review randomly the participant's source files for proper informed consent documentation.(usually about 10%, or may be higher)
- Observe the informed consent process, if possible,
- Check investigational product accountability is adequately controlled and documented throughout the product flow (arrival, dispensing, use, return from the participant and return/destruction after the study). Storage times, conditions and expiry dates must also be acceptable and sufficient supplies available wherever applicable.
- Observe laboratory and other facilities necessary for the study, if possible.
- Review the study/ source files to ensure appropriate documentation
- Verifying that the investigator follows the approved protocol and all approved amendment(s), if any.
- Ensuring that the investigator and the investigator's trial staff are adequately informed about the trial
- Verifying that the investigator and the investigator's trial staff 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.
- Verifying that the investigator is enrolling only eligible participants.
- Verifying that source documents and other study records are accurate, complete, kept up-to-date and maintained.
- Checking the accuracy and completeness of the CRF entries, source documents and other study related records against each other.
- 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). Case record forms would be checked to review the safety data i.e. Adverse Events (AEs) and Serious Adverse Events (SAEs) for the volume or severity of adverse events.
- Verify project account statements to tally expenditures and ensure that participants have been reimbursed as per study budget
- Collect views of the study participants, if possible.
- Investigator site file(s)

- Patient reimbursement status(if applicable)
- Fill the Study Monitoring Visit Report Form ANX1-VER2/SOP15/VER2 and write the comments.
- Exit/clarification meeting with the study team

15.4.4 AFTER THE VISIT

- The monitor will complete the report (use the form ANX1-VER2/SOP15/VER2) describing the findings of the monitoring visit and submit the same to the DSMB/sub-committee office. After the form is received at the office, it is checked for completeness. The preliminary comments may be shared with the PI, if required.
- Form is reviewed by DSMB secretary, and the form is forwarded to IRB Secretary for action
- The IRB Secretary/DSMB member representative/lead discussant for the project presents the monitoring visit findings including briefing about the study protocol, performance, SAE and previous monitoring reports if any in the IRB full board meeting.
- The Secretariat will place the report in the correct files.

- 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.
- The Principal Investigator should respond to the findings of the monitoring report within 4 weeks of receipt of the study monitoring report from the IRB. However, in case the PI needs additional time to respond to the findings, an official request has to be made to the IRB. The permission to extend the timeline to respond the findings of the study monitoring report may be granted to the PI at the discretion of the IRB on a case to case basis.
- Grounds for recommending suspension or termination of a clinical trial by the IRB include, but are not limited to:

    1. Zero accrual for 1-2 years or long-term, low accrual.
    2. Stopping rule violations

Stopping rules
A clinical trials term for statistical criteria which, when met by accumulating data, indicate that th e trial should be stopped early to avoid putting participants at risk unnecessarily or because the in tervention's benefit is so great that further data collection is unnecessary.

1. Multiple protocol violations during the conduct of the study affecting participants' rights, safety and well-being or the credibility of the produced data.
2. Safety issues
3. Compliance issues
4. The decision to recommend suspension or termination of a clinical trial is carefully considered and takes into account whether corrective actions had been requested at previous reviews and were not implemented.

IRB has the ultimate authority to effect termination or suspension of a clinical trial.

ANX1-VER2/SOP15/VER2

Study Monitoring Visit Report

Instructions for completing the monitoring report:

TITLE PAGE:

- This box must appear on the title page of the final document.
- Monitoring reports may also feature the monitoring report title and preparers' name and contact information more on the title page.

MONITORING REPORT:

- Instructions for completing the monitoring report can be found under the section headings in this template.
- Applicable study details (Title page, Section 1-4) can be entered before the commencement of the monitoring visit for effective time management at the site during monitoring.
- Sections which are not applicable may be left blank but should NOT be deleted from the final document.

All instructions, including this introductory text, should be deleted from the final document.

ProjectTitle & Shorttitle	
ProjectID ***(MCC IRB ProjectNo.)***	
MonitoringDate(s) ***DD-Month-YYYY***	
Prepared By	
Contact ***Telephone,email***	

1. SUMMARY OFFINDINGS

Study File related
IC Process related
Inclusion/Exclusion Criteria
Source Document related
Study Drugs related
Others (IRB, Compensation, Administration related)

2.Introductory Information	
2.1 Date/Time of monitoring visit ***DD-Month-YYYY***	
2.2 Purpose of monitoring*Site* ***Qualification Visit Site*** ***Initiation Visit Routine*** ***Monitoring Visit Site*** ***Close-OutVisit***	
2.3 Date of Last monitoring visit ***DD-Month-YYYY***	
2.4 Enumerate the open queries from the last monitoring visit if any	**1.** **2.** **3.** **4.** **5.**
2.5 Mention the study file numbers (subject IDs) which were reviewed at this visit	

3.Project Details	
3.1 Study Title	
3.2 Project Type*(Investigator initiated/sponsored)*	
3.3 Any changes in the study team since last monitoring visit	
3.4 If Yes mention the details	
3.5 Have the changes been notified to the IRB	
3.6 Project start date ***DD-Month-YYYY***	

4.Project Status	
4.1 Current protocol version and date	
4.2 Current status ***a. Ongoing*** ***b. Completed*** ***c. AccrualCompleted*** ***d. Follow-up*** ***e. Suspended*** ***f. Terminated*** ***g. Closed*** ***h. ClosedPrematurely***	
4.3 If the response to the above question is option e, f or h, kindly provide relevant explanation	
4.4.1 Total patients to be randomized	
4.4.2 Total Subjects screened	
4.4.3 Total subjects randomized **(a) Total number of patients registered form generalcategory** **(b)Total number of patients randomized form the privatecategory** *(Please specify the total and category specific randomization figures)*	
4.4.4 Recruitment status on schedule*(Yes/No)* ***Comments(if any)***	
4.4.5 Total subjects who withdrew consent	
2.4.6 Total Subjects who discontinued ***Comments/Reasons***	
2.4.7 Total Subjects who completed the study ***Comments/Reasons***	
2.4.8 Total Subjects who are active in the study	

5.Informed Consent						
Enumerate subject IDs of the monitored subjects' ICDs	***Subject ID***	***Any Findings (Yes/No)***	***Details***	***Reported to IRB (Yes/No)***	***Issues Closed/ Open***	***Corrective Action/Suggestions/Comments***
a. Has appropriate consent been obtained before beginning any study procedure						
b. Correct version of the ICF						
c. Source record documentation						
d. Signature/date of PI administration of ICP						
e. Has the subject been given a copy of the consent form						
f. Others please specify in details section						

6. Protocol specific deviations/violations						
	Subject IDs	***Any Findings (Yes/No)***	***Details***	***Reported to IRB (Yes/No)***	***Issues Closed/Open***	***Corrective Action/Suggestions/Comments***
a. Inclusion/Exclusion criteria related **b. Efficacy parameters related** **c. Visit windows related** **d. Labs related** **e. Others please specify in details section e.g. PK sampling related**						

7.SAEs						
Subject ID	***Any SAE (Yes/No)***	***SAE type***	***Source Documentation***	***Reported to IRB (Yes/No)***	***Issues Closed/Open***	***Corrective Action/Suggestions/ Comments***

8.Study Drug Management - delete section if non CTIMP (Not applicable)				
	Yes	No	NA	Comments (if applicable include a comment and describe any corrective actions that were initiated)
8.1- Is there sufficient IMP on site/held in the pharmacy?				
8.2- Are the drug accountability records correct and up-to-date?				
8.3- Are IMP returns being destroyed appropriately & destruction certificates available?				
8.4- Is IMP being stored in a secure location & under the correct storage conditions?				
8.5- Is there an automated or min/max temperature monitoring procedure in place?				
8.6- Has the temperature stayed within the correct range throughout the duration of the study?				
8.7- If not, has this been reported and resolved?				
8.8- Are the code-breaks intact / has the blind been maintained?				

9. Site Personnel, Facilities & Equipment / Study Supplies				
	Yes	No	NA	Comments (if applicable include a comment and describe any corrective actions that were initiated)
9.1- Has there been a repeated breach of GCP or protocol?				
9.2- If yes, has this been reported appropriately?				
9.4- Have there been any changes in facilities or equipment?				
9.5- Do the facilities & equipment remain adequate for the conduct of the study?				
9.6- Are there adequate study supplies (CRFs, lab kits etc) available on site?				
9.7- If yes, are lab ranges documented and updated?				
9.8-Does the study involve reimbursement of: **(a) Study specific investigations** **(b) Medical Management of SAEs** **(c) Travel**				
9.9- Have the proof of reimbursement been maintained in form of voucher/ledger/any other? Please specify in the comments section				

10. Ethics Committee Related				
10.1. General Information				
	Yes/No	**If Yes please provide details**	***Issues Closed/Open***	***Corrective Action/Suggestions/Comments***
10.1.1. Change in IEC membership		-	-	-
10.1.2. Change in IEC SOP		-	-	-
10.1.3. Change in IEC registration		-	-	-
10.2. Study Related Documents				
10.2.1. Latest version of study related documents submitted and approved?				
10.3. Details of Study Documents				
Documents	**Version Number**	**Version Date**	**Approval/ Notification**	**IEC approval/notification acceptancedate**
10.3.1. Protocol				
10.3.2.IB (if applicable)				
10.3.3. IB updates (if applicable)				
10.3.4.ICD				
10.3.5. ICD Back Translation				
10.3.6.CRF				

11. Source Data Verification				
	Yes	No	NA	Comments (if applicable include a comment and describe any corrective actions that were initiated)
11.1.Is the Source Data Verificationdone?				
11.2. Have the data queries been resolved?				

12.Investigators Site File				
	Yes	No	NA	Comments (if applicable include a comment and describe any corrective actions that were initiated)
12.1. Was the ISF reviewed for accuracy and completeness?				
12.2. Have the required documents being filed in the relevant section of the ISF?				
12.3. Was the ROMV visit recorded on the Site Visit Log?				

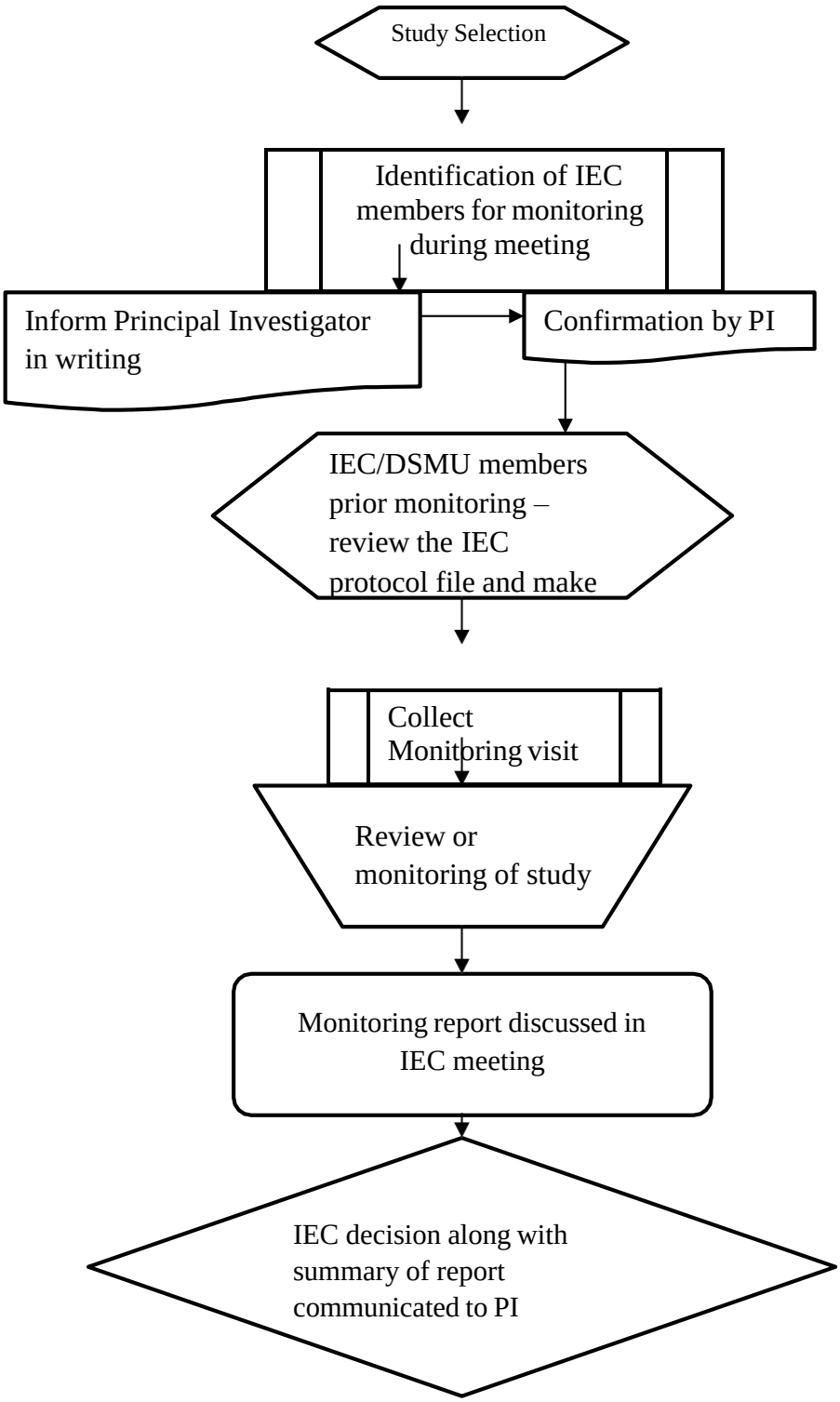
13.General Comments

(any information relevant to the study, other than Summary or specific sections e.g. deficiency identified in protocol, CRF vs Protocol etc.)

Name/Designation /Signature & Date of PI/study team member Name/Designation

/Signature & Date of DSMU member/monitor

Flow Chart


Study Selection
Identification of IEC members for monitoring during meeting
Inform Principal Investigator in writing
Confirmation by PI
IEC/DSMU members prior monitoring – review the IEC protocol file and make
Collect Monitoring visit
Review or monitoring of study
Monitoring report discussed in IEC meeting
IEC decision along with summary of report communicated to PI

CHAPTER 16

Dealing with Patients'/ Study Participants' Requests or Complaints

16.1 PURPOSES

The Institutional Review Board of the Malabar Cancer Centre takes care the protection of the rights and welfare of the human subjects participating in a clinical research approved by the committees under IRB, MCC, as its foremost responsibility. Informed Consent documents reviewed by the IRB inform the study participant that queries regarding their rights as a participant in the study may be addressed to the Member-Secretary, IRB and the IRB address and important phone numbers/ e-mail IDs are provided.

This SOP provides guidelines for dealing with and accommodating requests by participants/patients regarding their rights as a participant or to resolve their complaints in any approved study.

16.2 SCOPE

This SOP applies to all requests concerning the rights and well-being of the research participants participating in studies approved by the IRB, MCC.

16.3 RESPONSIBILITY

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

16.4 DETAILED INSTRUCTIONS

Informed Consent document of the research study provides the contact details of IRB. In case of any queries/concerns/complaints related to their rights, the participants can directly contact the IRB.

- When the IRB member/ administrative staff receives an inquiry or query or request from a research participant/ research participant's representatives/patient via phone/email/letter. The query, request and information will be recorded in the Query/Request/Complaint record (Form ANX1-VER2/SOP16/VER2)
- The Member Secretary will inform the Chairperson about the query/complaint received via phone/email/letter.
- The Chairperson / Members designated by the Chairperson will provide the information required by the research participant not exceeding 14 days
- In case of a complaint received from a research participant, the Chairperson will initiate a process to identify and address any injustice that may have occurred. Depending on the seriousness of the matter, the Chairperson will direct the Member Secretary to
    - Appoint a sub-committee of two or more IRB members or,
    - Call an emergency meeting of 2 or more IRB members for discussion or,
    - Consider the matter for discussion at the next full board meeting, for enquiry in order to resolve the matter
- The Chairperson/ Member Secretary/ designated IRB members will assess the situation and will mediate a dialogue between the research participant and the investigator in an attempt to resolve the matter.
- The IRB will insist on factual details to determine the reality between the truth and individual perception.
- The final decision will be informed to the investigator by the secretariat. Investigator must answer the participant queries suitably and report to the IRB about the same.
- The information including any action taken or follow-up will be recorded in the form ANX1-VER2/SOP16/VER2 by the investigator and the form will be signed and dated.

The IRB members will be informed about the action taken and the outcome in the forthcoming IRB meeting.

16.5 REQUEST DOCUMENT FILLING UP

The record form will be filed in the "response" file by the Member Secretary/Administrative staff. A copy of the same will be kept in the study file. The file will be stored in a secure place.

ANX1-VER2/SOP16/VER2

Study Participant Request/ Complaint Record Form

INSTITUTIONAL REVIEW BOARD (IRB)
Malabar Cancer Centre (MCC), Thalassery- 670103
India

Date of Receive: **Received By:**	
Request from:	* Telephone Call No. & Date:…… * Fax No. &Date : ……. * Letter &Date :……. * E-mail / Date :…….. * Walk-in/Date/Time :…… * Other, please specify:……..

Participant's Name :

Contact Address :

Contact No. :

Title of the Study/ PI Name :

Starting date of participation:

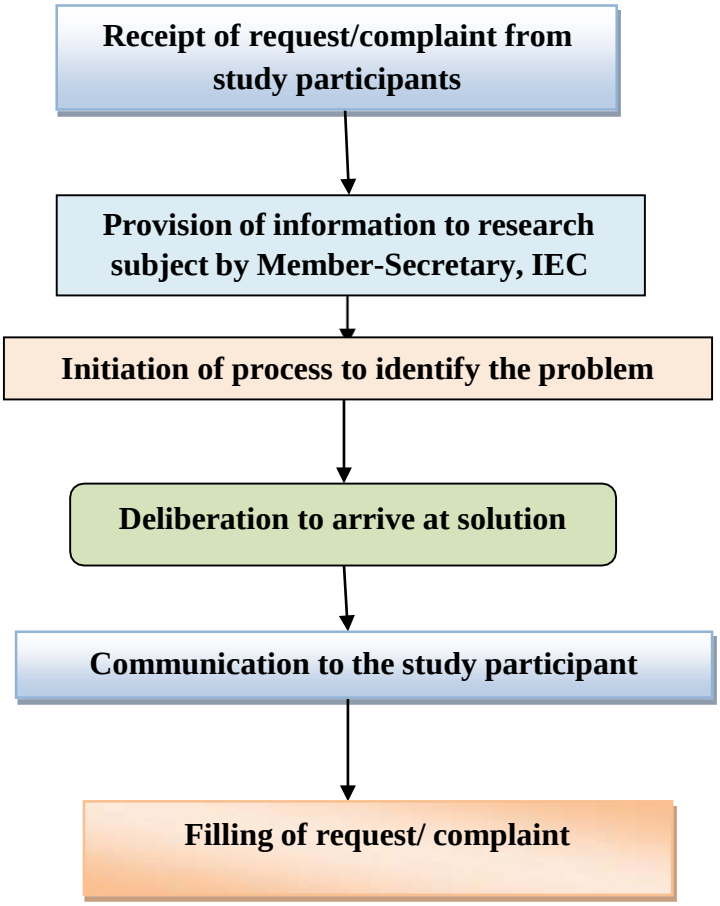
Request :

Action Taken :

Outcome :

…….
Name & Signature of the Member-Secretary, IEC Date

FLOW CHART


Receipt of request/complaint from study participants
Provision of information to research subject by Member-Secretary, IEC
Initiation of process to identify the problem
Deliberation to arrive at solution
Communication to the study participant
Filling of request/ complaint

CHAPTER 17

Protection of Vulnerable Population in Clinical Research

17.1. PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to describe procedures to review research protocol involving vulnerable population. The SOPs provides clear, instructions so that the related activities of the Ethics Committee are conducted in accordance with Indian laws and relevant National and International Guidelines. It describes the requirements concerning review of research that involves groups that could be potentially vulnerable to coercion with regard to autonomy, and present conditions that may affect risk/benefit determinations or bearing unequal burden in research.

17.2. SCOPE

This SOP applies to all policies and procedures of review and assessment applied to all research dealing with vulnerable population that require additional consideration or protection, submitted and approved by the IRB.

17.3. GUIDELINES FOR REVIEW OF RESEARCH INVOLVING VULNERABLE POPULATION

The word vulnerability is derived from the Latin word vulnarere which means ‘to wound’. 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.

Vulnerable groups*:* Effort may be made 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.

a. Research on genetics should not lead to racial in equalities.
b. Persons who are economically or socially disadvantaged should not be used to benefit those who are better off than them.
c. Rights and welfare of mentally challenged and mentally differently able persons who are incapable of giving informed consent or those with behavioral disorders 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.
d. 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.

- 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.

- "Vulnerable" or "special" classes of participants include as listed below:

1. Incapable of making a voluntary informed decision for themselves or whose autonomy is compromised temporarily or permanently, for example
   a) people who are unconscious,
   b) differently abled,
   c) Able to give consent, but whose voluntariness or understanding is compromised due to their situational conditions/contexts.

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.

2. Economically and socially disadvantaged (unemployed individuals, orphans, abandoned individuals, persons below the poverty line, ethnic minorities, sexual minorities – lesbian/ gay/bisexual and transgender (LGBT), etc.)
3. 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
4. Children (up to 18years)

5. Women in special situations (pregnant or lactating women, or those who have poor decision-making powers/poor access to health care).
6. Tribal and marginalized communities
7. Refugees, migrants, homeless, persons or populations in conflict zones, riot areas or disaster situations.
8. Afflicted with mental illness and cognitively impaired individuals, differently abled – mentally and physically disabled.
9. Terminally ill or are in search of new interventions having exhausted all therapies.
10. Suffering from stigmatizing or rare diseases have diminished autonomy due to dependency or being under a hierarchical system (students, employees, subordinates, defense services personnel, health care workers.)
11. Institutionalized individuals, under trials and prisoners.

17.4 PRINCIPLES OF RESEARCH AMONG VULNERABLE POPULATIONS

Vulnerable populations have an equal right to be included in research so that benefits accruing from the research apply to them as well. If any vulnerable group is to be solely recruited then the research should answer the health needs of the group. Participants must be empowered, to the maximum extent possible, to enable them to decide by themselves whether or not to give assent/consent for participation.

In vulnerable populations, when potential participants lack the ability to consent, a Legally Authorized Representative (LAR) should be involved in decision making. Special care must be taken to ensure participant's privacy and confidentiality, especially because breach of confidentiality may lead to enhancement of vulnerability.
If vulnerable populations are to be included in research, all stakeholders must ensure that additional protections are in place to safeguard the dignity, rights, safety and wellbeing of these individuals.

17.5 ADDITIONAL SAFEGUARDS/PROTECTION MECHANISMS

When vulnerable individuals are to be recruited as research participants additional precaution should be taken to avoid exploitation/retaliation/reward/credits, etc., as they may either feel intimidated and incapable of disagreeing with their caregivers, or feel a desire to please them. In the first case, they may be subjected to undue pressure, while in the second, they may be easily manipulated. If they perceive that their caregivers want them to participate in research, or if the caregiver stands to benefit from the dependent's participation, the feeling of being pressed to participate may be irresistible which will undermine the potential voluntariness of the consent to participate.

Researchers must justify the inclusion of a vulnerable population in the research. ECs must satisfy themselves with the justification provided and record the same in the proceedings of the EC meeting.

Additional safety measures should be strictly reviewed and approved by the ECs. The informed consent process should be well documented. Additional measures such as recording of assent and re-consent, when applicable, should be ensured. ECs should also carefully determine the benefits and risks of the study and examine the risk minimization strategies. As potential participants are dependent on others, there should be no coercion, force, duress, undue influence, threat or misrepresentation or incentives for participation during the entire research period. Vulnerable persons may require repeated education/information about the research, benefits, risks and alternatives, if any.

Research on sensitive issues such as mental health, sexual practices/preferences, HIV/AIDS, substance abuse, etc. may present special risks to research participants. Researchers should be cognizant of the possibility of conflicting interests between the prospective participant and LAR and should be more careful. Participants may be prone to stigma or discrimination, specifically when the participant is enrolled as a normal control or is recruited from the general population in certain types of research. Efforts should be made to set up support systems to deal with associated medical and social problems. Protection of their privacy, confidentiality and rights is required at all times – during conduct of research and even after its completion. Whenever possible, ancillary care may be provided such as setting up of a facility, school for unattended children of the participants or a hospital, or counseling centre.

17.6 STAKEHOLDERS OBLIGATION / DUTIES

Researchers

- Recognize the vulnerability of the participant and ensure additional safeguards are in place for their protection
- Justify inclusion/exclusion of vulnerable populations in the study.
- COI issues must be addressed.
- Have well defined SOPs to ensure a balanced benefit-risk ratio.
- Ensure that prospective participants are competent to give informed consent.
- Take consent of the LAR when a prospective participant lacks the capacity to consent.
- Respect dissent from the participant.
- Seek permission of the appropriate authorities where relevant, such as for institutionalized individuals, tribal communities etc.
- Research should be conducted within the purview of existing relevant guidelines/regulations.

Ethics Committees

- During review, determine whether the prospective participants for a particular research are vulnerable.
- Examine whether inclusion/exclusion of the vulnerable population is justified.

- Ensure that COI do not increase harm or lessen benefits to the participants.
- Carefully determine the benefits and risks to the participants and advise risk minimization strategies wherever possible.
- Suggest additional safeguards, such as more frequent review and monitoring, including site visits.
- Only the full committee should do initial and continuing review of such proposals. It is desirable to have empowered representatives from the specific populations during deliberations.
- ECs has special responsibilities when research is conducted on participants who are suffering from mental illness and/or cognitive impairment. They should exercise caution and require researchers to justify cases for exceptions to the usual requirements of participation or essentiality of departure from the guidelines governing research. ECs should ensure that these exceptions are as minimal as possible and are clearly spelt out in the Informed Consent Document (ICD).
- ECs should have SOPs for handling proposals involving vulnerable populations.
- Opine if AV consenting will be permitted or only Audio consenting may be recommended.

Sponsors

- The sponsor, whether a government, an institution or a pharmaceutical company, should justify the inclusion of vulnerable groups in the protocol and make provisions for protecting their rights/safety.
- The sponsor must enable monitoring and ensure that procedures are in place for quality assurance (QA) and quality control (QC).
- The sponsor should ensure protection of the participants and research team if the research is on sensitive topics.

17.7 THE FOLLOWING IS REQUIRED WHEN CHILDREN ARE ENROLLED IN RESEARCH:

As per the National Commission for Protection of Child Rights, a child is defined as a person from 0 to 18 years of age

17.7.1 Research proposals should be scientifically sound.

Risk or harm is a very important consideration in research involving children. Risk refers to a potential harm that can occur to the child as a direct or indirect consequence of the research procedure. The risks entailed in research procedures need to be considered when they are over and above the routine care of the participant.

Research may include any procedure the participant undergoes for research including questionnaires, investigations such as blood sampling, bone marrow aspiration, liver biopsy etc., or therapeutic interventions such as medication or surgery, over and above the routine standard of care for the patient. Harm occurring from participating in research may be physical (such as pain from a needle prick for blood sampling), psychological (such as fear of separation from parents) or social (such as missing school and friends

etc.). Risks must be assessed in relation to benefits.

A benefit is a good outcome. The benefit is usually potential, which means positive but uncertain outcome. The benefit may be direct, as in a direct benefit to the participant; or indirect.

Examples of direct benefits include the possibility of recovery, reduction in pain, improvement in disease severity, etc. Indirect benefits include the opportunity to understand more about the disease, develop social relationship with other patients, etc. Payments for participation should not be considered in the benefit-risk- ratio. Also, patients and participants may consider other benefits such as better access to doctors, access to investigations which are not otherwise freely available, being special patients as part of research, etc. These indirect benefits may be more misunderstood by illiterate patients from poor socioeconomic strata.

The equation between the potential benefit and the risk or potential harm should be at least as favorable for the proposed research procedure as for the alternatives available to the children.

- There should be benefit to children in general and, in most cases, to the individual child participant. 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. 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.
- The need for the study should be justified by a thorough review of literature.
- The research should be conducted by a team of investigators who have the requisite expertise. One or more members of the team should be a pediatrician and/or have prior experience of conducting research involving children.
- Research involving children should take into consideration the unique physiology, anatomy, psychology, pharmacology, social situation and special needs of children and their families.
- Research involving children must be conducted in a child-friendly environment, as far as possible. The settings of the research provide the child and parent adequate medical and psychological support. Both pain and emotional discomfort should be prevented as much as possible. When unavoidable, it should be adequately managed and reduced. To do this, non-invasive procedures should be preferred.

- In general, drugs should be tested for safety, pharmacokinetics, and at least initial indications of efficacy in adults established before they are tested in children. It may often be appropriate to defer pediatric testing until adult testing has reached Phase III or beyond, when substantial data are available on the safety and efficacy of a drug in adults. However, there may be situations where studies involving children would be needed without prior adult studies, for example, surfactant use in premature babies with respiratory distress syndrome. For studies prior to phase III the drug has a therapeutic value in a primary disease of the children.

- Children will not be involved in research that can be carried out equally well with adults.
- 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.
- Interventions that are intended to provide therapeutic benefit are likely to be at least as advantageoustotheindividualchildparticipantasanyavailablealternativeinterventions.
- A parent or legal guardian of each child has voluntarily given fully informed consent.
- The assent of the child should be obtained 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.
- Investigators must seek to involve children in discussions about research and obtain their assent to participation as in accordance with their developmental level and decision-making capacity. The parental/LARs' permission for the child's participation in the research is termed as 'consent', whereas the child's agreement to participate is termed as 'assent'.

17.7.2 Consent process for illiterate parents /LARs

- When a participant is willing to participate but not willing to sign or give thumb impression or cannot do so, then verbal/oral consent may be taken on approval of the EC, in the presence of an impartial witness who should sign and date the document. This can be documented through audio or video recording of the participant, the PI and the impartial witness, all of whom should be captured in the frame. However, verbal consent should be an exception for specific reasons carried out with the approval of EC and not to be followed routinely.
- In non-regulatory, observational studies, sometimes literate or illiterate, parents /LARs may verbally agree to participate but refuse to give their thumb impression. In such cases, again, the documentation of the consent process needs to be done by a literate impartial witness.

In some cases, fresh or re-consent may need to be taken, such as when:

- New information becomes available which would necessitate amendment/deviation of protocol (excluding any new safety related information which can harm the participant if not immediately implemented by the investigator).

- A research participant regains consciousness from an unconscious state or becomes mentally competent to understand the study (procedures to address such a possibility should be spelt out in the informed consent form).
- Long term follow-up or study extension is planned at a later stage.
- There is change in treatment modality, procedures, site visits.
- Attains 18 years of age, or the legally acceptable representative has changed.
- There is possibility of disclosure of identity through data presentation or photographs (which should be camouflaged adequately) in an upcoming publication.
- Future research may be carried out on stored biological samples if not anonymized.

17.7.3Determinants of risk

1. *Age and developmental status*: Risk assessment in children must take into account their age, developmental status and maturity. For example, taking 10 ml blood sample may be low risk for a 10-year-old but high risk for a preterm neonate.
2. *Underlying medical condition*: In some cases, a research procedure that may be of minimal or low risk to a healthy child could be of high risk to a child with underlying medical condition. For example, intramuscular injections that may be safe for healthy children are risky for children with clotting disorders. **Ethics committees should ensure that children with underlying medical conditions that place them at risk due to research procedures are excluded from the study.**
3. *Cumulative characteristics of risk during research*: Determinations about risk should consider the cumulative characteristics of research interventions or procedures and the time period for which they are done. For example, a single chest X-ray is a minimal risk procedure, but if the child has to undergo multiple chest X-rays over a short duration of time, the risk category should be higher.

17.7.4 Type of assays and sample collection

In research involving children, due consideration should be given to the number and type of body fluid assays and investigations.

- Blood samples should be age and/or bodyweight appropriate. Depending on the nature of the study the ethics committee may obtain an independent opinion from a pediatrician regardingthesafetyofbloodvolumesproposedtobedrawnforthepurposeofthestudy.
- The samples should be obtained using appropriate facilities and materials.
- Alternative sampling (for example, urine or saliva sampling) for pharmacokinetic studies should be preferred when possible. However, the ability to use alternative samples may depend on the validation of the analytical methodology and clinical utility of measurements made in these matrices.
- For blood and tissue assays, micro volumes and micro-assays should be used, whenever possible.
- For painful and/or invasive procedures standard pain relief methods should be employed.
- Timing of sampling should be coordinated with the routine standard of care sampling of the patients to avoid repeated needle pricks.

- Sampling should be performed by trained staff.
- The number of attempts for sampling should be limited. Timing of sampling and number of sampling attempts should be defined in the protocol. For example, it is recommended that after one unsuccessful attempt, another experienced person should take over the procedure.

17.7.5 Pediatric formulations to be used in pediatric studies

Formulations used in a study should be described in the protocol. Age-appropriate formulations should be used to avoid the risk of adverse reactions (for example, young children choking on tablets), the risk of dosing errors or inaccuracy. Whenever available, pediatric formulations should be used. Excipients used for the formulation should take into consideration the age of the children included in the study (for example, benzyl alcohol is contraindicated in neonates). Conditions to avoid bacterial contamination and degradation of the medicinal product should be specified in the protocol.

17.8 GUIDELINES FOR ETHICAL APPROVAL BASED ON DEGREE OF RISK

For research procedures that are intended to provide potential direct diagnostic, therapeutic or preventive benefit for the individual child participant, a risk category higher than minimal risk may be justified. For studies having interventions not intended to directly benefit the individual child participant, the risk-levels should be minimum risk or low risk.

17.9 CONCERNS REGARDING INFORMED CONSENT

1. The process of obtaining consent and assent should not be a mere formality, limited to gettingtheparticipants'signaturesontheforms.Insteadthisshouldbeaprocess,wherein the onus is on the investigator to ensure that the parents and children (as far as their developmental level and maturity permits) understand what is going on in the research. This process should also include opportunities for the parents and children to ask questions. The consent process is not a one-time process but should be an ongoing interaction between the researcher and the participant, to help resolve the queries which may arise in the participant's mind during the course of the study.
2. The language of the patients/participant information sheet (PIS) should be simple and easily understood by the parents. Many times, in order to protect themselves from any future litigation, investigators fill PIS with technical terms (medical and legal) which the parents find difficult to understand. While translating to a local language difficult technical words must be avoided, and simple daily-use words that the participant is able to understand should be used.
3. When checking that parents understand all the aspects of research participation, a particular concern is whether they understand that they will be participating in research and that the purpose of research differs from the purpose of normal clinical care. The purpose of research is to generate knowledge, usually for the benefit of patients or individuals in the future. The misbelief that the purpose of research is treatment is termed as therapeutic misconception.

17.9.1 Children's assent

Assent is defined as a child's affirmative agreement to participate in research. A mere failure of the child to object should not be interpreted as assent. The assent process should take into account the children's developmental level and capability of understanding. Cultural and social factors also play an important role. Children vary considerably in the ability to understand abstract concepts depending on their age

and maturity. The assent form chosen should be appropriate for the child's age and reading ability. Children with chronic illness may have been challenged to develop increased capacity to make independent judgments based on previous experiences. The other important issue here is the child's general level of independence and autonomy.

Content of the assent form has to be in accordance with the developmental level and understanding capacity of the child. For example, a child aged 8 years should be told what exactly she/he is going to undergo, although they may not understand the concept of research. Younger children are better able to grasp the more practical aspects of research (e.g., what they are expected to do or what will happen) than they are to understand the abstract concepts such as randomization. For a 15-year-old, however, the assent process should be similar to the informed consent process. If the study is of a long duration study, the researchers may have to repeat the assent process with more information, as the child grows older.

17.9.2 Age and method of obtaining assent

For children between 7 (84 months and above) and 11 years of age, oral assent must be obtained in the presence of parent/LAR. For children between 12 and 18 years of age, written assent must be obtained. If a child becomes 13 years old during the course of the study, then written assent must be obtained in addition to parent/LAR consent. This is a joint decision- making process between the child and the concerned adult. In cases of verbal assent, the parent /LAR's counter-signature must be obtained confirming that the child's verbal assent has been taken. Re-assent must be taken in all the same situations as re-consent as mentioned above. For children less than 7 years of age, parental consent is sufficient. As assent is part of the informed consent process, the regulations as per the CDSCO guidelines for regulatory clinical trials apply for assent as well.

17.9.3 Content of assent form –

The type and amount of information given needs to be simplified as per the child's cognitive and developmental level. The information should be simple, and age-appropriate.

17.9.4 Waiver of assent

Waiver of assent may be provided by the ethics committees in the following situations:

1. If the research has the potential of directly benefiting the child and this benefit is available only in the research context. In such situations, the child's dissent may be overruled.
2. Waiver of assent may also be considered if the research involves children with mental retardation and other developmental disabilities, where the children may not have the developmental level and intellectual capability of giving assent.
3. Assent may also be waived under the same conditions in which adult's informed consent maybe waived.

Dissent or refusal of a child to participate must always be respected. Explanation must be given to ensure that the child understands that she/he may withdraw her/his assent at any time during the study.

17.10 RESEARCH IN NEONATES

Neonates represent the most vulnerable group within the pediatric population. Study protocols in this population should take into account this, and the potential long-term effects of interventions, including developmental effects. ECs' reviewing any research proposed in neonates should have an advisory member with expertise in neonatal research/care.

ECs' should carefully scrutinize all research proposed in neonates for potential risks. Risks if any should be carefully weighed against possible benefits in this fragile population. ECs' should ensure a proper scientific review of the protocol by a competent person/s to remove any risks resulting from poor methodology. Neonates should be researched when the findings of the study will have potential implications for neonatal healthcare. All measures to reduce risks should be undertaken. When possible, older children should be studied before conducting studies in younger children and infants. Within neonates, those who are critically ill should be considered for research even more carefully. Parents or caretakers of these babies face stresses that may interfere with their ability to make an informed decision on behalf of their baby. Strategies such as continuous consent can to some extent reduce such problems. The consent of one parentis required for studies in neonates with research exposing them to no or minimal risk or in studies that offer the prospect of direct benefit to the participant. However, for studiesthat do not offer the prospect of direct benefit or are high risk, consent from both parentsis required. The exception being when only one parent has legal responsibility for the careand custody of the child, one parent is deceased, unknown, incompetent, or not reasonablyavailable. In such cases, it is the duty of the investigators to provide adequate justification.

If one of the parents is a minor, then consent should not be taken from her/him. If both parents are minors, then enrolment of such a baby should be avoided as far as possible. To enroll such neonates for research, the investigators should provide adequate justification to the EC. A legally acceptable representative should provide an informed consent in such situations.

When adults are unable to consent, the IRB determines:

- A non-therapeutic clinical trial (i.e. a trial in which there is no anticipated direct clinical benefit to the participant) should be conducted in participants who personally give consent and who sign and date the written consent document.
- Non-therapeutic clinical trials may be conducted in participants with consent of a legally acceptable representative provided the following conditions are fulfilled:
    - The objectives of the clinical trial cannot be met by means of a trial in participants who can give consent personally.
    - The foreseeable risks to the participants are low.
    - The negative impact on the participant's wellbeing is minimized and low.
    - The clinical trial is not prohibited by law.
    - The opinion of the IEC is expressly sought on the inclusion of such participants, and the written opinion covers this aspect.

- 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.

17.11 THE FOLLOWING IS REQUIRED WHEN PREGNANT OR NURSING WOMEN ARE ENROLLED IN RESEARCH:

Pregnant or nursing women: 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 fetus or nursing infant and the object of the research is to obtain new knowledge about the fetus, pregnancy and lactation. As a general rule, pregnant or nursing women should not be participants of any clinical trial except such trials as are designed to protect or advance the health of pregnant or nursing women or fetuses or nursing infants, and for which women who are not pregnant or nursingwould not be suitable participants.

a) The justification for participation of these 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 fetal abnormalities and for conditions associated with or aggravated by pregnancy etc. Women should not been courage to discontinue nursing for the sake of participation in research and in case she decides to do so, harm of cessation of breast-feeding 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.

b) 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.

c) Research related to pre-natal diagnostic techniques: In pregnant women such research should be limited to detect the fetal 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 fetus.

17.12 FOLLOWING IS REQUIRED DURING GENETIC STUDIES:

Genetic Counselling

a) Pre- and post-test counselling should be given by persons who are qualified and experienced in communicating the meaning of genetic information as some conditions may require termination of pregnancy or selection of embryos to avert birth of a genetically abnormal child/foetus. While disclosing the result, appropriate options should be provided to the family to enable them to come to a decision.

b) While general principles of counselling require the presence of both spouses, necessary care and caution must be taken so as not to break families. Truthful counselling with extreme caution and patience is essential to explain the situation in a proper perspective in order to minimize psychosocial harm.

Informed Consent:

Stringent norms and caution should be followed in the consent process when done for research purposes. For routine genetic diagnostic testing, written consent may or may not be needed as per institutional policies; however, for any research it is required. Informed written consent is essential for procedures such as pre-symptomatic testing, next generation sequencing (NGS), prenatal testing, genomic studies, carrier status etc. It needs to be emphasized that consent for screening or a subsequent confirmatory test does not imply consent to any specific treatment or termination of the pregnancy or for research. If the research or testing involves a child, appropriate age-specific assent (verbal/oral/written) should be obtained along with parental consent. In addition to the general contents specified in section 5, the consent form for genetic testing for research may have explanations/details on the following elements:

- the nature and complexity of information that would be generated;
- the nature and consequences of return of results and choice offered to the participant whether to receive that information or not and incidental findings, if any;
- direct/indirect benefits and their implications including if there are no direct benefits to the participants;
- How the data/samples will be stored, for how long, and procedures involved in anonymisation, sharing , etc.
- Choice to opt out of testing/withdraw from research at any time; • whether the affected individual or the pro band would like to share her/his genetic information with family members who may benefit from it; and • issues related to ownership rights, IPR concerns, commercialization aspects, benefit sharing.
- Group consenting or community consenting also can be involved were population based studies are involved. Community head or culturally appropriate authority consent must be taken. However, this doesn't exempt individual informed consent.

Geriatric Population:

1. The geriatric population age comprises arbitrarily 65 years and older (importantly of older age range 75 and above, to the extent possible.
2. Geriatric population must be included in phase 3 database (or phase 2 or studies conducted exclusively in geriatric participants at the sponsor's option) in meaningful number. Sufficient representation of geriatric population is expected as compared to younger population so that accurate comparison of drug response, effectiveness and adverse event rates can be done.

3. Drug to drug interactions and pharmacokinetic differences (related to excretory function) are the recognized examples in geriatric population for their different behavior when compared to younger population. Determination of such difference if exists is of prime importance and subsequently becomes one of the major objectives of the study.
4. It is recognized that certain drugs and applications (some topically applied agents, some proteins) do have low systemic drug levels may limit minimize difference to a certain insignificant level.

17.13 CATEGORIZATION OF PROTOCOLS

Vulnerable population will be subjected to full board Initial review (SOP 4aVER2. Research involving vulnerable populations is not eligible for expedited review or exemption from review.

ReviewProcess

- The IEC evaluates whether additional safeguards have been included in the study to protect the rights and welfare of vulnerable participants.
- The IEC requires at least one or more individuals who are knowledgeable about or have experience in working with these participants as part of the review process.
- New 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 and as per SOP04a/04b.

The research protocol involving vulnerable population will be reviewed according to current requirement and guidelines. The decisions are arrived at using the approved checklist for lead discussants (Refer Annexure1-5).

If the research includes a vulnerable population that is not covered in the above list or there are no national or international guidelines for ensuring protections, IRB willevaluate the research proposal to ensure that precautions are taken to protect the participants.

The protocol should be reviewed keeping in mind the following points:

- Measures to protect autonomy,
- Risk/benefit determinations with respect to the vulnerability
- Whether vulnerable participants are bearing unequal burden in research.

Member of the IRB who would be reviewing such protocols should be well versed with the potential harm or risk of such population participating in the study. The checklist for different vulnerable population provided in Annexure (A-F) should be used. Special justification is required for inviting vulnerable individuals to serve as research participants and, if they are selected, the means of protecting their rights and welfare must

be strictly adhered to.

The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations. The central issue for the IEC to consider is whether the potential subject's ability to exercise free choice is limited in some way.

Reviewing research protocol involving vulnerable population: When researchers are likely to approach participants, who lack the ability to consent, the IRB evaluates whether:

- ✓ The proposed plan for the assessment of the capacity to consent is adequate
- ✓ Before requesting assent/ surrogate consent to participate in clinical trial the Investigator must provide the LAR and/or impartial witness with the following information in a language that is non- technical and understandable by the LAR and/or impartial witness and the same shall be recorded through audio-visual means.
- ✓ Assent/surrogate consent of the participants is a requirement wherever possible, and, if so, whether the plan for assent/ surrogate consent is adequate.
- ✓ There is adequate room for ensuring the involvement of the LAR and/or impartial witness in the consenting process.
- ✓ Details of such questions if any, asked by the LAR/ or impartial witness and his/her understanding on consent are also to be recorded through the audio video means. The process of signing/putting thumb impression by the LAR/ or impartial witness should also be video recorded.
- ✓ When a research participant regains consciousness from unconscious state or is mentally competent to understand the study. If such an event is expected then procedures to address it should be spelt out in the informed consent form.

Responsibility

The IRB Secretariat is responsible for receiving, verifying, and managing the hard copies of the received research protocols pertaining to vulnerable groups based on new and evolving applicable regulations and guidelines as per the checklist.

The Secretariat should create a study specific file, distribute the packages and study assessment forms to the IEC members for review with the updated checklist (1-5), and communicate the review results to the investigators.

- It is the responsibility of the IEC Secretariat to maintain up-to-date tools (e.g. checklist) for review of research pertaining to vulnerable groups based on new and evolving applicable national and international regulations and guidelines.
- Maintain file for update-checklist (1-5) which conforms to recent / current applicable regulations and guidelines

The Member Secretary will assign two or more members of the IRB who have a thorough understanding of the ethical review process and experience in the field of research to review such type of protocols. The lead discussants should be familiar and trained in the concept of vulnerability and protections for participants with diminished autonomy.

IRB Chairperson/ Member Secretary is responsible for ensuring that IRB members are well versed in new and evolving regulations and guidelines pertaining to vulnerable populations through regular training programs, for selecting lead discussants with appropriate expertise to conduct the reviews of such research, and for securing appropriate consulting expertise as needed for selected reviews.

IRB members are responsible for verifying, and reviewing the research protocols pertaining to vulnerable populations using study assessment form and checklist (Refer SOP17, Annexure 1-5).
IRB member is responsible for conducting appropriate review of research planned for vulnerable populations, including an assessment of potential for coercion, in consultation with any appropriate experts and resources as described in this SOP.

IRB Members will review the protocol and the informed consent document or assent form (Refer SOP 4a.5.4) and opine.

IRB Meeting

- The details of review procedures and communication of decision is described in detail inSOP05/V6
- Document review of risk assessment in IEC minutes for the protocols involving vulnerable population.
- IEC Member Secretary will minute the discussions.

Annexure1

ANX1/VER2/SOP17/VER2

Checklist 01- Requirements for Research Involving

Investigator IRB:

Study Title:

RISK DETERMINATION	BENEFIT ASSEMENT	IEC ACTION
⌋ Minimal risk	With direct potential benefit to child□ Without direct potential benefit to child□	Approved□ Not Approved□
	No direct benefit to individualbut offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	Approved□ case by case (with special safeguards Not Approved□
⌋ Less than minimal risk	With direct potential benefit to child□ Without direct potential benefit to child□	Approved□ Not Approved□
	No direct benefit to individualbut offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	Approved□ case by case (with special safeguards Not Approved□
☐ Minor increase over minimal risk or Low risk	With direct potential benefit to child□	Approved□ Not Approved□

	Without direct potential benefit to child□	
	No direct benefit to individualbut offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	Approved□ case by case (with special safeguards Not Approved□
☐More than minimal risk or High risk	With direct potential benefit to child□ Without direct potential benefit to child□	Approved□ Not Approved□
	No direct benefit to individualbut offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	Approved□ case by case (with special safeguards Not Approved□

i. 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
ii. Risk may not be more than a minor increase over minimal risk, consent of both parents required under normal circumstances.
iii. Approval to proceed with this category of research must be made by the IEC with input from selected experts

Risk and Benefit assessment in Children	**Yes**	**No**	**NA**
Does the research pose greater than minimal risk to children?	☐	☐	☐
If yes: Are convincing scientific and ethical justification given?	☐	☐	☐
If yes: Are adequate safeguard in place to minimize these risks?	☐	☐	☐
Does the study involve normal volunteers?	☐	☐	☐

Risk and Benefit assessment in Children	**Yes**	**No**	**NA**
If yes: Is the inclusion of normal volunteers justified?	☐	☐	☐
Have appropriate studies been conducted on animals and adults justified?	☐	☐	☐
If No: Is the lack of appropriate studies conducted on animals and adults justified?	☐	☐	☐
Will older children be enrolled before younger ones?	☐	☐	☐
Is permission of both parents necessary? If Yes- please justify	☐	☐	☐
Will efforts be made to ensure that parents' permission to involve their children in research studies is free from coercion, exploitation, and /or unrealistic promises?	☐	☐	☐
Are provisions made to obtain the assent of children over 7 and, where appropriate, honoring their dissent?	☐	☐	☐
Are provisions made to protect participants' privacy and the confidentially of information regarding procedures?	☐	☐	☐
Are there special problems that call for the presence of a monitor or IEC member during consent procedures?	☐	☐	☐
Are special needs of adolescents such as counseling and confidentiality accounted for in the research design?	☐	☐	☐
Are there any special problems such as confidentiality and reporting that might arise in sensitive research about child abuse or sexual practices of teenagers?	☐	☐	☐
Does the research involve implications for other family member? (for example, genetic risk , HIV infection , Hepatitis C)	☐	☐	☐
If Yes: Are adequate mechanisms in place to deal with other members of the family?	☐	☐	☐
Should parents be required to be present during the conduct of the research? (Are proposed participants very young? Are the procedures involved painful? Must subject stay overnight in the hospital when they otherwise would not have to?)	☐	☐	☐

Comments:

_____

Name & Sign of Lead discussant:
Date:

Annexure 2

ANX2- VER2/SOP 17/VER2

Checklist 02 - Requirements for Research Involving Pregnant or nursing women, Fetuses & nursing infant

Investigator: ***IRB#:***

Study Title:

Research Involving Pregnant or nursing women, Fetuses & nursing infant

RISK DETERMINATION	BENEFIT ASSESSMENT	IEC ACTION
☐Minimal	With or without direct benefit	Approvable
☐Less than minimal risk	With or without direct benefit	Approvable
☐Minor increase over minimal risk or Low risk	With or without direct benefit	Approvable
☐More than minimal risk or High risk	Potential benefit	Approvable
☐More than minimal risk or High risk	No direct benefit to individual but offer general knowledge aboutdisorder and may benefit to the societyor future generations are likely to benefit.	Approvable on case to case basis with special safeguards

	Yes	**No**	**NA**
Where scientifically appropriate, has preclinical studies including studies on pregnant animals, and clinical studies including studies on non-pregnant women been conducted and data made available for assessing potential risks to pregnant or nursing women, nursing infant and fetuses	☐	☐	☐
The risk to the fetus or nursing infant is not greater than minimal, or any risk to the fetus which is greater than minimal is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus or nursing infant;	☐	☐	☐

Any risk, is the least possible, for achieving the objectives of the research	☐	☐	☐
The woman's consent or the consent of her legally authorized representative is obtained in accordance with the informed consent provisions , unless altered or waived in accord with Sops	☐	☐	☐

	Yes	**No**	**NA**
The woman or her legally authorized representative, as appropriate, is fully informed regarding the reasonably foreseeable impact of the research on the fetus or resultant child;	☐	☐	☐
If the research involves minors who are pregnant, assent and permission will be obtained in accordance with the NDCT rules and ICMR guidelines	☐	☐	☐
No inducements, monetary or Otherwise will be offered to terminate a pregnancy;	☐	☐	☐
Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and	☐	☐	☐
Individuals engaged in the research will have no part in determining the viability of a fetus.	☐	☐	☐
Does this research promises therapeutic or preventive benefits (e.g. 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 fetal abnormalities and for conditions associated with or aggravated by pregnancy)	☐	☐	☐
Does the study involves discontinuation of nursing for the sake of participation in research Is the cessation of breast-feeding to the nursing child justified? Is breast feeding harmful to the infant? Does the research has provisions for compensation in terms of supplying supplementary food such as milk formula?	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
Can this research be conducted in women who are not pregnant or nursing	☐	☐	☐

Does this research protect or advance the health of pregnant or nursing women or fetuses or nursing infants,	☐	☐	☐
Is this research related to termination of pregnancy and is as per the Medical Termination of Pregnancy Act, GOI, 1971.	☐	☐	☐
	Yes	**No**	**NA**
Does this research violate any provisions of the Medical Termination of Pregnancy Act, GOI,1971	☐	☐	☐
Is this research related to pre-natal diagnostic techniques in pregnant women	☐	☐	☐
Is this research limited to detect the fetal 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 fetus	☐	☐	☐
Does this research violate any provisions of the Prenatal Diagnostic Techniques (Regulation and Prevention of Misuse) Act, GOI,1994	☐	☐	☐

THIS RESEARCH INVOLVES FETUSES AFTER DELIVERY

	Yes	**No**	**NA**
1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to fetuses;	☐	☐	☐
2. The individual(s) providing consent is fully informed regarding the reasonably foreseeable impact of the **research** on the fetus or resultant child;	☐	☐	☐
3. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;	☐	☐	☐
4. Individuals engaged in the **research** will have no part in any decisions as to the timing, method, or procedures used to terminatepregnancy;	☐	☐	☐
5. Individuals engaged in the **research** will have no part in determining the viability of a fetus.	☐	☐	☐

AND

A. Fetuses of uncertain viability	Yes	No	NA
1. Does the research hold out the prospect of enhancing the probability of survival of the particular fetus to the point of viability, and any risk is the least possible for achieving the objectives of the research;	☐	☐	☐
OR			
The purpose of the **research** is the development of important biomedical knowledge which cannot be obtained by other means and there will be no risk to the fetus resulting from the **research**;	☐	☐	☐
2. The legally effective informed consent of either parent of the fetus or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained.	☐	☐	☐

And/or

B. Nonviable fetuses	Yes	No	NA
1. Vital functions of the fetus will not be artificially maintained;	☐	☐	☐
2. There will be no risk to the fetus resulting from the research;	☐	☐	☐
3. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and	☐	☐	☐
4. The legally effective informed consent of both parents of the fetus will be obtained in accord with the ICMR guidelines except that the waiver and alteration provisions do not apply. However if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable fetus will suffice to meet the requirements of this paragraph. The consent of a legally authorized representative of either or both of the parents of a nonviable fetus will not suffice to meet the requirements of this paragraph.	☐	☐	☐

Comments: _____

Name& Sign of Lead discussant:

Date:

Annexure 3

ANX3- VER2/SOP 17/VER2

Checklist 03- Research Involving Cognitively Impaired Adults

- The purpose of this checklist is to provide support for IRB members or the Designated Lead discussant when reviewing research involving cognitively impaired adults as participants.

For review, this checklist is to be completed by the Designated Reviewer to document determinations required by the regulations and protocol specific findings justifying those determinations.

1. **Research Involving Cognitively Impaired Adults in which there is Anticipated Direct Benefit to the subject** (All items must be "Yes")		
☐Yes	☐No	One of the following is true (Check the box that is true) • The risk to the participants is presented by an intervention or procedure that holds out prospect of direct benefit for the individual subject. • More than minimal risk to participants is presented by monitoring procedure that is likely to contribute to the participants well – being.
☐Yes	☐No	The risk is justified by the anticipated benefit to the participants.
☐Yes	☐No	The relation of anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.
☐Yes	☐No	The proposed plan for the assessment of the capacity to consent is adequate.
☐Yes	☐No	Assent is required of: (One of the following must be "**Yes**") One of the following is true (**Check box that is true**) < All Participants < All Participants capable of being consulted. < None of the participants
☐Yes	☐No	The consent document includes a signature line for a legally authorized representative.

2. **Research Involving Cognitively Impaired Adults in which there is No Anticipated Direct Benefit to the subject** (All items must be "Yes")		
☐Yes	☐No	The proposed plan for the assessment of the capacity to consent is adequate.
☐Yes	☐No	The objectives of the trial cannot be met by means of study of

		participants who can give consent personally.
☐Yes	☐No	The foreseeable risks to the participants are low.
☐Yes	☐No	The negative impact on the subject‘s well-being is minimized and low.
☐Yes	☐No	The trial is not prohibited by law.
☐Yes	☐No	Participants have a disease or condition for which the procedures in the research are intended.
☐Yes	☐No	Participants will be particularly closely monitored.
☐Yes	☐No	Participants will be withdrawn if they appear to be unduly distressed.
☐Yes	☐No	The proposed plan for the assessment of the capacity to consent is adequate.
☐Yes	☐No	Assent is required of (One of the following must be “**Yes**”) One of the following is true (**Check box that is true**) < All Participants < All Participants capable of being consulted. < None of the participants
☐Yes	☐No	The consent document includes a signature line for a legally authorized representative.

Comments-

Name &Sign lead discussant:
Date:

Annexure 4

ANX4- VER2/SOP 17/VER2

Checklist 04-Research Involving Students, Employees or Residents

Participants who are students, employees or residents require special considerations.

The proposed plan for the assessment of the capacity to consent is adequate.	□Yes	□No
Have the participants been assured that their status (education, employment, and/or promotion) will not be affected by any decision to participate or not?	□Yes	No □
Have the risks to participants been minimized?	□Yes	□No
Have participants been assured that participation is voluntary (no signs of coercion)?	□Yes	□No
Have participants been assured that confidentiality will be protected or maintained?	□Yes	□No

Comments-
Name & Sign of Lead discussant
Date:

Annexure 5

ANX5- VER2/SOP 17/VER2

Checklist 05 - Considerations for Genetic Research
Investigator: **IRB#**
Study Title:

1. Will the samples be made anonymous to maintain confidentiality? If yes, stophere	☐Yes	☐No
2. Has the investigator established clear guidelines for disclosure of information,including interim or inconclusive research result?	☐Yes	☐No
3. Has the appropriateness of the various strategies for recruiting participants andtheir family members been considered?	☐Yes	☐No
4. Does the proposed study population comprise family members?	☐Yes	☐No
5. Will family members be implicated in the studies without consent?	☐Yes	☐No
6. Will the samples be destroyed in the future?	☐**Yes**	☐**No**
7. Is genetic counseling being offered?	☐Yes	☐No

Comments-
Name & Sign of Lead discussant:

Date:

Annexure 6

ANX6- VER2/SOP 17/VER2

Checklist –Requirements for Research involving terminally ill patients

Principal Investigator
Proj. No.-
Study Title:

RISK DETERMINATION	BENEFIT ASSEMENT	IEC ACTION
☐ Minimal	☐ With direct benefit ☐ Without direct benefit	☐ Approved ☐ Not Approved
	☐ Potential benefit	☐ Approved ☐ Not Approved
	☐ No direct benefit to individual but offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	☐ Approved case by case (with special safeguards ☐ Not Approved
☐ Less than minimal risk	☐ With direct benefit ☐ Without direct benefit	☐ Approved ☐ Not Approved
	☐ Potential benefit	☐ Approved ☐ Not Approved
	☐ No direct benefit to individual but offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	☐ Approved case by case (with special safeguards ☐ Not Approved
☐ Minor increase over minimal risk or Low risk	☐ With direct benefit ☐ Without direct benefit	☐ Approved ☐ Not Approved
	☐ Potential benefit	☐ Approved ☐ Not Approved

	☐No direct benefit to individual but offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	☐Approved case by case (with special safeguards ☐Not Approved
⌋ More than minimal risk or High-risk	☐With direct benefit ☐Without direct benefit	☐Approved ☐Not Approved
	☐ Potential benefit	☐Approved ☐Not Approved
	☐ No direct benefit to individual but offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	☐Approved case by case (with special safeguards ☐Not Approved

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

Risk and Benefit assessment in terminally ill patients.	**Yes**	**No**	**NA**
Does the research pose greater than minimal risk to patients?	☐	☐	☐
If yes: Are convincing scientific and ethical justification given?	☐	☐	☐
If yes: Are adequate safeguard in place to minimize these risks?	☐	☐	☐
Are appropriate studies that have been conducted on animals and adults justified?	☐	☐	☐
If No: Is the lack of appropriate studies conducted on animals and adults justified?	☐	☐	☐
Do the anticipated benefits justify requiring the subjects to undertake the risks	☐	☐	☐
Is inclusion of vulnerable population warranted?	☐	☐	☐
Can the research question be answered by using a non-vulnerable population?	☐	☐	☐
Will efforts be made ensure that participants are free from coercion, exploitation, and /or unrealistic promises?	☐	☐	☐
Are provisions made to obtain the consent?	☐	☐	☐

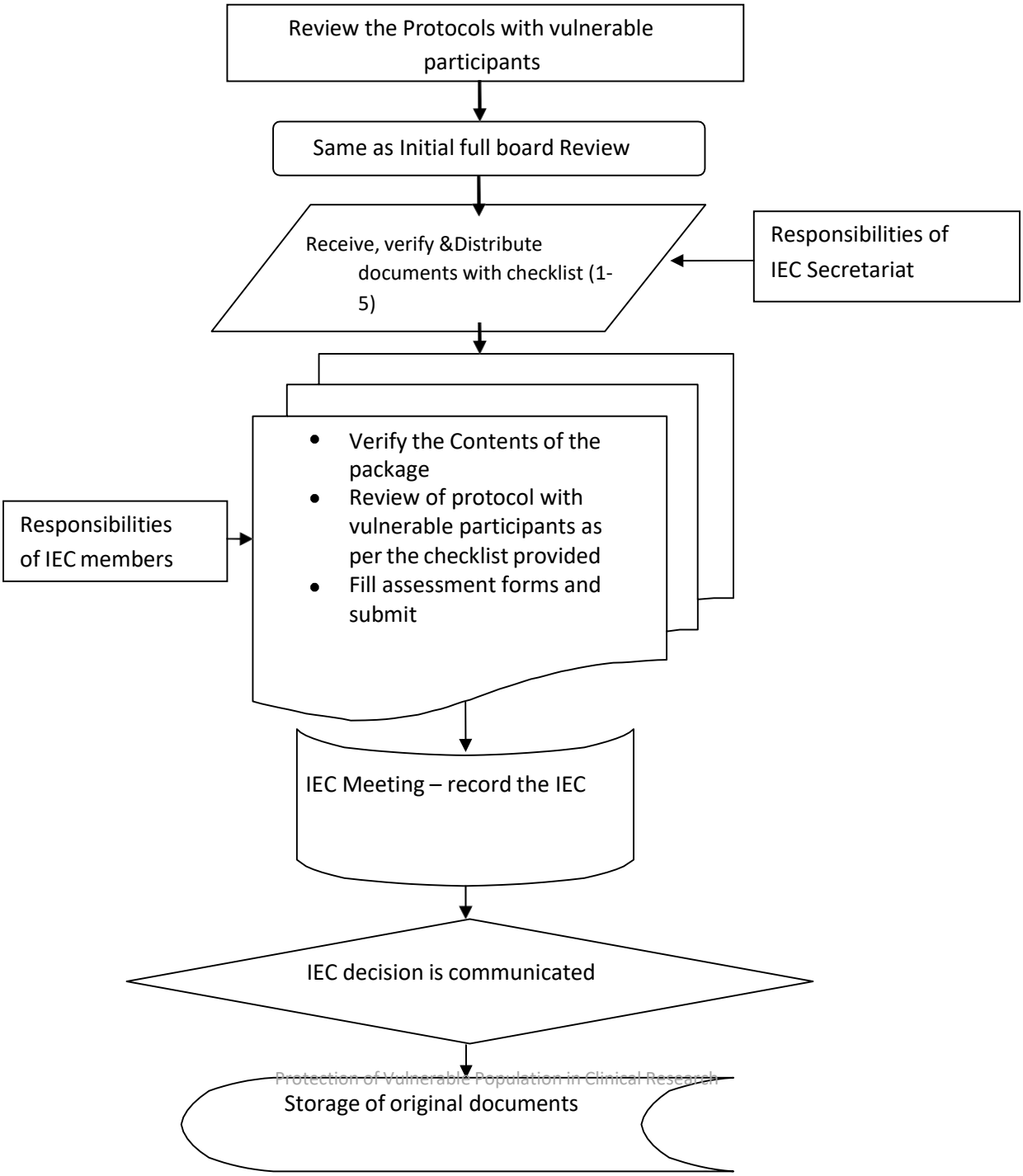
Are provisions made to protect participants' privacy and the confidentially of information regarding procedures?	☐	☐	☐
Are there special problems that call for the presence of a monitor or	☐	☐	☐

Risk and Benefit assessment in terminally ill patients.	**Yes**	**No**	**NA**
IEC member during consent procedures?			
Are special needs of counseling and confidentiality accounted for in the research design?	☐	☐	☐
Are there any special problems such as confidentiality and reporting that might arise in this research	☐	☐	☐

Comments-

Name & Sign of Lead Discussant:
Date:

Flow Chart



CHAPTER 18

Review of Academic Clinical Trial

18.1 Purpose

The IEC should review and must approve, every research study involving human participants and other forms of studies, before the research is initiated. The IEC should evaluate the scientific rationale, scope and, methodology, and the ethical aspects of the study. The committee should evaluate the possible risks to the participants with proper justification as well as the expected benefits to participants/community. The adequacy of documentation for ensuring privacy & confidentiality should also be reviewed.

The purpose of this Standard Operating Procedure (SOP) is to describe the procedures for submission, review, IRB communications for academic clinical research.

18.2 Scope

This SOP applies to the submission, review and IEC communications of all academic clinical trials submitted for initial review and review of revised and resubmitted protocols submitted for approval of the IEC. The specific points/items in the Assessment Form must be adequately addressed in the protocol and/or protocol-related documents submitted for the review. Relevant comments made during discussion and deliberation about a study should be recorded in the minutes of the meeting.

Detailed instructions

Academic Clinical Trial

As per the New drugs and Clinical Trials rules, 2019, no permission is required for conduct of academic clinical trials from the licensing authority, where .
(i) The clinical trial in respect to the permitted drug formulation is intended solely for academic research purposes for a new indication or new route of administration or new dose or new dosage form,
(ii) Theclinicaltrialreferredtoinclause(i)hasbeeninitiatedafterpriorapprovalbytheEthics Committee for clinical trial,
(iii) the observations generated from such clinical trial are not required to be submitted to the Central Licensing Authority, and
(iv) the observations of such clinical trial are not used for promotional purposes.

In the event of a possible overlap between the academic clinical trial and clinical trial or

a doubt on the nature of study, the MCC Ethics Committee shall inform the Central Licensing Authority in writing indicating its views within thirty working days from the receipt of application to that effect. In case the Central Licensing Authority does not send the required communication to MCC Ethics Committee within thirty working days from the date of receipt of communication from the MCC Ethics Committee, it shall be presumed that no permission from the Central Licensing Authority is required.

In such trials, the investigator has the dual responsibility of being an investigator as well as the sponsor. 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.

The trials must be registered in CTRI and there should be mechanism for appropriate methods for informed consent, conduct of trial and proper follow-up of patients.
For students conducting clinical trials as part of their academic thesis, the guide and the academic institution should take up the responsibilities of the sponsor.

Submission

- PI should submit mandatory documents as per checklist**ANX1-VER2/SOP18/VER2**
- In case of clinical trials involving drugs/devices, it is mandatory to submit drug safety and toxicity profile, adverse events data (incidence, DSMB reports etc.), Technical specifications of devices, risk – benefit assessment

Full board Review

All academic clinical trials submitted for IRB approval will be reviewed in the full board meeting.
IEC has to approve such studies after due consideration of benefits and risks and all other ethical aspects and inform to the licensing authority if there is a possible overlap between academic clinical trial and clinical trial as per the New Drugs and Clinical Trials rules, 2019.
Refer SOP 04a and SOP05 for detailed review process.

Communicating Decision

IRB shall intimate the licensing authority about the approval of clinical trials intended for academic purposes such as use of approved drug formulation to study new indication or new route of administration or new dose or new dosage .The IRB shall await for comments from the CLA for a period of 30 days from the date of receipt of communication from the IRB. If no communication from CLA is received in the specified time frame, IRB shall presume that no permissions are required from the licensing authority and will issue the final approval letter for the study. The researcher can delink data to maintain confidentiality and safeguard the information for basic research. However, If the result of the research is of benefit to the health of the participant then, with approval of the EC, data could be re-linked for communication of the result.

Annexure

AX1-VER2/SOP18/VER2

Checklist of Documents

Item No.	Mandatory Documents	Yes	No	NA
1	Project Submission Form (both hard and soft copies) duly signed by the Principal Investigator			
	A. Grouping of Project			
	B. Project Fact Investigators Declaration Conflict of Interest Consent of Head of the PI's Department Consent from Working Group			
	C. Project Submission Overview			
	D. Budget Sheet for the Proposed Study Detailed Budget for the Proposed Study			
2	Study Protocol			
	Participant Information Sheet & Informed consent forms (ICFs) in English, Marathi & Hindi (and if required any other language)			
3	Back translations of ICFs (not mandatory for Hindi and Marathi)			
4	Case Record Form			
5	Questionnaire (if applicable)			
6	Questionnaire Validation certificates (if applicable)			
8	Investigator Brochure			
9	Package insert/label			
10	Insurance policy			
11	NOC from ICMR/HMSC			
12	Clinical Trial Agreement(CTA)/ Memorandum of Understanding(MOU)/ Material Transfer Agreement(MTA) if applicable			
13	Brief resume of Principal Investigators and Co-investigators (1 Page each)			
14	MMC registration of Principal Investigators and Co- investigators			
15	Copy of Valid Good Clinical Practice training certificate for all investigators			
16	Cover letter from the investigator			

CHAPTER 19

Training of IRB

19.1Purpose

This SOP defines the procedure for training IRB members/IRB Secretariat to ensure optimal review of research protocols submitted to IRB.

19.2 Scope

This SOP is applicable to all members of the IRB and administrative staff of IRB.

19.3 Responsibility

The Chairperson and Member Secretary of the respective Committees will be responsible for ensuring trainings of IRB.

Procedure

- At the time of reconstitution of the IRB, the latest SOPs will be circulated to all members of the IRB via e-mail. Members will be encouraged to familiarize themselves with the SOPs before attending the IRB meeting.
- Member Secretary and other members will be selected at least 3 months and 1 month in advance respectively. Member Secretary designate will be inducted into the IRB as an observer before he/she takes on the mantle in the new IRB. Other member- designates may attend the board meeting as observers before starting their tenure as IRB members.
- At the time of appointment to the IRB, each member should have a valid GCP (Good Clinical Practice) certificate as a pre-requisite to induction in the IRB as GCP certificate is the universal standard in Clinical Research.
- The members will be required to update their GCP certification periodically.
- The Chairperson and/or Member Secretary will conduct a presentation of the MCC IRB SOPs in the first meeting of the newly constituted IRB. Regular trainings will be conducted on the various SOPs through the term of the IRB.
- In addition to the SOP and GCP training, the IRB Secretariat will organize regular training for the IRB members. An annual training calendar will be prepared by the IRB Secretariat.
- The topics of training will be finalized by the Chairperson/Member Secretary. The training will be conducted by Chairperson, or any other member of the IRB specialized in a given topic. The IRB may also request a non-IRB member specialized in a topic of importance to impart training to the IRB members. The training programme will be scheduled and spread over the year.
- The topics of training will be selected to help members understand their roles and responsibilities while reviewing the research protocols. The topics will also include, but are not limited to regulatory guidelines, advancements in health

research that could impact review of research protocols, research ethics, and concept of fairness and equity in research participation, conflict of interest, Informed consent and its significance, privacy and confidentiality matters, IPR etc.

- On finalization of the training calendar, the IRB Secretariat will circulate the same to all members of the IRB.
- The IRB Secretariat will also maintain logs of the training and certificates attended by the IRB members.
- Members will also be encouraged to attend training in Research Ethics, Bioethics Conferences, Workshops, Seminars conducted at other organizations. The members should submit the certificates of such Ethics Conferences/Workshops/Seminars to the IRB Secretariat for IRB record.

The training program for the new and existing members of the IRB on the following,

1. The New Drugs and Clinical Trials Rules 2019
2. National Ethical Guidelines for Biomedical and Health Research Involving Human Participants.
3. ICH – GCP E6-R2
4. Good Clinical Practice Guidelines for Clinical Trials in India Other National & International regulations and Guidelines, as applicable.
5. IRB Policies and Standard Operating Procedures.
6. Members will be trained in the update/revisions in the guidelines.

List of Annexures

- Training Calendar (ANX1-VER2/SOP19/VER2)
- Training Log (ANX2-VER2/SOP19/VER2)

ANX1-VER2/SOP19/VER2

IRB Training Calendar

Sr. No.	Training Session	Speaker	Date	Target Audience
1.				
2.				

ANX2-VER2/SOP19/VER2

Training log

Topic:
Training date:
Training Time:
Venue:
Training Conducted by:
Target Audience
Audience:

Trainees:

Sr. No	Name	Designation	Signature and date
1.			
2.			

CHAPTER20

Assessment and Internal Audit of IRB

20.1 PURPOSES

This SOP outlines the procedure for the self-assessment of the IRB members/staff and internal audit of the IRB to maintain high standards of research conducted at MCC

20.2 SCOPE

This SOP is applicable to the IRB members and staff

20.3 RESPONSIBILITY

Chairpersons, Member Secretaries and IRB staff will be responsible for the assessment and audit of IRB.

20.4 PROCEDURE

Assessment of IRB members and IRB Secretariat

- The Chairperson will perform assessment of the IRB members annually. This assessment will cover regularity in attendance to IRB meetings, quality of review, time taken to review documents, completion of study assessment forms etc.
- The Chairperson will also perform self-assessment annually.
- The member secretary will perform assessment of the Administrative Staff of the IRB annually. Evaluation forms will be circulated to individual members and the respective IRB staff via email and a copy of the same will be maintained in the IRB records

Internal Audits

- Periodicity of Self-Assessment / Internal Audit

- 03 to 04 internal audits will be conducted in a year
- IRB staff will conduct quarterly internal audits as per the checklist ANX5-VER2/SOP20/VER2

Preparation for the audit

- On receipt of written/ mailed communication regarding audit, the IRB Staff will prepare and make necessary arrangements.
- The information and files requested by the auditors should be made available by the Secretariat.

Audit Procedure

- The audit involves review of IRB records, minutes, membership files, protocols, IRB correspondence etc...

Report of Internal Audit

- The internal audit report will be prepared by the auditors. A signed copy of the report will be forwarded to the IRB Member Secretary.

Correction of deficiencies observed at audit

- The audit report will be discussed in the IRB meeting. Based on the IRB recommendations corrective/preventive action plan will be implemented within 2 months of receipt of the IRB recommendations
- Action plan will be communicated by the Member Secretary to the Auditor

Records of the Audit

- The Member Secretary/ designated IRB member/ Secretariat must keep record of the audit reports and action plans in a separate audit file

LIST OF ANNEXURES

1. ANX1-VER2/SOP20/VER2- IRB Evaluation Form of Chairs & Co-chairs
2. ANX2-VER2/SOP20/VER2- IRBE valuation Form of IEC Member Secretary/Members
3. ANX3-VER2/SOP20/VER2- IRBE valuation Form of Staff
4. ANX4-VER2/SOP20/VER2- IRB Audit NABH Checklist
5. ANX5-VER2/SOP20/VER2- IRB Internal Audit Checklist

ANX1-VER2/SOP20/VER2

IRB Evaluation Form of Chairs & Co- chairs

Part A

1. Mention (□) the individual who is performing the evaluation: Self – evaluation : ☐
2. Name of the person who is evaluated :

_____

Period –

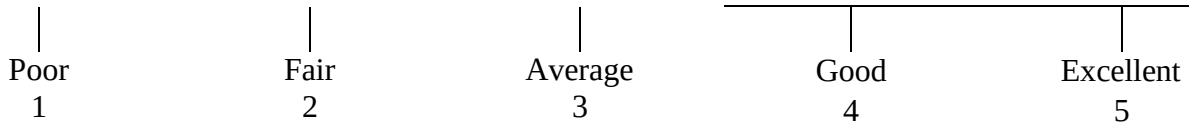
3. Number of Meetings attended out of total meetings: ☐ ☐
4. Number of exempt determination made: ☐
5. Number of new protocols reviewed by the expedited procedure: ☐
6. Number of new protocols reviewed that went to the convened full board IEC: ☐
7. Number of continuing review completed as the primary reviewer: ☐
8. Completion of educational requirements related to IEC :☐Yes ☐No
9. Attendance at educational sessions (Make tick (□) in the column)
   - □ Regular
   - □ Irregular
10. Number of educational sessions conducted: ☐

Evaluation of Chairs & Co- chairs

Part B

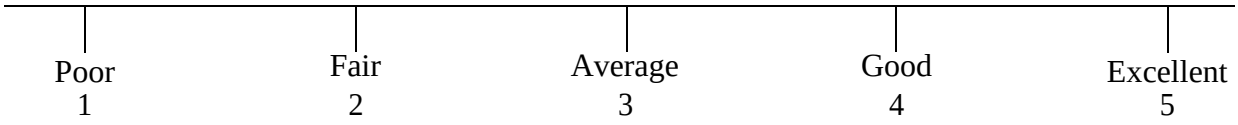
i) Preparedness for meetings

Scale



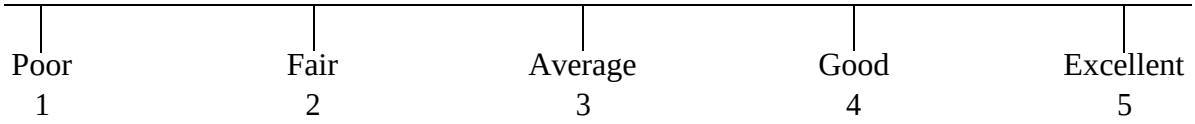
ii) Contribution to IRB

meetings Scale



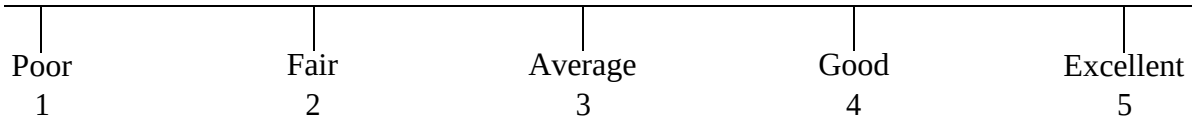
iii) Quality of

reviews Scale



iv) Communication with IRB

staff Scale



Feedback- _____

_____

_____

_____

Signature:

Date:

ANX2-VER2/SOP20/VER2

IRB Evaluation Form of IRB Member Secretary/Members

Part A

1. Mention (□) the individual who is performing the evaluation: Self – evaluation :□
   Member secretary IRB :□
2. Name of the person who is evaluated: _____
3. Number of Meeting attended out of total meetings :□/□
   □Poor (1-4) □Average (5-8) □Good (9-10) □Excellent (11-12)
4. Time taken to respond to modification sent
   □Good (1 week) □Average (2weeks) □Poor (above 2 weeks)
5. Number of exempt determination made:□ □NA
6. Number of new protocols reviewed by the expedited procedure:□ □NA
7. Number of new protocols reviewed that went to the convened full board IRB :□
8. Number of continuing reviews completed as the primary reviewer :□
9. Number of reviews completed as the primary reviewer for study amendments:□
10. Completion of study assessment forms: (tick (□) in the box)
    □Yes (out of) □No (out of)
11. Completion of educational requirements related to IEC : (tick (□) in the box)
    □Yes □No
12. Attendance at educational sessions : (tick (□) in the box)
    □Regular (out of) □Irregular (out of)
13. Number of educational sessions conducted:□ □NA

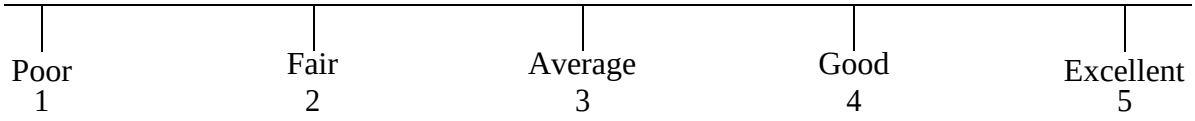
IRB Evaluation Form of IRB Member Secretary/Members

Part B

Name of the person who is evaluated- _____
Period–

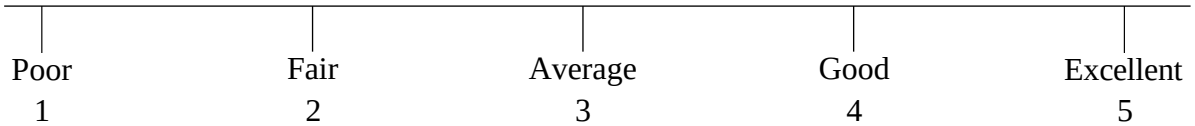
i) Preparedness for meetings

Scale



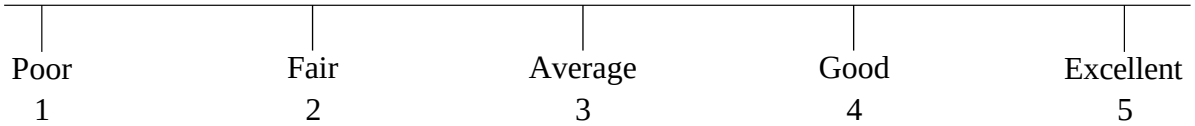
ii) Contribution to IRB

meetings Scale



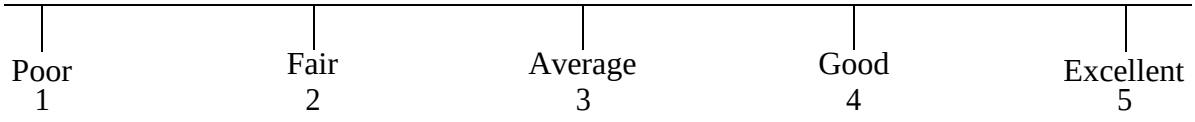
iii) Quality of

reviews Scale



iv) Communication with IRB

staff Scale



Feedback- _____

_____

_____

Signature:

Date:

ANX3-VER2/SOP20/VER2

IRB Evaluation Form of Staff

1. Mention (□) the individual who is performing the evaluation: Member secretary IRB:
   Name of the person who is evaluated:

   _____
   Period –

2. Handles workload efficiently : (tick (□) in the box) Yes:☐ No: ☐
3. Number of new protocol processed that were reviewed by the expedited procedure: ☐
4. Number of new protocols processed that went to the convened IRB: ☐
5. Completion of required checklists and documentation : (tick (□) in the box) Yes:☐ No: ☐
6. Maintains paper files efficiently and correctly : (tick (□) in the box) Yes:☐ No:☐
7. Drafting Agenda and Minutes in timely manner : (tick (□) in the box) Yes:☐ No: ☐
8. Maintain IRB rosters efficiently and correctly : (tick (□) in the box) Yes:☐ No: ☐
9. Prepare IRB records efficiently and correctly : (tick (□) in the box) Yes:☐ No: ☐
10. Completion of educational requirement related to IRB: (tick (□) in the box) Yes:☐ No: ☐
11. Attendance at educational sessions : (tick (□) in the box)
    Yes:☐ No: ☐
12. Number of educational sessions conducted: ☐
13. Preparedness for meetings : (tick (□)in the box)
    Good:☐ Average:☐ Poor: ☐
14. Quality of pre-reviews : (tick (□) in the

box) Good:☐ Average:☐ Poor: ☐

15. Communication with IRB chair and vice-chair : (tick (□) in the box) Good:☐ Average:☐ Poor:☐

16. Communication with supervisor: (tick (□) in the box) Good:☐ Average:☐ Poor:☐

17. Communication with investigators : (tick (□) in the box) Good:☐ Average:☐ Poor:☐

18. Ability to help investigator:
Good:☐ Average:☐ Poor:☐

Feedback- _____

_____

_____

_____

Name of Member Secretary

Signature:

Date:

ANX4-VER2/SOP20/VER2

IRB Audit						
Auditors:						
Date of Audit Conducted:						
Standard 1	**Authority for formation of Ethics Committee: There shall be documented procedures to establish the authority for formation of Ethics Committee as per applicable rules and regulations.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
	Tick the box to indicate the requirement is met:					
1.1	Does IRB follow procedures to specify the authority under which the Ethics Committee is established and administratively governed?	SOP				
1.2	Is there any documented policy to ensure the independence of the Ethics Committee in its functioning and decision making?	SOP				
1.3	Does Ethics Committee function as per applicable rules and regulations	SOP				
	Compliance					
Standard 2	**Standard Operating Procedures (SOPs): The Ethics Committee has and follows written SOPs for its different functions as per applicable rules and regulations.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
2.1	Do the IRBs have procedures in place and well defined for the development, review and revision of SOPs?	SOP				
2.2	**List of mandatory procedures for EC**					
A	**Terms of reference for EC**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Is the composition (names and qualification of the members) as per DCGI: for new induction, resignation, replacement or removal	SOP, roster, circular, membership files				

	of members.					
ii)	Is there a clause for Declaration of Conflict of Interest and Confidentiality Agreement?	SOP/member file				
iii)	Frequency of ethics committee meetings.	SOP				
iv)	Is there any policy regarding training for new and existing committee members?	SOP, training records				
v)	Is there any policy of communication with different stake holders?	SOP				
	Compliance					
B	**Protocol Submission**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**N A**	**Comments**
i)	Is there any procedure for receipt of applications – original, revised, amended with supporting annexes?	SOP/Manual				
	Compliance					
C	**Ethical review**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**N A**	**Comments**
i)	Is appropriate review and decision making of proposals done by IRB?	• Minutes • RB decision letters				
ii)	Is there any procedure to be followed for vulnerable population?	• SOP • Study assessment form • Minutes				
iii)	Is there any procedure for risk-benefit analysis?	• SOP • Study assessment form • Minutes				
iv)	Is there any procedure for review of Informed Consent Document (subject Information Sheet and Informed Consent Form) and informed consent process?	• SOP • ICF assessment • Minutes				

Compliance						

D	**Decision making , Minutes recording , post meeting activities including monitoring**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**N A**	**Comments**
i)	Is there any procedure for deliberations and maintaining minutes?	• SOP • Minutes				
ii)	Is there any procedure for reporting, analysis of SAEs and making opinion on compensation?	• SOP • Procedure for report of any onsite/offsite SAEs • Minutes				
iii)	Is the CRA reviewed by IRB ? • Conduct of on-site monitoring in the past	• SOP • Minutes				
iv)	Procedure for handling issues related to non-compliance, protocol violation, negligence, complaints by the participants and other stake holders.	• SOP Review of deviation/violation/non compliance reports • Minutes				
v)	Procedure for review of protocol amendments.	• Procedure for filing an amendment review appropriate - How is the amendment reviewed by IRB?				
Compliance						
E	**Documentation and archiving**					

Sr. No.	Check Parameters	Documents /evidence to be checked against the parameter	Yes	No	NA	Comments
i)	Procedure for control and archiving of records with confidentiality.	• Procedure for control and archiving of records with confidentiality •Does EC maintain an Archival record?				
	Compliance					

Standard 3	**Ethics Committee Composition: The Ethics Committee meets the requirement for membership as per applicable rules and regulations. Procedures are documented and followed.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Is the Composition of IRB multidisciplinary, multi-sectorial and appropriate for its functioning?	• IRB Roster • Circulars • SOP/manual				
ii)	Are any Subject Experts and representatives of vulnerable subjects invited as required with prior intimation?	• IRB Roster • Minutes of IRB meeting • SOP/manual				
iii)	Are Membership, appointment, reconstitution and resignation defined as per terms of reference.?	• Does the Membership File have proper documentation of reconstitution, appointment and resignation of EC members • SOP				
iv)	Are the roles and responsibilities of members well defined?	• SOP • TOR (Do appointment letters mention roles and responsibility of member)				
v)	Are the Ethics Committee members trained (initial and ongoing) in applicable rules and regulations and Ethics Committee SOPs?	• SOP • Training Calendar				

vi)	Are Conflict of Interest and Confidentiality addressed at the time of composition?	• Membership file				
	Compliance					
Standard 4	**Protection of subject rights, safety and wellbeing: The Ethics Committee follows documented procedures for subject protection.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Are the rights and responsibilities of subjects documented and specified in the SOP/ ICF template?	• SOP/ ICF template • ICF review/assessment form				
ii)	Subject's participation and withdrawal from the trial shall be voluntary and with prior intimation?	• SOP/ ICF template • ICF review/assessment form				
iii)	Subjects shall be informed and should comprehend (initial and ongoing) the associated risks and benefits of the trial.	• SOP/ ICF template • ICF review/assessment form				
iv)	Are Confidentiality and Privacy of Subjects protected?	• SOP/ ICF template • ICF review/assessment form				
v)	Monitoring of trials shall be done to ensure equitable selection of Subjects, with special attention to vulnerable and high risk	SOP				
vi)	Is compensation provided to Subjects for participation in the trial appropriate and as per the rules and regulation and is reflected in the contract?	• SOP/ ICF template • ICF review/assessment form Insurance				
vii)	Is the review of Serious Adverse Events adequate with provision for medical care and an appropriate reporting mechanism is followed as per applicable rules and regulations?	DSMB/IRB minutes				
viii)	Is the Compensation for injury to the subject as per the rules and regulations and are they monitored for compliance?					

ix)	How are Complaints and concerns of subjects addressed and managed appropriately, if the	SOP				

	need arises?					
Compliance						

Standard 5	**Administrative support: The Ethics Committee follows documented procedures / terms of reference (TOR) to ensure that administrative support for its activities is adequate.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Are adequate finance, human resource allocation and Secretariat for administrative work and record keeping with due care and Confidentiality provided?	• HRPP manual • SOP				
ii)	Is there adequate financial transparency of Ethics Committee activities and functioning?	• HRPP manual • SOP				
iii)	Is there any procedure for communication between ethics committee, investigator/ relevant site staff, institution and regulatory authority?	• HRPP Manual • SOP				
Compliance						

Standard 6	**Review Process: The Ethics Committee follows documented procedures for initial review of the trial related documents, review of amendments and periodic review.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Is the review done in a formal meeting within a reasonable time by the Ethics Committee following appropriate submission of documents by investigator as per rules and regulations and Ethics committee requirement?	• SOP				
ii)	Does the initial review of proposed clinical trial evaluate the scientific validity of the protocol, risk to subjects, expected benefit and ethical	• SOP • Study assessment Forms • Minutes of meeting				

	standards as per applicable rules and regulations?					
iii)	Are Informed consent document, assent form (as applicable) and translations reviewed for appropriateness of language, accuracy and completeness of information?	• SOP •ICF assessment Form, • Minutes of meeting				
iv)	Does Ethics Committee review the informed consent processes proposed to be followed at the site for a particular trial to ensure that subject/LAR/ impartial witness are provided appropriate information, adequate time is given and impartial witness used as applicable?	• SOP				
v)	Recruitment strategies	• SOP				
vi)	Proposals involving special group and vulnerable population shall be evaluated as per rules and regulations.	• SOP • Study assessment Form • Minutes of meeting				
vii)	Is Contract and budget evaluated, for indemnity, compensation, roles and responsibilities as per applicable rules and regulations.	• SOP				
viii)	Are the amendments to the originally approved protocol, consent forms and investigators brochure reviewed in formal meetings to evaluate the risk to trial subjects.	• SOP • Minutes of meeting				
x)	Periodic review of trial shall be done for continuation, risk evaluation and adverse event monitoring.	• SOP • DSMB IEC minutes				
	Compliance					

Standard 7	**Decision making and post meeting activities: The Ethics Committee follows documented procedures for decision making process and post meeting activities.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Are decision making process (approval/disapproval/pending/revokin g) as per applicable rules and regulations, ensuring quorum and consensus/voting requirements fulfilled.	• SOP • Decision letters				
ii)	Does SOP mention statement that the subject shall be recruited into the trial only after written approval from Ethics Committee and approval by regulatory authority.	• SOP				
iii)	Do minutes capture about declaration of Conflict of Interest prior to the review and voluntary withdrawal during decision making process.	• SOP • Minutes of meeting				
iv)	Whether decisions are based on risk assessment, scientific validity and adherence to ethical principles for the initial and periodic approvals.	• SOP • Minutes of meeting				
v)	Are deliberations and decisions made during the meetings documented, approved, signed and maintained as minutes of meeting.	• SOP • Minutes of meeting				
vi)	Are Protocol deviations and non-compliances reviewed and appropriate actions taken as perrules & regulations.	• SOP • Minutes of meeting				
vii)	Are serious adverse events analyzed and compensation amount assessed and reported to Regulatory Authority as per rules and regulations.	•SOP • DSMB IEC minutes				
viii)	Does PI notify all decisions/opinions in writing.	• SOP • IRB decision letters				
	Compliance					
Standard 8	**Monitoring: The Ethics Committee follows documented procedures for monitoring and for- cause assessment.**					

Sr. No.	Check Parameters	Documents /evidence to be checked against the parameter	Yes	No	N A	Comments
i)	Are subject's rights, safety and wellbeing monitored appropriately	• SOP • Study assessment Form				
ii)	Is adequacy and continuity of consent process ensured	• SOP • Study assessment Form				
iii)	For-cause assessments shall be conducted following non-compliance and/or complaints for the trials approved by the ethics committee.	• SOP • DSMB/IEC minutes				
iv)	Have any opportunities for improvement identified and appropriate actions initiated.	• SOP • DSMB/IEC minutes				
	Compliance					

Standard 9	Self-assessment: The Ethics Committee has and follows documented procedures for self- assessment.					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**N A**	**Comments**
i)	Does periodic self assessments conducted.	• SOP • Member Evaluation File				
	Compliance					

Standard 10	Record keeping and archival: The Ethics Committee follows documented procedures for record keeping and archiving.					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Are security, confidentiality and integrity of all proposals and associated documents reviewed from time to time and administrative communication and maintained as per regulatory	• SOP				

	requirement and with Confidentiality.					
ii)	Are documents and records archived after completion /termination of trial as per applicable rules and regulations	• SOP • Archival Log				
iii)	Are record retrieval policies and procedures in place to ensure access to information for inspection and audit and continual protection of trial subjects, post trial closure with prior permission in writing.	• SOP • Document request form				

ANX5-VER2/SOP20/VER2

Institutional Ethics Committee Internal Audit							
	Auditors:						
	Date of Audit Conducted:						
	IEC:						
	Date of Meeting Minutes:						
	A.	**Documentation of Attendance**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate the requirement is met:					
	1	Name of members present					
	2	Name of members absent					
	3	Name of alternate members and the members they are replacing					
	4	Inclusion of consultants or permanent members, with competence to review issues that require additional expertise					
	5	Researchers or other guests present					
	Compliance						
	B.	**Documentation of Quorum:**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate whether the requirement is met:					
	1	Statement that a quorum is met					
	2	a lay (non-scientist) person from the community.					
	3	a basic medical scientist/clinical pharmacologist.					
	4	a non-affiliated member*					
	5	a clinician (if research falls under FDA regulations, the physician must be licensed)					
	6	a legal expert					

	7	a philosopher, ethicist, theologian (or similar person), social scientist, representative of a non-government agency					
	Compliance						
	C.	**Quality of protocol review**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate the requirement is met:					
	1	Incomplete assessment form					
	2	Unsuitable reviewer					
	3	Appropriate independent expert (if required)					
	4	Independent expert comments documented					
	5	Appropriate review of recruitment strategies					
	7	Failure to assess PI competence/Conflict of interest					
	8	Failure to recognize vulnerability					
	9	Failure to address vulnerability					
	10	Inappropriate risk/benefit assessment					
	11	Inappropriate study design					
	12	Appropriate review of ICD					
	13	Appropriate review of parent ICF					
	14	Appropriate review of assent form					
	15	Whether criteria for expedited has been met					
	16	Whether criteria for waiver of consent has been met					
	17	Documentation of IRB deliberations as per SOP					
		Compliance					
	D.	**Documentation of Conflict of Interest**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate the requirement is met:					

	1	Minutes specify Conflict of Interest declaration by members					
	2	When members report conflicts, they do not participate in discussion or vote, except to provide information to the IRB					
	3	Minutes list criteria for Conflicts of Interest that organization should declare					
		Compliance					
	E.	**Membership / Experts file review**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate that all IRB membership files have following elements:					
	1	Latest CV signed and dated					
	2	GCP training certificate					
	3	GCP certificate valid					
	4	Confidentiality agreement					
	5	SOP training and other training documentation					
	6	COI declaration					
	7	Letter of resignation if applicable					
	8	Resignation intimation within specified period as per SOP 02					
	9	Letter of replacement /removal with reasons (if applicable)					
	10	Confidentiality agreement (Independent expert)					
		Compliance					
	F.	**Documentation of whether files contain additional information for continuing review of ongoing studies**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate whether IRB records also include the following additional information at the time of continuing review:					
	1	Mandatory documents submitted					

	2	Records of continuing review activities					
	3	Modifications to previously approved research					
	4	Unanticipated problems involving risks to participants or others					
	5	Documentation of non-compliance (whether there is non-compliance in fact, whether non-compliance is serious, whether non-compliance is continuing)					
	6	Significant new findings					
	7	Documentation of patient complaints/concerns if any addressed adequately					
	8	All correspondence between the IRB, researchers/ site staff, institution, regulatory authorities (e.g., approval letters and other correspondence)					
		Compliance					
	G.	**IRB Records**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate the requirement is met:					
	1	all minutes					
	2	all attendance records, if kept separately from minutes					
	3	the Constitution and composition of the IRB					
	4	standard operating procedures of the IEC					
	5	agenda of all IRB meetings					
	6	record of all notification issued for premature termination of a study with a summary of the reasons					
	7	Members Evaluation form					
	8	CV and GCP of IRB staff					
	9	Archival log &shredding log					
	10	Procedures followed for record retrieval					
		Compliance					

	H	**Review of Records (Random records reviewed)**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
	1	IRB approval letter					
	2	Has the study undergone continuing review?					
	3	Does an amendment/s have IRB approval?					
	4	Has there been a premature termination / suspension of the study and whether reason for the same is documented					
	5	Regulatory study					
	6	DCGI approval					
	7	Import/export license					
	8	Recruitment methods and materials are approved by IRB					
	9	Protocols or research plans					
	10	Investigator brochure					
	11	Insurance validity					
	12	CTA available					
	13	HMSC approval					
		Compliance					
	I.	**Authority for IRB Formation**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate that all IRB records for each study include:					
	1	Letter of Authority (sign and dated)					
	2	Valid period of Authority					
	3	Terms of reference (sign and dated)					
	4	Valid period of TOR					
		Compliance					

	J.	**Quality of Initial/Ongoing Review of Submission**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate the requirement is met:					
	1	Mandatory documents submitted					
	2	IRB fees collected					
	3	Document Receipt form present					
		Compliance					
	K.	**Review of protocol deviation/violation**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate the requirement is met:					
	1	Protocol deviation/violation Review in IEC meeting					
	2	Action taken on deviation /violation (Noted, Warning to the PI, etc…)					
		Compliance					
	L.	**SAE Review**					
		Check Parameters					
	Sr. No.	Tick the box to indicate the requirement is met:	**Yes**	**No**	**NA**	**Comments**	
		Review in DSMB					
	1	DSMSC minutes ratified in the IEC meeting					
	2	Causality assessment **appropriate**					
	2	IRB reporting to DCGI					
	3	**Reporting** timelines met for **forwarding** IEC assessment to CDSCO/DCGI					
	4	DCGI orders for SAE compensation					
	5	IRB intimation to PI for payment of compensation					

	6	Documentary evidence submitted for compensation/reimbursement paid by the sponsor **to IRB**					
		Compliance					
	M	**CRA Review**					
		Check Parameters					
	Sr. No.	Tick the box to indicate the requirement is met:	**Yes**	**No**	**NA**	**Comments**	
	1	CRA reminder timelines met					
	2	Is the CRA delayed (Has submission timelines as per SOP met by PI)					
	3	Action taken by IRB for delayed submission of CRA					
	4	Review by DSMB Member Secretary					
	5	Appropriate CRA review					
	6	Action taken by IRB in case of lapse in IRB approval					
	7	Whether CTRI registration done for the studies which are applicable for CTRI					
		Compliance					
	N	**Completion Report Review**					
		Check Parameters					
	Sr. No.	Tick the box to indicate the requirement is met:	**Yes**	**No**	**NA**	**Comments**	
	1	IEC review of Completion Report					
	2	Action taken by IRB in case of any adverse findings					
	3	Study file archived as per SOP					
		Compliance					
	O	**Monitoring Review**					
		Check Parameters					
	Sr. No.	Tick the box to indicate the requirement is met:	**Yes**	**No**	**NA**	**Comments**	
	1	Is the monitoring sample size as per the SOP i.e.≥ 10%					
	2	ICF monitoring					
	3	Risk evaluation and SAE					

		monitoring					
	4	Protocol deviation/violation reported by the PI to IRB					
	5	For cause monitoring done					
	6	Study Monitoring Visit Report completed					
	7	Report reviewed by DSMB secretary					
	8	Report reviewed by IRB					
	9	Findings communicated to PI					
	10	PI response review by IRB					
		Compliance					

CHAPTER 21

Review of proposals for conducting research in urgent / Emergency situations

21.1 PURPOSES

To provide guidance on procedures to be followed by Institutional Ethics Committee, MCC during humanitarian emergency situations.

21.2 SCOPE

This SOP describes procedures to be followed by the IRB and IRB Secretariat to receive and review humanitarian emergency research proposals from principal investigators at MCC, and continued review of new and ongoing non-emergency research proposals during humanitarian emergencies

21.3 PROCEDURES

Once an outbreak/disaster has been declared as a matter of national emergency by the Health Authority of India, any research submitted to the IRB shall be categorized into 3 types namely:

1. New research directly related to the emergency situation (outbreaks, epidemic)
2. Ongoing non-emergency research
3. New non-emergency research
4. General principles

The Principal Investigators shall submit research submissions via the IRB online portal (if applicable). All study documents mandated in IRB SOP (SOP 3 and 4a) needs to be submitted. Proposals applying for expedited reviews and Exemption from IRB shall follow IRBSOP 4b and 4c.

a) In an emergency situation, proposals may be submitted with only PrincipalInvestigator's signatures. However, approval by email from Head of Department needsto be attached by PI. Each co-investigator will send an email to the PI stating the following: Title of the project
b) Acceptance of specific roles and responsibilities
c) Declaration of conflict of interest.

The PI should submit these emails along with project submission.

Once new research proposals are received at the IRB office, these are made available to the Member Secretary and the Chairperson via the IRB online portal and/or email communication.

The Member Secretary /Chairperson identify the research proposals submitted to the IRB Office that qualifies for an expedited review, fast-track unscheduled full board meeting or a scheduled full board meeting.

Depending on the type of humanitarian emergency situation- such as an epidemic or a highly contagious outbreak, the mode of conduct of meeting will be identified by the Member

Secretary in coordination with the IRB Secretariat. The meeting may be conducted as face- to-face meetings or teleconferences /virtual meetings.

- In situations where face-to-face meetings would pose a health risk to committee members and strict social distancing is mandated, the IRB meetings shall be conducted as virtual meetings after first identifying the available software platform accessible to all IRB members.
- All the IRB members need to report the IRB member secretary through administrative staff about the conflict of interest if any at least 3 days prior to the meeting. The digital platform used should be secure and have facilities to exclude members with a conflict. The commonly used digital platforms are Microsoft Teams, WebEx, and Cisco. Skype isn't feasible for group meetings while zoom has concerns of privacy and confidentiality of data exchange. The members with conflict will be kept in the waiting lobby by the member secretary in coordination with administrative staff as applicable.
- No unauthorized person enters the room when the virtual meeting is in progress.
- Agenda of virtual meetings should be kept short, however, EC may meet more frequently for fast track review within in 24-48 hrs.
- The meeting shall be digitally recorded (audio/video) and will be stored securely and accessible to authorized personnel only.
- The IRB Secretariat will document the attendance of members during the meeting in the Minutes of the meeting

Rules of Order: Opening the Meeting:

1. The chairperson will call for the attendance. The attendance list is displayed by the meeting host in coordination with IRB administrative staff (if applicable).
2. Agenda items with conflict of interest will be moved to the end of the agenda will be communicated to the Chair and Meeting Host before the meeting by the IRB administrative staff.
3. When a Board Member's name is called, they should audibly confirm their presence and that they can hear and speak. Members who are calling from a phone-only connection should self-identify, as they will be unable to participate in on-screen voting and will have their votes taken audibly for each item.
4. At the conclusion of roll call, the Meeting Host audibly turns the meeting over to the Chairperson.
5. The Meeting Host opens the vote poll and announces to all attendees that the voting poll is open. Members cast their votes via the on-screen poll, while the Meeting Host unmutes phone-only members, and calls each member's name to request an audible vote one at a time. After all audible votes are cast and recorded, the on-screen poll is closed and recorded. Members who fail to log their vote either audibly or via the poll will be counted as abstaining. Members who abstain from 3 or more consecutive votes during the meeting will be called out during the meeting to ensure they are still present and connected to the meeting. When the voting has concluded, the Meeting Host audibly turns the meeting over to the Chairperson for the first review.

Rules of Order: Application Reviews, Discussion, and Voting Procedure

1. The Meeting Host displays the agenda on the shared screen. If there are any Business or Information Items, they will be displayed at this time.
2. The Chair introduces the first item for board review and turns the meeting over to the Primary Reviewer for their presentation (if applicable).
3. The Primary Reviewer presents their review of the item, presents any questions they wish to have the board address, and then concludes with a motion.
4. The Chair asks the membership if they have any questions or comments in response to the reviews presented.
5. Board Members with questions or comments should raise their hand if option available, ask their question in the chat box, or audibly say "I have a question" at this time. The Meeting Host helps the Chair identify individuals who would like to speak. Members should wait for the Chair or Meeting Host to turn the meeting to them before speaking to ensure attendees do not talk at the same time.
6. The Chair and Meeting Host will manage questions and comments in an orderly fashion, ensuring each member's question or comment is addressed. The Meeting Host will unmute members who raise their hands or ask questions aloud and audibly turn the meeting to them.
7. After the presentation and discussion of an item has concluded, the Chair will repeat the conclusion for the item to ensure all membership has heard it. • E.g., "The study is submitted." The Chair audibly turns the meeting over to the Meeting Host.
8. The Meeting Host opens the vote poll and announces to all attendees that the voting poll is open.
9. Same procedure will be followed for each item.

Rules of Order: Items with Attendee Conflicts of Interest

1. The Chair announces that the next item discussed will be an agenda item where a voting member has a conflict of interest (CoI). The Chair audibly excuses the conflicted Member with a CoI from the meeting, signaling the Meeting Host to use the "waiting Lobby" function to temporarily excuse the Member from the virtual meeting.
2. The Meeting Host audibly confirms the member has been excused to the Waiting Lobby, stating the Member's name for the minutes.
3. The conflicted Member waits in the Lobby until they are invited to rejoin the meeting by the Meeting Host.
4. After the discussion and vote, the Chair audibly asks the Meeting Host to invite the excused Member back into the virtual space. The Member states that they are back and can hear and see.

Rules of Order: Closing the Meeting

1. The Chair announces that the last item has been discussed and asks if there are any
1. Outstanding items, questions, comments, or Expedited items that need additional discussion.
2. Members who have items to discuss should raise their hand, type their question/commentin the Chat box, or for phone-only participants, audibly indicate they have something to say.
3. The Meeting Host will take note of all members who have questions or comments, and will either: 1. Go through each member's question/comment one at a time, naming the member who commented and allowing them time to speak, or 2. Audibly confirm to the Chair that there are no pending matters to discuss.

4. The Chair will audibly confirm that all pending matters have been satisfactorily resolved and declares that the IRB board meeting is over, signaling to the Meeting Host to disconnect the online session.

5. The Meeting Host will audibly confirm that attendees may disconnect from the meeting. • "This IRB meeting is now concluded. Attendees, you may now disconnect from the virtual space."

Guidance for review of new research directly related to the emergency situation (outbreaks, epidemics)

- Research during emergencies can be reviewed through expedited review / unscheduled full committee meetings on a case-to-case basis depending on the urgency and need. If an expedited review/e-expedited review is done, full ethical review will follow whenever next possible

- Given the unprecedented nature of the emergency, the IEC may identify subject experts who may or may not be part of the parent institute, to review these projects. **Irrespective of the institutional affiliation, the research proposals shall be made available to the experts only after obtaining a signed confidentiality agreement from them.**
- Quorum for decision-making should have a minimum of five members, including both medical/non-medical and technical/non-technical members with one non-affiliated member, depending upon the nature of the project being reviewed
- The EC may plan a prior review by subject experts/obtain clarifications from researchers before the meeting or/ invite independent consultants (non-voting) or representative from a specific patient group as special invitee. The special invitees invited for the web-meeting maybe asked to leave the meeting before final decision making.
- The findings/queries may be sent to the PI via email to fast track query resolution.
- The IRB decision on approval shall be sent out by the IRB Secretariat via official letter.

Ethics Considerations for research during humanitarian emergencies:

- Research should be coordinated nationally and internationally to avoid wasteful duplication and underpowered study.
- All international collaborations shall be undertaken only after obtaining approval from Health Ministry's Screening Committee (HMSC).
- Collaborative research may be undertaken only after MOUs/CTAs/MTAs are finalized.EC shall ensure that all emergency research proposals (clinical trials/biomedical research) are registered on Clinical Trial Registry of India (CTRI).
- EC should ensure that the research proposals do not impede response efforts by taking away personnel, equipment, facilities, and other resources from those required for response to the emergency situation.
- EC should critically consider the research context, background information, risks of the research, and the most appropriate means of answering specific research questions with rigorous and reliable data to ensure the results are both valid and useful in shaping future response.
- EC should review the participant selection criteria and ensure that it minimizes risk, maximizes social value and upholds the scientific validity of the study.

Vulnerable groups may not be routinely excluded from the research participation without evidence based scientific and ethical justification such as an unfavorable benefit-risk ratio.

- EC should be vigilant that such humanitarian emergencies may render individuals vulnerable to coercion as they may not have access to formal or informal support during these times
- The EC, while reviewing the ICDs for both humanitarian emergency research proposals and non-emergency proposals during such times, should consider the limitations to obtain written consent due to quarantine, social distancing, severity of medical condition, the high risk of exposure to both study personnel and participants etc.
- Alternate methods of consenting such as electronic consents, telephonic consents, verbal consents etc. may be permitted to document and record consent.
- The consenting process for participants, vulnerable group should be as per National Ethical Guidelines and Regulatory mandate.
- Participants and stakeholders should be fully informed about the collection, storage, future use, bio-banking and export of human biological material. A broad consent shall be used for research on residual clinical samples with an individual opt-out option provided.
- The EC shall continually evaluate progress of ongoing proposals, review SAE reports, protocol deviations/violations/ non-compliance/ DSMB reports/ any new information/ and assess final reports.
- The EC shall periodically monitor emergency research studies.
- The EC reserves the right to halt or terminate such studies in case of violations or non-compliance or due to new safety information that has an adverse risk-benefit ratio.

Elements of an ICD	**Additional elements (optional)**
1. Statement mentioning that it is research	1. Alternative procedures or treatment
2. Purpose of research and methods	2. Insurance coverage
3. Duration, frequency, methods	3. Possible stigmatizing condition
4.Benefits to participant, community or Others	4.Biological material and data, Including

5.Foreseeable risks, discomfort or Inconvenience	i. Current and future uses
6. Confidentiality of records	ii. Period of storage, secondary use, sharing
7. Payment/reimbursement for participation	iii. Right to prevent use of biological sample
8. Treatment and/or compensation for injury	iv. Provisions to safeguard confidentiality
9. Freedom to participate/withdraw	v. Post-research plan/benefit sharing
10. Identity of research team and contact Persons	vi. Publication plan/photographs/pedigrees

Review of on-going studies and new research proposals (no-emergency research)

- The IEC encourages investigators to adopt precautionary measures as mandated by the national regulatory agencies for ensuring the safety and well-being of participants during conduct of ongoing studies during humanitarian emergencies.
- Studies that are ongoing or near term or have shown direct benefit to the participants may follow the measures such as

• Cancellation or postponements of physical visits unless these involve procedures carried out at MCC and are strictly necessitated.
• Conduct of follow up via telephone/videoconferencing/email etc… in lieu of physical visits.
• Re consenting of participants via phone or video-calls and obtaining oral consents supplemented with email confirmation to implement urgent changes
• Home delivery of drug to participants while ensuring compliance with applicable privacy and data protection regulations.

- Incorporating amendments in the proposal(s) to align to the research needs

arising from the emergency including issues related to re-consent from participants

This is not an exhaustive list and any alternate procedures adopted by PI in place of routine protocol procedures need to be notified to IRB for review and approval.

- The IRB may also suspend or temporarily halt studies that are not initiated at the time of declaration of the emergency situation.
- New non-emergency research proposals that are submitted during such times maybe postponed to subsequent IEC meetings at the discretion of the Member Secretary based on the workload at the IRB Secretariat.
- The IRB shall consider the existent emergency situation and assess if a planned study may have a negative impact on participants' safety or increase risk to participants and make relevant suggestions for additional safeguards for conducting research before giving approval.

IRB may permit remote monitoring and Source Document Verification activities by Sponsors upon written request from the Principal Investigator. In case it is imperative that a monitoring be done, the PI may remotely share the EMR screen with the sponsor to conduct a live monitoring of source data. However, IRB would not permit sending patient related documents including source documents to the sponsor either electronically or manually.

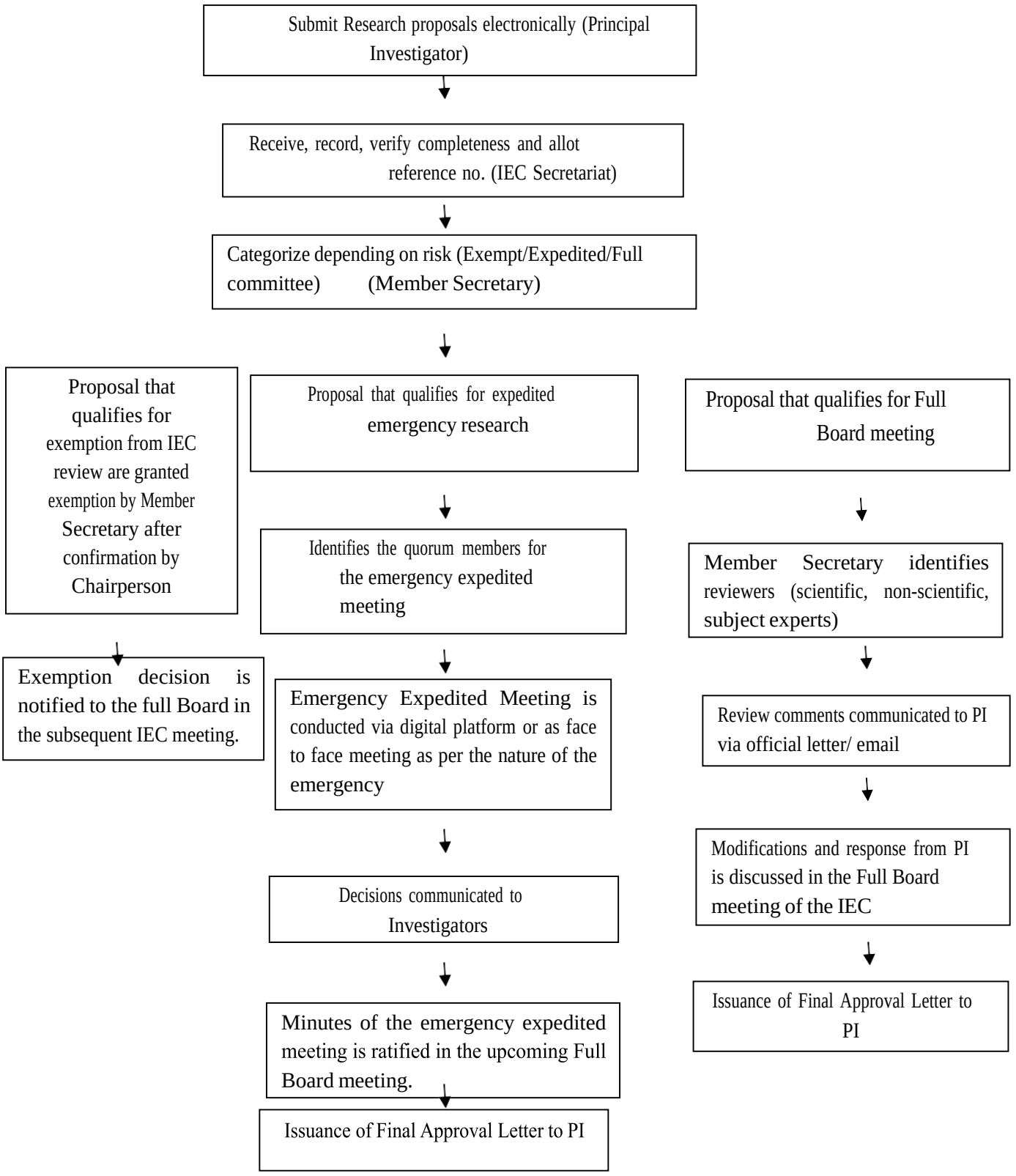
- If study interventions can increase the risk of developing the emergency health condition then the condition may be considered a SAE related to participation and the EC may ask PI to budget for the cost of treatment of participants who develop the condition.

In case of an outbreak of infectious diseases, monitored emergency use of unregistered and experimental interventions (MEURI) may be approved with the following precautions:

- Thorough scientific review followed by an ethics review / locally or by national level lRB
- Tackle public concerns and ensure oversight by a local lRB.

- Use GMP products; make rescue medicines/supportive treatment accessible.
- Meticulous documentation of therapeutic processes including adverse events
- Fast track research and possible sharing of data on safety and efficacy for further research
- Consent process is important and must be carried out with care.
- Community engagement and ensuring fair distribution of scarce supply
- Facilitate post-trial access of the successful investigational drug/ vaccine free

PROCESS FLOW



Review of proposals for conducting research in urgent/ emergency situations

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