MALABAR CANCER CENTRE

(An Autonomous Centre under Government of Kerala)

INSTITUTIONAL REVIEW BOARD

Standard Operating Procedures

(*SOPs*)

Edited by

Subhradev Sen

Directed by

Dr. Satheesan B

OFFICE OF IRB

Division of Clinical Research & Biostatistics

Malabar Cancer Centre

(An autonomous Institute under the Government of Kerala)

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Standard Operating Procedure (SOPs)
Institutional Review Board (IRB) - Malabar Cancer Centre (MCC)

SOP Codes SOP01/VER1, SOP02/VER1, SOP03/VER1, SOP04/VER1, SOP05/VER1, SOP06/VER1, SOP07/VER1, SOP08/VER1, SOP09/VER1, SOP10/VER1, SOP11/VER1, SOP12/VER1, SOP13/VER1, SOP14/VER1, SOP15/VER1

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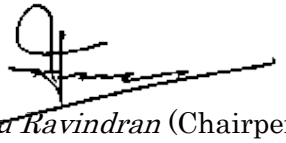
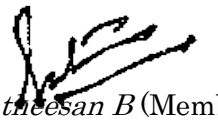


Dr. Babu Ravindran (Chairperson)



Dr. Satheesan B (Member Secretary)

Accepted by

Dr. Satheesan B
Director, Malabar Cancer Centre

FOREWORD

Dr. Satheesan B, *M.B.B.S, MS, M.Ch, DNB*

The Malabar Cancer Centre at Thalassery (MCC) fosters a research environment that promotes respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of the centre.

In the review and conduct of research, actions by MCC will be guided by the principles (respect for persons, beneficence, and justice) set forth in the ethical principles and guidelines for the protection of human participants of research and will be performed in accordance with the ICMR revised guidelines on "*Ethical Guidelines for Biomedical Research on Human Participants (2006)*" and ICH-GCP regulations. The actions of MCC will also conform to all other applicable federal, state, and local laws and regulations.

The Centre maintains an Institutional Review Board (IRB) with its delegate sub-committees to review research protocols involving human participants and to evaluate both risk and the protection against risk for participants. It is the function of the IRB to

- ✓ Determine and certify that all projects reviewed by the IRB conform to the policies and procedures in this document and the regulations and policies set forth under the Common Rule regarding the health, welfare, safety, rights, and privileges of human participant
- ✓ Assist investigators in complying with national and international regulations
- ✓ Ensure that research meets the centre's ethical standard of "*Research & Academic freedom*" which the institute is committed to.

This compiled version of Standard Operating Procedures (SOPs), through which the IRB functions, are developed for last two years and simultaneously made into action. I am happy that the first version of the SOPs is finally into a shape of a single book for publication.

I congratulate the Office of IRB, Division of Clinical Research & Biostatistics, for bringing out the first version.

March'2015

DIRECTOR

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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 Organizatio
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)

SOP 01/ VER1

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), Malabar Cancer Centre (MCC).

The SOPs will provide clear, unambiguous instructions to conduct activities of the IRB in accordance with the ICMR guidelines 2006, Schedule 'Y" (Drugs and Cosmetic Act 1940: Amendment 20th Jan 2005), WHO Operating Guidelines for Ethical Review Committee that Review Biomedical Research, and ICH (International Conference on Harmonization) - Good Clinical Practice (GCP)

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 IRB members. SOP team will be responsible to amend the SOPs as and when required.

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.

- SOP team will consist of Member Secretary 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 SOPs. 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
- 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)

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-VER1/SOP01/VER1)*. This Formulation of new SOP/ Revision of an SOP Form (*ANX5-VER1/SOP01/VER1)* 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-VER1/SOP01/VER1)*

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 / VER y** 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/VER1 is SOP number 01 with VER = Version Number 1

Each Annexure (ANX) is unique code with format **ANXn–VERp/SOP xx/VERy**. **e.g.** *ANX1–*
VER1/SOP01/VER1 indicates ANX is Annexure, 1 is Annexure number, VER1 is version 1, belonging to the SOP 01/VER1

Each Appendix will be given unique code with the format **APNn/VERy** e.g. APN1/VER1 indicates APN is Appendix, 1 is Appendix no 1, VER1 is Version no.1.

Each SOP will be prepared according to the template for Standard Operating Procedures (ANX2 – VER1/*SOP01/VER1)*. Each page of the SOP will bear a header with the effective date which is the 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 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.

1.4.6 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.

1.4.7 Implementation, distribution and filing of SOPs

- Approved SOPs will be implemented from the Effective Date.
- 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 –VER1/SOP 01/VER1)*.
- 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 –VER1/SOP 01/VER1)*

1.4.8 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 –VER1/SOP01/VER1*).

*** **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.***

References

1. Schedule Y (Drugs and Cosmetic Act 1940; amendment 20th January 2005) Retrieved from *http://www.cdsco.nic.in/html/Schedule-Y 20 (Amended 20Version- 2005)*
2. WHO Operational Guidelines for Ethical Review Committee that Review Biomedical Research (Geneva 2000) Retrieved from - *www.who.int/tdr/publications/publications*
3. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) (1996) Retrieved form - *http://www.ich.org/LOB/media/MEDIA482.pdf*
4. ICMR Ethical Guidelines for Biomedical research on Human Participants, ICMR (2006) Retrieved from - *http://www.icmr.nic.in/ethical guidelines.pdf*

GLOSSARY

Effective date: The date of approval of the SOPs signed and dated by the Chairperson, IRB, MCC and by Director, MCC, and subsequently the SOP is implemented from that date

Master SOP files: An official collection of the Standard Operating Procedures (SOPs) of IRB, MCC accessible to all staffs, IRB members, auditors and government inspectors as a paper copy with approval signatures

Previous SOPs of the IRB: A collection of previous official versions of a SOPs and relevant information regarding changes and all preplanned deviations

Requestors: Investigators, Sponsors, Contract Research Organizations, Regulatory authorities, Hospital administrators, and such others

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

Recipients**:** Stakeholders who would receive a copy of SOP, viz., two categories
IRB Members i.e. SRC Members & IEC Members 2) Non-IRB members i.e. investigators/sponsors/Institutes or Research Organizations undersigned MoU with MCC/ Academic departments of MCC/ Administrative Officers, MCC/ Accounts Officer, Heads of Departments/Divisions of MCC/ Librarian, MCC and other concerns as per MCC administrative decision.

SRC members: Individuals serving as regular members of the Scientific Review Committee of IRB, MCC. The Committee has been constituted in accordance with the requirements set forth in ICMR guidelines.

IEC members: Individuals serving as regular members of the Institutional Ethics Committee of IRB, MCC. The Committee has been constituted in accordance with the requirements set forth in schedule Y (20th January 2005)

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

SOP Team: A team of members selected from the IRB, MCC including the Member Secretary, In Charge of Clinical Research & Biostatistics division and any other member of IRB –SRC and/or Academic staff of MCC departments, as identified by the Chairperson/ Member-Secretary of IRB-IEC, MCC, who oversee the creation, preparation, review and periodic revision of the IRB.

ANX1-VER1/SOP01/VER1

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/VER1
2	Constitution of Institutional Review Board	SOP02/VER1
3	Management of Research Study Submission	SOP03/VER1
4	Preparation of Agenda, Procedures for conducting Meetings, Minutes recording	SOP04/VER1
5	Continuous Protocol Review	SOP05/VER1
6	Review of Protocol Deviation/ Violation/ Waiver/ Non-compliance	SOP06/VER1
7	Review of Reports on Serious Adverse Events (SAEs)	SOP07/VER1
8	Maintenance of Active project Files, Disposal/Archival of Closed project, Documents Retrieval	SOP08/VER1
9	Documentation of IRB Activities	SOP09/VER1
10	Study Completion Report Review	SOP10/VER1
11	Management of premature Termination/ Discontinuation/ Suspension of the Studies	SOP11/VER1
12	Review of request for waiver of Written Informed Consent	SOP12/VER1
13	Site Monitoring	SOP13/VER1
14	Dealing with patients'/ study participants' Requests or Complaints	SOP14/VER1
15	Protection of Vulnerable Population in Clinical Research	SOP15/VER1

ANX2-VER1/SOP01/VER1

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-VER1/SOP01/VER1
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-VER1/SOP01/VER1

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-VER1/SOP01/VER1

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:	

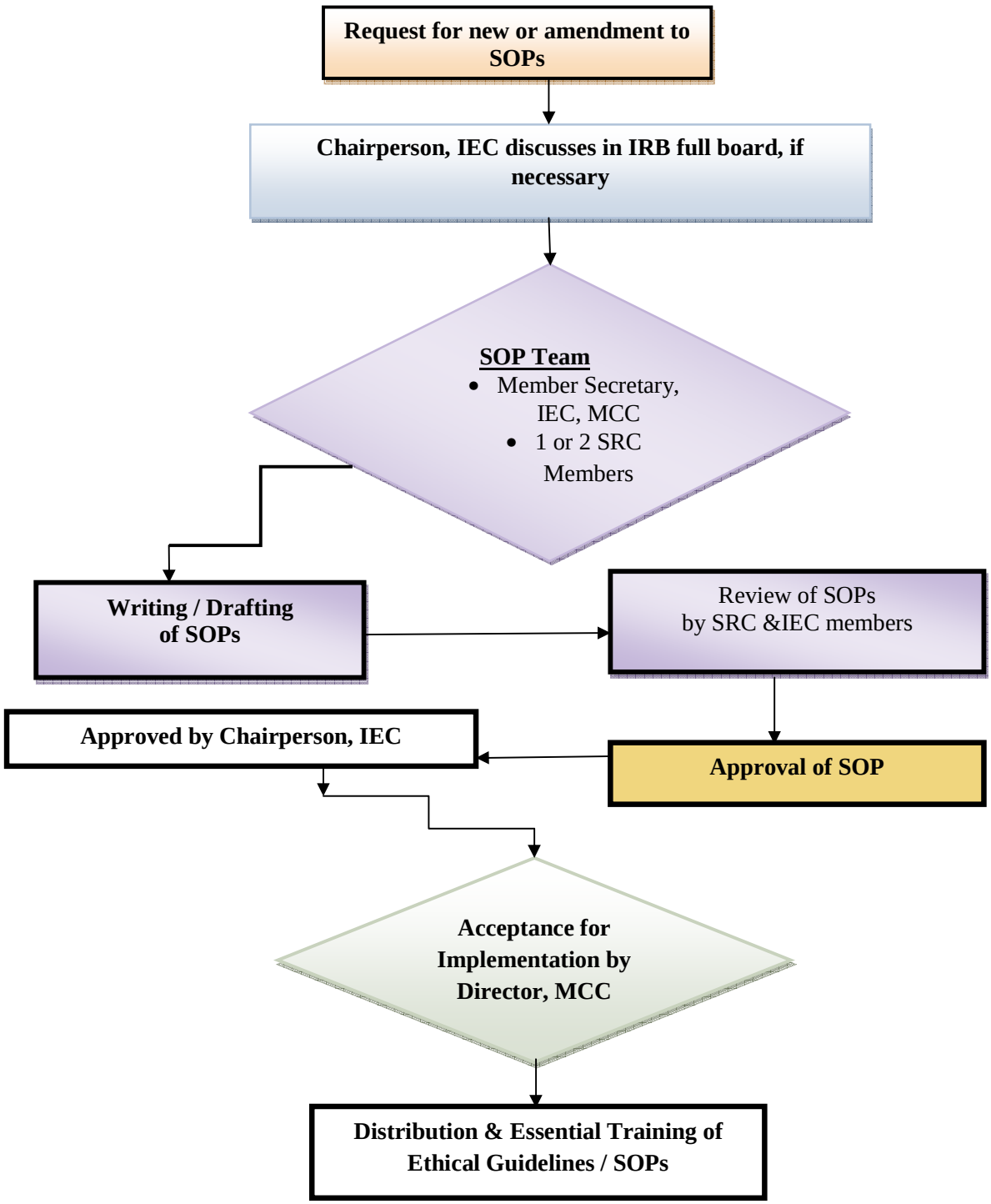
ANX6-VER1/SOP01/VER1

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					

FLOW CHART


Request for new or amendment to SOPs
Chairperson, IEC discusses in IRB full board, if necessary
SOP 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 2

Constitution of Institutional Review Board

SOP 02/ VER1

CHAPTER 2

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 been developed as a State of Art cancer centre with equal thrust on Clinical Care, Education and Research. MCC has a clear vision to establish & evolve itself as a hub for Core Research on Oncology through investigator-initiated trials, intervention studies, and development of newer technologies, experimental medications, therapeutics, processes and scientific techniques to fight against the deadly disease, Cancer.

The Institution feels to continue oncology based research by developing itself on qualities of being extremely thorough, exhaustive and accurate. This gave rise to the need for impeccable and efficient management of its research activities and clinical trials to ensure the protection of human rights as mandated by Indian law (Schedule Y), and to satisfy 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 of the 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 and CRO/SMO based clinical trials.

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 been taken up.

However, as per the decision of the Director, MCC, in order to manage the review process more efficiently, the MCC Scientific Review Committee and the Institutional Ethics Committee are been merged to form the Institutional Review Board (IRB). Therefore, in MCC, IRB works in review process for research study proposals with two mutually exclusive wings, viz., SRC & IEC.
Each IRB reviews both, the scientific and ethical aspects, if any, of the study.

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 the 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.

2.1 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.

2.2 MANDATE

The Institutional Review Board (IRB) through its delegated sub-committee(s) functions independently for maintaining a systematic, reliable and consistent scientific as 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

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

2.3 SCOPE

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

2.4 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.

2.5 SCIENTIFIC AND ETHICAL BASIS

- The committee consists of members who collectively have the qualifications and 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 mainly based on the ICMR guidelines (2006), Schedule Y (Drugs and Cosmetics Act 1940., amendment 20th Jan 2005), Operational Guidelines for Ethics Committees that Review Biomedical Research (WHO 2000), and ICH-GCP, 1996 and the local regulations, CFR 45 (US FDA)

- IRB seeks to fulfill the requirements for international assurances and is established and functions in accordance with the national law and regulations

2.6 COMPOSITION OF IRB

Institutional Ethics Committee (IEC)

- IRB will be multidisciplinary and multi-sectorial in composition. IRB-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, Co-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.

Composition of IEC

The composition should be as follows:-
1. Chairperson (not – affiliated to MCC)
2. Member Secretary (MCC Staff member)
3. 1-2 clinicians (not affiliated to MCC)
4. 4-8 clinicians (can be MCC staff members)
5. Basic medical scientist
6. Clinical Pharmacologist
7. One legal expert or retired judge or medico-legal expert
8. One social scientist / representative of Non-governmental Voluntary Agency/ Philosopher/ Ethicist / Theologian
9. One lay person from the community

2.6.1 SCIENTIFIC REVIEW COMMITTEE (SRC), MCC

2.6.1 (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 & 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 members are agreed in a SRC meeting and recommend the study proposal to Institutional Ethics Committee (IEC) for reviewing ethical issues, if any. 8 to 15 qualified persons constitute the SRC, MCC. The entire members are directly appointed by Director, MCC with composition as follows:

2.6.1 (b) Composition of Scientific Review Committee (SRC), IRB, MCC

- Chairperson: Director of MCC
- Vice-Chairperson : One Senior Professor (preferably from MCC)
- Members: Faculty members with or above the ranking of Associate Professor in academic divisions, MCC
- 2 Biostatistics Faculty Members from MCC to see the Statistical bases for the study proposals
- 1 or 2 External Experts in selected cases
- 1 or 2 Selected faculty members of high academic reputation or rare specialization

SRC meets on every 2nd Saturday of a month or on 3rd Saturday, if the 2nd Saturday falls on a holiday and as and when required.

2.6.2 MEMBERSHIP OF IRB, 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 and/or in the Executive Council, in cases. The Director of MCC himself/herself will hold the position of Member Secretary for IRB-IEC.

- **<u>Criteria for selection of members</u>:**

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 2.6.3 of this SOP.

2.6.3 Terms of Appointment

2.6.3. (A) Duration

- The members of the IRB, MCC will be appointed for a duration of 3 years (especially for IEC)
- 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.
- The members can be continued and there will be no limit on the number of times the membership is extended. 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 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. In case the Director, MCC resigns from the post of Member-Secretary, IEC, the Vice - Chairperson of SRC will automatically be the Member-Secretary of IEC. In case of unwillingness of Vice -Chairperson of SRC in becoming Member-Secretary of IEC, the IRB constitution has to be fully modified & the matter must be placed to MCC Academic Council.
- In case of the transfer/resignation/discontinuation of the Director, MCC, from his/her post at the centre, the Secretary of SRC will act as Member-Secretary (in-charge) of IEC with full office and authority as per the IRB constitution until a new Director for MCC is appointed.

2.6.3. (B) Renewal

- The membership will be renewed after the stated term of 3 years.
- The process of renewal will be as follows :

  Selection of Chairperson and other members should be done at least 3 months 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 – VER1/SOP02/VER1)* at the beginning of the IRB meeting and/or before scientific and ethical review tasks of the IRB commence

- If a *regular member resigns*, or *ceases to be a member due to disqualification/ dissatisfaction*, or *in case of death*, a new member will be appointed for the remaining term as per the Conditions of appointment stated below – section 2.6.3

2.6.3. (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 the resigning member. Appointments may be made in consultation with Academic Council members and /or Chairperson of IEC.

2.6.3. (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 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.

2.6.4 Conditions of Appointment

1. Name, age, gender, profession, and affiliation of IRB members will be publicized.
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. Conflict of interest, if any, must be disclosed.
5. Members must apprise themselves of the relevant documents, codes, ICH -GCP guidelines and the ICMR code and IRB, MCC SOPs.
6. Members are required to sign the confidentiality agreement (*ANX1-VER1/SOP 02/VER1*) at the start of their term. The confidentiality agreement protects the privacy and confidentiality of all parties whose information may be disclosed to the IRB in the course of its work.
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.

2.7 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.

2.7.1 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.

2.7.2 Member-Secretary, IRB-IEC

The Member Secretary will be 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.
In the absence of the Member-Secretary of IEC, the Chairman or Vice-Chairman of IEC will function as an acting Member-Secretary of IRB-IEC and vice-versa for routine IRB work.

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 mention MCC staff for coordinate and manage the activities of the IRB for that meeting.

.2.7.3 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.

<u>Duties of the administrative officers/staffs:</u>

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.

2.8 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.
- 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.

2.9 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 a 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.

These 5 members should have the following representation:

a) ***basic medical scientists (preferably one clinical pharmacologist)***
b) ***clinicians***
c) ***legal expert;***
d) ***social scientist or representation of non-governmental voluntary agency or philosopher or ethicist or theologian or similar person***
e) ***lay person from the community***

- A quorum should include at least one member whose primary area of expertise is in a non-scientific area, a clinician, and at least one member who is independent of MCC/research site and have no immediate family member affiliated to MCC.
- No quorum should consist entirely of members of one Profession/ one Gender.
- In the absence of the Chairperson, the Co-Chairperson will chair the meeting. In the absence of both, Member-Secretary of IEC, MCC will chair the meeting as the Acting Chairperson.
- When an alternate member attends a meeting as a substitute for a regular member, the alternate member's participation counts toward the quorum requirements.

2.10 EDUCATION OF IRB MEMBERS

IRB members have a need for initial and continued education regarding the science and ethics of biomedical research. All IRB members must be conversant with ICMR

Guidelines for Research involving Human Subjects 2006, Schedule Y of Drugs and Cosmetics Act and ICH-GCP guidelines.
IRB members will receive introductory training material in research bioethics and functioning of IRBs and will be exposed to ongoing opportunities for enhancing their capacity for ethical review.
Training of the IRB members in Research Bio-Ethics:

- ✓ A new member may be inducted 1 month prior to his/her appointment and will be requested to be an 'Observer' for the first board meeting. The Member Secretary or IRB Secretariat/ Office of the IRB, MCC, will impart an introductory training.
- ✓ The IRB members will be encouraged to receive ongoing training by attending workshops at least once every year.
- ✓ The IRB will conduct workshops from time to time to impart training to the IRB members and Institutional faculty members.

2.11 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.

2.12 HONORARIUM

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

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References

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1. CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects Retrieved from- *http://www.cioms.ch/frame guidelines nov2002.htm*
2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH- GCP) 1996. Retrieved from-*http://www.ich.org/LOB/media/MEDIA482.pdf*
3. ICMR Ethical Guidelines for Biomedical research on Human Participants, ICMR (2006)- Retrieved from - *http://www.icmr.nic.in/ethical guidelines.pdf*

4. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000. (Geneva 2000) Retrieved from- w*ww.who.int/tdr/publications/publications*/

5. Code of Federal Regulations 45 CFR 46.108
htttp://www.hhs.gov/ohrp/humansubjects/guidance

6. European Convention on Human rights and Biomedicine (1997). Retrieved from *http://conventions.coe.int/treaty/en/treaties/html/164.htm*

7. Schedule Y (Drugs and Cosmetic Act 1940; amendment 20th January 2005*)* Retrieved from - *http://www.cdsco.nic.in/html/Schedule-Y 20(Amended 20Version-* 2005) 20 original .htm

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GLOSSARY

Confidentiality: Prevention of disclosure to other than authorized individuals, of information and documents related to IRB

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

Independent Consultants: Professionals with advanced training and expertise in the medical or non-medical areas related to the protocol being reviewed.

Scientific member : Individual who possesses the clinical and/or scientific knowledge and ability to effectively evaluate the research and clinical investigation.

Non-Scientific member: Individual who possesses expertise and/or experience outside scientific areas and serves to represent either vulnerable populations or local cultural and community attitudes relative to the rights and welfare of human research participants.

Non-affiliated member: Individual who is a scientific or non-scientific member, is knowledgeable about clinical or scientific matters or local cultural and community attitudes, and has no association with MCC.

ANX1-VER1/SOP02/VER1

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 the delegate of any organization or private interest; Whereas, the fundamental duty of an IRB member is 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 of human 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 nature shall 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 participate in 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 I have made as part of my Committee duties) to the Chairperson upon termination of my functions as 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-V1/SOP02/VER1

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**

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**

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 observership / 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 3

Management of Research Study Submission

SOP 03/ VER1

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
- ✓ Protocol amendments and any other amendments.
- ✓ Annual Status Reports/Continuing review of the study
- ✓ Study completion/termination

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

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-VER1/SOP03/VER1*)
  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.
- State clearly the missing documents as per the form (*ANX3-VER1/SOP03/VER1*)
- 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: 20 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 Department of Biostatistics & Health Research. 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. Project Submission Overview
d. Budget Sheet for the Proposed Study

B. Essential Documents

a) ***Participant Information Sheet & Informed Consent Forms*** (ICFs), for studies in children, parent consent form and in case of children between age 7-18 years of age- Child Assent Forms and Parent consent forms in Malayalam and English are mandatory and any other language required (See *ANX2-VER1/SOP 03/VER1*)
b) Investigator's Brochure (if applicable)
c) Case Record Form
d) One page, recent, signed and dated curriculum vitae of the investigators indicating qualifications and relevant experience.
e) Agreement to comply with national and international GCP protocols for clinical trials
f) Regulatory clearance from appropriate regulatory authorities i.e. DCGI approval / ICMR /Health Ministry Screening Committee (HMSC) (if applicable)
g) For international/ national collaborative study Memorandum Of Understanding (MoU) between the collaborating partners
h) Clinical Trial Agreement (if applicable)
i) Insurance/Indemnity policies, indicating who are covered (if applicable)
j) Any other important information relevant to the study
k) 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 contains 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 ANNUAL CONTINUING REVIEW FOR *APPROVED RESEARCH STUDIES*

- The IRB will send reminders for annual report to Individual PI at least 30 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/VER1*) for the approved research study
- The Office of IRB will verify the completeness of the Continuing Review Application Form (*ANX1-VER1/SOP05/VER1*) 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

3.9 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 10/VER1*) **termination.**
- The Office of IRB will verify the completeness of the Study Completion Report Form (*SOP10/VER1*) **termination** filled by the PI.
- The study completion/ **termination** report will be tabled in the board meeting of IRB.

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Reference:

1. International Conference on Harmonization - Guidance on Good Clinical Practice (ICH -GCP) 1996 Retrieved from - http://www.ich.org/LOB/media/MEDIA482.pdf .
2. IRB SOPs by Tata Memorial Hospital, Mumbai, India.

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GLOSSARY

***Amendment*:** A written description of a change(s) to or formal clarification of a protocol.

***Case Record Form*:** A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject

***Clinical Trial Agreement*:** A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters.

***Essential Documents*:** Documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.

Informed Consent: A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.

***Investigator's Brochure*:** The Investigator's Brochure (IB) is a compilation of the clinical and non-clinical data on the investigational product(s) that are relevant to the study of the product(s) in human subjects.

***Study Protocol*:** A document that describes the objective(s), design, methodology, statistical considerations and organization of a trial

***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-VER1/SOP03/VER1

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) PRJECT FACT SHEET

1. Study/Project Number(to be filled up by IRB Office, MCC)	
2. Project Title	
3. Date of receipt by IRB, MCC	
4. Keywords for Title (2 to 4 options)	
5. Principal Investigator	
6. Number of ongoing study the PI is involved (as PI only)	
7. Full address & Contact details of PI *(provide e-mail ID & contact no. along with complete mailing address in CAPITAL LETTERS)*	
8. Co-Investigator(s)	
9. Name of the Study Site	
10. Agency or Sponsor or	

Funding resource	
11. Total estimated Budget (in Rs.)	
12. Duration of the project (in months)	
13. Total number of patients to be accrued in study (including MCC, if multi-institutional study)	
14. Expected Date/Month of starting the project	
15. Will biological products be sent out of the country? (Yes/No) **If yes, attached the copy of regulatory clearance obtained [DCGI/ ICMR /Health Ministry Screening Committee (HMSC)]**	
16. Any Conflict of interest, (Yes/No) **If Yes Please specify**	
---------- **Signature of PI**	**----------** **Date**

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 subjects in accordance with the ICH-GCP and ICMR ethical guidelines, 2006. 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 understood 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 DSMSC, 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 used 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 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, 2006. 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	J. Examination of patients on follow-up
B. Design	K. Data collection and monitoring of data
C. Screening of patients	L. Interpretation of data
D. Selection & Recruitment and consenting of patients	M. Statistical analysis & Interpretation
E. Laboratory investigations	N. Maintaining patients file and master file of project
F. Laboratory report interpretation	O. Drafting final report
G. Treatment decision	P. Publication
H. Patient evaluation	Z. Any other, please specify
I. AE and SAE management, evaluation and reporting	

***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-VER1/SOP03/VER1

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

GUIDELINE FOR PREPARATION OF THE INFORMED CONSENT FORM	
While submitting your project to the IRB, ensure that you have included an informed consent form that is prepared as per the guidelines for ICMR ethical guidelines 2006, Schedule Y, ICH-Good Clinical Practice (ICH – GCP) and the Declaration of Helsinki.	
Kindly Note:	
i.	Informed consent forms in English and Malayalam are mandatory and any Language if applicable
ii.	Font: Times New Roman for English & Meera/ Karthika for Malayalam
iii.	Font Size: 12
iv.	Each page of consent forms must have Date, Study Name & Page number **in the footer**
v.	Separate forms should be prepared when minors (children) are study participants; assent form for the mature minors (age 7-18 years) and consent form for the parents

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

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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 names of Principal Investigator and all other investigators.]

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.

Purpose:
The purpose of this study is to_____

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 subject.
- If this is a randomized trial, details of both arms of the trial must be explained .
- State the amount of time required by the subject 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. If case tissues or biological samples, are being retained for research, describe what will be done to the tissues in simple lay person's terms. (If applicable)

Alternative treatments:

Disclose appropriate alternative treatments available, if any.

Risks:

List the foreseeable risks, 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.

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 by sponsors/Principal Investigator/s of the project, and study participant.

Reimbursement for Participation

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

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Emergency Medical Treatment

(If applicable, add here)

In case of the physical injury to the subject 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. 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 charwill be housed (specify the location). Data will be stored securely and will be madavailable 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 subject unless deemed necessary.

Compensation for study related Injury
Compensation of subjects for disability or death resulting from such research related injury;
Describe the details of compensation or insurance for study related injury to the trial subject. Explain who will bear the cost in case of trial related injury? Research subjects 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 subject to confirmation from Director, MCC. In case of death, their dependents are entitled to material compensation.

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 questions about your rights as a participant, contact the Member -Secretary, IRB, MCC, [Name], 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

Study Title:
Study Number: [For Office Use Only]
Subject' Initials:_____ Subject's Name:_____
Date of Birth / Age:_DD/MM/YYYY /_____

1) I confirm that I have read 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 that the Sponsor of the research study, others working on the Sponsor's behalf, IRB and the regulatory authorities will not need my permission to look at my health records in respect of both 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.

4) 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)

5) I agree to take part in the above study.

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

Participant's name (in Capital Letters):	
Participant's signature & date	
Address(capital letters): Phone Nos.:	
Legal Acceptable Representative name : Legal Acceptable Representative : Signature & Date	
Address (capital letters): Phone Nos.:	
Impartial Witness's name :	
Impartial Witness's signature & date:	
Address (capital letters): Phone Nos.:	
Name of PI or Co-PI/Co-I:	
PI or Co-PI/Co-I & 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 IRB 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 Form 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.

A Xerox copy of the Informed Consent Form(ICF) must be given to prospective participant.
A receipt of copy of ICF by the subject should be documented by the investigator in the source documents. Copies of the consent form must be available in English & Malayalam.
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 us 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 form is more than one page, there should be a line at the bottom of each page for the subject'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 form front to back. Please make provision for the assent of the child to the extent of the child's capabilities such as in the case of 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 form, and of a 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

ANX3-VER1/SOP 03/VER1

Child Information Sheet and Assent Form **Study Title: " ……"**
Introduction
You have come to meet the doctor as you are suffering from ……..... You may be having symptoms…… Describe briefly the purpose of this study If this is a randomized trial, details of both arms of the trial must be explained in writing to the subject being enrolled. Disclose appropriate alternative treatments available, if any.
We invite you to participate in this study. **What will you have to do?**

To participate in this research study, you will be examined by your doctor and if found to fulfill pre-specified criteria, you will be eligible to be enrolled in this research study.
Since you are in the age group of 5-18 years, we ask you to sign this assent form if you agree to participate. 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 abide by the trial procedures. Your accompanying parent / guardian will also sign a similar form called as the Parent Informed Consent Form.
List all procedures, which will be employed in the study.
Point out any that are considered experimental/or otherwise, and explain technical and medical terminology in simple, non-technical & direct language.
In addition, to record the same parameters daily your parent/ guardian will also be provided with a dairy where they will enter the same findings accordingly. You will have to tell them about your symptom and they will mark accordingly in the diary.

Side effects

All medicines/procedures produce some side effects – the medicine you will take/the procedure you will undergo can produce (Describe the side effects). Your Physician will take due precautions so that you do not experience these side effects.
If you experience any of these listed effects or any other unlisted effects do contact your study doctor immediately. The study doctor will treat you accordingly.
Your parents will not have to bear the cost of the medical treatment/ hospitalization as a result of these side effects.

In addition during the trial period if you suffer from any other diseases, if you consider some of the side effects as serious or you undergo hospitalization during the study period, please immediately contact the study doctor:
Dr. **Phone:**

The occurrence of any of the side effects (known/ unknown) and concomitant diseases will be noted by the physician at every visit. The assessment of acceptability of the formulation/procedure will be performed by the treating physician at the end of the study.

Risks and discomforts

There is no foreseen significant risk / hazard to your health, if you wish to participate in the study. You 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 Sponsor will pay for the medical expenses for the treatment of that injury.

Benefits

If you participate in the study you will receive ……If you appear to have any acute illness ……you will be offered free treatment for those visits in accordance with local standard medical care. You will not be offered free treatment for chronic diseases or conditions not related to study procedures.

Your participation in the study may help others, because this participation will help us determine if the study drug/procedure is safe.

Confidentiality

Your existing medical records may be accessed; personal health information about you may be collected and processed by study investigators for the purpose of performing the study. Information about you will be collected and stored in files with an assigned number, and not directly with your name. The document linking your name with the assigned study number will be kept for 5 years in a locked cabinet at the study site, after which the linking document will be destroyed. All documents related to the study will only be accessed by the study investigator, sponsor, the Ethics Committee and the Regulatory authority

Your parent / guardian will have the right to access personal information about you at any time with the study doctor and the right to correct this personal information. Your parent / guardian can take away your authorization to collect process and disclose data about you at any time.

Right to refuse or withdraw

You do not have to take part in this research if you do not wish to do so. Refusing to participate will not affect your treatment. You will still have all the benefits that you would otherwise have got at this clinic/hospital. You may stop participating in the research at any time you wish without losing any of your rights. Your treatment will not be affected in any way The study doctor may decide to withdraw you from the study if he/she considers it is in your best interest You will be informed of important new findings developed during the course of the study so you will be able to consider your participation in the study in light of new information

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Whom to contact

If you have any questions, please ask them now. You may also ask questions later. If you wish to ask questions later,

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

If you have any queries regarding your medical rights and ethical responsibilities you may contact,

<Name of Member-Secretary of IRB > **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 are prematurely discontinued from the study. It is also your responsibility and your parent / guardian to report any expected or unexpected reactions (side effects) that you notice during the study period.

It is also the responsibility 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_____, exercising my free power of choice, hereby give my consent for participation in the study entitled:

"……
……."

I have been informed, to my satisfaction, by the attending physician, about the purpose of the study and the nature of the procedure to be done. I am aware that my parents/guardians do not have to bear the expenses of the treatment if I suffer from any trial related injury, which has causal relationship with the said trial drugs/procedures/therapies/any other form of interventions.

I am also aware of right to opt out of the trial, at any time during the course of the trial, without having to give reasons for doing so.

_____
Name and Signature of the study participant Date:

_____
Name and Signature of the attending Physician Date:

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/Therapy/Procedure/Any other form of Intervention

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 anytime and ask to see [names of Nurse, Doctor and 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 will 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.*

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 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.

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, 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 any way.

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 IRB], 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 IRB-Institutional Ethics committee (IEC), MCC.

Dr. Phone:

Consent To Participate In Research & Authorization To Use And Share Personal Health Information: For Subjects less than 18 Years of Age

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.

_____ _____
Signature of Parent/Guardian Date

_____ _____
Signature of Subject (when appropriate) Date

_____ _____
Signature of Person Obtaining Consent/Authorization Date

_____ _____
Signature of Witness Date

CHAPTER 4

Preparation of Agenda, Procedures for conducting Meetings, Minutes recording

SOP 04/ VER1

CHAPTER 4

Preparation of agenda, procedures for conducting Meetings, minutes recording

4.1 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 unless otherwise specified.
IEC meets at 03:00 pm on the last Friday of every two months and/or as and when required.
Venue: Conference Hall, Malabar Cancer Centre, Thalassery.

4.2 SCOPE

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

4.3 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.

4.4 DETAILED INSTRUCTIONS

4.4.1 BEFORE IRB MEETING

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

IEC Meeting:
Prepare the agenda of the IEC meeting (*ANX1-VER1/SOP04/VER1*)
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.

4.4.2 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 3 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.

4.4.3 MEETING PREPARATION

- Reserve the Conference Hall of MCC on the scheduled meeting date and time. The meeting will be held in the Conference Hall, MCC, unless otherwise specified.
- Ensure that the room, equipment (projectors, recorder, etc) and facilities are available in good housekeeping conditions on the day of the meeting.
- On the previous day of the meeting, keep all original files of protocols on the agenda in the meeting room for ready reference during the meeting.

4.4.4 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 (*SOP 02/VER1 section no. 2.9*) requirements are met, otherwise he/she may wait for a maximum period of 30 minutes, 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.

4.4.5 DECISION MAKING PROCESS

IRB provide complete and adequate review of the research proposals submitted to them. The SRC reviews the scientific merits and demerits of all the submitted study proposals to the IRB.
The retrospective studies do not go for IEC approval and such proposal gets IRB approval directly on the basis of SRC clearance and recommendations. The SRC approved and forwarded prospective study proposals go to IEC for final approval.
The IEC will review new project proposals, amendments, annual progress of ongoing projects, SAE reports, and assess final reports of all research activities through a scheduled agenda.

1. A SRC/IEC member will withdraw from the meeting for the decision procedure concerning an application where a conflict of interest exists.
2. If SRC/IEC member has her/his own proposal for SRC/IEC review he/she will not participate in the discussion on that particular project in the corresponding meeting. Decision may only be taken when sufficient time has been allowed for review and discussion of an application in the absence of non-members (e.g., the investigator, representatives of the sponsor, independent consultants) from the meeting, with the exception of IRB staff.
3. IEC or SRC decisions will only be made at meetings where a quorum (*SOP 02/VER1* section no. 2.9) is present.

4. The documents required for a full review of the application should be complete and the relevant elements considered before a decision is made.
5. Only IEC members who attend the meeting will participate in the decision.
6. Decisions will be arrived at through consensus. When a consensus is not possible, the IEC will vote.
7. If the full board approves a research proposal in principle subject to minor modifications, the revised project proposal submitted by the PI will be reviewed and approved by the
8. Member Secretary, IEC or in some cases by the primary reviewer on behalf of the full board. Such revised proposals will not be taken up for the full board review. However, in case of major changes, the revised documents will be discussed in full board meeting.
9. An IEC may decide to reverse its positive decision on a study if it receives information that may adversely affect the risk/ benefit ratio.
10. Any advice that is non-binding will be appended to the decision.
11. In cases of conditional decisions, clear suggestions for revision and the procedure for having the application re-reviewed will be specified.
12. 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 IRB Office
13. The discontinuation of a trial will be recommended if the IEC finds that the goals of the trial have already been achieved midway or unequivocal results are obtained.
14. 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 viewpoint.
15. Subject expert/s may be invited to offer their views, but expert/s should not participate in the decision making process. However, his / her opinion must be recorded.
16. The proceedings of the SRC meetings will be documented and signed by the all the members attended that particular meeting.
17. The proceedings of the IEC meetings will be documented and signed by the Member Secretary and Chairperson.

4.4.6 AFTER THE SRC/IEC MEETING

4.4.6 (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

- The Member Secretary will compile the proceedings of IEC meeting in a concise and easy-to-read style and will e-check spelling, grammar and context of the written minutes.
- The minutes of the meeting will be compiled within a week.

4.4.6 (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.

4.4.6 (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.

4.4.7 COMMUNICATING DECISION

For IEC

1. The decision will be communicated in writing to the PI, preferably within a period of 10 days of the IEC meeting at which the decision was made.
2. The communication of the decision will include, but is not limited to, the following,
3. MCCC Project No. and title of the research proposal reviewed
4. The clear identification of the protocol of the proposed research or amendment, date and version number (if applicable).
5. 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.
6. The name and title of the Principal Investigator, The name of the site(s)
7. The date and place of the decision, A clear statement of the decision reached

8. Validity of approval usually will be yearly for multiyear projects, however may change on case to case basis.
9. Any suggestions by the IEC.
10. A conditional decision (i.e. approval with recommendations or modifications, suggestions for revision and the procedure, any other requirements by the IEC), will be valid only for six months from the date of issue of letter. If the PI does not comply with the IEC suggestions during these three months, a reminder will be issued. The modifications will be re-reviewed by Member Secretary, IEC or primary reviewer/s and /or may be referred for full board review (*ANX3-VER1/SOP04/VER1*).
11. In the case of a positive decision, the PI is notified of the following requirements through an approval letter (*ANX2-VER1/SOP04/VER1*)
    - a statement of the responsibilities of the PI; for example, confirmation of the
    - acceptance of any requirements recommended by the IEC
    - submission of progress report(s) decided on case to case basis, usually yearly.
    - the need to notify the IEC in cases of protocol amendments (other than amendments involving only logistical or administrative aspects of the study)
    - 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 IEC
    - 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
12. In the case of a negative decision, the reasons should be clearly stated in the communication to the PI.
13. The PI will also be notified of the duration of the approval, which will not exceed one year.
14. All decision and approval letters will be signed by the Member Secretary, IEC.
15. Every page of consent forms (English and Malayalam) of investigator initiated trials and first page of ICFs of sponsored trials (English and Malayalam) will be signed and dated by Member Secretary, IEC. These approved ICFs will be sent to the PI along with the approval letter.
16. The Chairperson / Member Secretary, IEC, will sign and date the approval letter and approval certificate in the original research protocol.

For SRC

Each and every proposal must have an SRC clearance.

1. The decision will be communicated in writing to the PI, preferably within a period of 10-15 days of the SRC meeting at which the decision was made.
2. The communication of the decision will include, but is not limited to, the following,
3. MCC Project No. and title of the research proposal reviewed

4. The clear identification of the protocol of the proposed research or amendment, date and version number (if applicable).
5. 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.
6. The name and title of the Principal Investigator, The name of the site(s)
7. The date and place of the decision, A clear statement of the decision reached
8. Validity of approval usually will be yearly for multiyear projects, however may change on case to case basis.
9. Any suggestions by the SRC
10. No conditional decision (i.e. approval with recommendations or modifications, suggestions for revision and the procedure, any other requirements by the SRC), will be valid for SRC Clearance. In case any modification required, the office of IRB will intimate and request for the same by e-mail and will request for a modified version for submission in the Office of IRB. A deadline for such submission will be indicated clearly on the mail. The modifications will be re-reviewed by Chairperson, SRC or primary reviewer/s and /or may be referred for full board review or IEC clearance, if necessary.
11. A positive decision, the PI is notified of the following requirements through an approval letter (*ANX4-VER1/SOP04/VER1*). In case of negative decision no letter will be issued, Office of IRB will e-mail such decisions to the PI and corresponding proposal will be discarded within 7 days from the e-mail communication.
12. In case a proposal is forwarded by SRC and recommended to IEC for ethical review, a letter of decision will be communicated to the PI (*ANX5-VER1/SOP04/VER1*).

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References

1. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996 Retrieved from- http://www.ich.org/LOB/media/MEDIA482.pdf
2. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, (Geneva 2000)- Retrieved from- www.who.int/tdr/publications/Publications

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GLOSSARY

Agenda: A list of things to be done; a program of business for the meeting

Minutes: An official record of proceedings at a meeting

Quorum: Number of members required to act on any proposal presented to a committee for action.

ANX1 –VER1/SOP04/VER1

I. Agenda format
II. Minutes
III. Projects for Initial Review
IV. Amendments
V. Letters
VI. Minutes of DSMB & SAEs (It Applicable)

ANX2 –VER1/SOP04/VER1

FORMAT FOR APPROVAL LETTER OF ETHICS COMMITTEE

IEC File No. Date: Month Day-Year (e.g. January 1st -2013)

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

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

Ref: Project No./Title

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

The Institutional Ethics Committee of Malabar Cancer Centre reviewed and discussed your application (dated) to conduct the research study entitled "_____" during the IEC meeting held on (date).

The following documents were reviewed and approved:

1. Project Submission form.
2. Study protocol (including protocol amendments), dated_____, version no(s).
3. MCC-Scientific Review Committee approval letter dated _____
4. Patient information sheet and informed consent form (including updates if any) in English and/Vernacular language.
5. Investigator's brochure, dated_____, version no._____
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
_____ Chairman of the Ethics committee
_____ Member secretary of the ethics committee
_____ Name of each member with designation

The Research Proposal is approved in its presented form. The approval is valid until one year from the date of sanction. You may make a written request for renewal / extension of the validity, along with the submission of annual status report.

Following points must be noted:

1. IEC should be informed of the yearly progress of the study.
2. IEC has approved recruitment of ____ patients on this study.
3. PI and other investigators should co-operate fully with DSMB, who will monitor the trial
4. from time to time.
5. The decision was arrived at through consensus. Neither PI nor any of proposed study team
6. members was present 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, Status report, including accounts details should be submitted to Secretary, DSMB and extramural sponsors.
8. The IEC functions in accordance with the ICH-GCP/ICMR/Schedule Y guidelines.
9. In case of any new information or any SAE, which could affect any study, must be informed to IEC, DSMB and sponsors. The PI should report SAEs occurred for IEC approved studies within 7 days of the occurrence of the SAE. If the SAE is '*Death*', the Office of IRB will receive the SAE reporting form within 24 hours of the occurrence.
10. 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 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 trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the SRC and 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 Ethics committee.
g. Any deviation/violation/waiver in the protocol must be informed to the IEC.

Thanking You,

Yours Sincerely,

Member Secretary,
Institutional Ethics Committee ***IRB OFFICE ROUND SEAL***
OFFICE SEAL

ANX3 –VER1/SOP04/VER1

FORMAT FOR CONDITIONAL APPROVAL FOR PROJECT/AMENDMENTS

IEC File No. Date:

Conditional Approval

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

Sub.: Decision Forwarding-IEC Meeting-MCC-Reg
Ref: Project No./Title

Dear Dr./Mr./Mrs.…

The above referenced project was tabled, reviewed and discussed during the Institutional Ethics Committee meeting held on date/time/place

List of documents reviewed.
1.
2.
The following members attended the meeting.
1.
2.
The committee suggested the following:
a.
b.
c.
The approval will be granted subject to the compliance with all the above suggestions of the IEC.
Kindly resubmit the two copies of revised proposal or documents within three months for re-review.

This conditional approval is valid only for *SIX* months from the date of issue of letter.

Thanking you,

Yours sincerely,
Member Secretary, IEC ***IRB OFFICE ROUND SEAL***
Office Seal

ANX4 –VER1/SOP04/VER1

FORMAT FOR APPROVAL LETTER OF SRC
(In case of Retrospective studies, Audits, etc.)

SRC File No. Date: Month Day-Year (e.g. January 1st -2013)

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. HOD's approval, No objection from Cancer Registry Department if registry data is under utilization.

The Research Proposal is approved by SRC in its presented form.
The approval is valid until one year or mentioned study duration (whichever is earlier) from the date of sanction. You may make a written request for renewal / extension of the validity, along with the submission of annual status report.

Following points must be noted:

1. No clinical intervention for the purpose of the study is allowed in the proposed study site.
2. 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
OFFICE SEAL

IRB OFFICE ROUND SEAL

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

ANX4 –VER1/SOP04/VER1

FORMAT FOR APPROVAL LETTER OF SRC
(In case of Prospective Study Proposals)

SRC File No. Date: Month Day-Year (e.g. January 1st -2013)

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

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. You are requested not to start the study until the IEC clearance is obtained
2. Please keep in touch with the Office of IRB for the IEC status of your study proposal

Thanking You,

Yours Sincerely,

Chairperson*
Scientific Review Committee
OFFICE SEAL

IRB OFFICE ROUND SEAL

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

CHAPTER 5

Continuous Protocol Review

SOP 05/ VER1

CHAPTER 5

Continuous Protocol Review

5.1 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.

5.2 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.

5.3 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.

5.4 DETAILED INSTRUCTIONS

5.4.1 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

5.4.2 Notify the Principal Investigator or the study team

- Reminders in writing/email are sent from Office of IRB to the Principal Investigators on every two months basis for submission of an annual status reports/ Continuous Review applications for projects that were approved by IRB previously.
- Principal Investigator should submit three hard copies of the report (1+2) and a soft copy.

5.4.3 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/VER1)

5.4.4 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

5.4.5 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.

5.4.6 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

5.4.7 Review Process

- ➢ The IRB-IEC Chairperson/ Member Secretary/ members will use the Continuing Review Application Form (*ANX1-VER1/SOP05/VER1*) to guide the review and deliberation process.

The IRB members could arrive at any one of the following decisions at the IRB meeting:

1. Noted and the project can be continued without any modifications
2. Modifications recommended - Studies for which modifications have been suggested by the IRB-IEC may not proceed until the conditions set by the IRB have been met. Studies should be amended and submitted to the IRB within one month for re-review
3. Disapproved.

- ➢ 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.

- 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.

5.4.8 Store original documents

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

5.4.9 Communicate the IRB decision to the Principal Investigator

The Office of IRB will notify the Principal Investigator of the decision. If IRB has recommended modifications, the decision will be notified to the Principal Investigator and he/she will be requested to resubmit the relevant documents within 1 month for the approval till then the project is suspended. Principal Investigator will be communicated about the decision within 14 working days after the minutes are finalized.

References

1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, (Geneva 2000) www.who.int/tdr/publications/publications/
2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996- http://www.ich.org/LOB/media/MEDIA482.pdf

ANX1-VER1/SOP05/VER1

CONTINUOUS REVIEW APPLICATION (CRA)
Institutional Review Board (IRB)
Malabar Cancer Centre (MCC), Thalassery- 670 103, India

PART-I

MCC Study No.:

Date of Registration:

Protocol title:

Principal Investigator:

Phone No:

Email Id:

Institute:

Source of funding: Intramural / Extramural | If extramural which _____

Account No:

In case of a Pharma funded studied please provide:

Sponsor Name:

Address:

Phone No: Email:

Date of IRB approval:

Start Date of study:

If the start date is > 6 months from the IRB approval date kindly provide the reasons for the same

Duration of study(overall) :

No of study arms:

CONTINUOUS REVIEW APPLICATION (CRA)

PART-II

1) **Project Status**

- Ongoing (Kindly select one option from below)
  ____ Active Enrollment ongoing
  ____ Accrual completed /Follow-up ongoing
- Suspended (If 'Suspended' state Reason and provide date of suspension)

……

……

- Not started/Not initiated (If 'Not started' state Reason)

……

2) **Provide the date of last status review report submitted to IRB for this project**

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

3) **Summary of Protocol participants**:

o Target accrual of trial (entire study) _____
o Total patients to be recruited at MCC _____
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: _____
o Any Impaired participants

- None_____
- Physically _____
- Cognitively _____
- Both _____

MCC Case No.	Reason for withdrawal

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

- YES / NO

If 'Yes', attach in format below

MCC Case No	SAE Event	Report Type	StudyArm	Submission date to DSMB

b) In case of multicentre trials state whether reports of offsite SAEs have been submitted to the IRB –

- Yes / No

5) Have any Deviations/Violations been noted since the last status report?

- YES / NO

If 'Yes', attach in format below

MCC Case No.	Type of Deviation	Study Arm	Date of Submission

PART-III

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

- YES / NO

If 'YES', were these Protocol Amendments approved by IRB?

- YES / NO

If 'YES', please provide in format below

7. a) Have any Informed Consent documents been amended since the last status report?

YES / NO

b) If 'YES', were these Informed Consent Document amendments approved by IRB?

YES / NO

c) If 'YES', fill in format below

d) 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

Amendment No. Version Dated	Date of Submission	Date of Approval

8) **Is the recruitment on schedule?**

- YES / NO

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

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

- YES / NO

(If 'YES', Kindly attach a sheet explaining the changes)

10) **Have any participants withdrawn from this study during the last one year?**

- YES / NO

(If 'YES', Kindly attach a sheet stating reasons for drop-outs)

11) Have any participating investigators been added or deleted since the last status report was submitted to IRB?

- YES / NO

(If 'YES', Kindly attach a sheet with details regarding the changes)

12) Have any new collaborating sites (institutions) been added or deleted since the last status report was submitted to IRB?

- YES / NO

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

13) **Does the protocol have an inbuilt monitoring plan?**

- YES / NO

(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, TMH)

14) **When was study last monitored?**

Date of monitoring __ __ / __ __ / __ __ __ __ (DD/MM/YYYY)

Monitored by _____

Number of subjects monitored _____

15) Is the Data Safety and Monitoring Board report available?

- YES / NO (If 'YES', submit as an attachment)

16) Did the monitoring team have any adverse comments regarding the study

- YES / NO (If, 'YES', please attach a copy of their comments)

17) Is the report on interim data analysis available?

- YES / NO (If 'YES', kindly submit as an attachment)

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

- YES / NO (If 'YES' kindly attach a sheet providing the details)

19) Has there been any presentation/publication related to the data generated this trial?

- YES / NO (If, 'YES', kindly attach a sheet enclosing the details)

20) **Details regarding the budget**

Total budget proposed for the project _____ (in Rs.)

Total budget sanctioned for the project _____ (in Rs.)

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

- YES / NO (If YES, kindly append a statement of disclosure for the same)

……..

SIGNATURES:

Principal Investigator:

Signature with Date :

ANX2-VER1/SOP05/VER1

Reminder letter by the IRB to investigator

(Will be communicated twice as Reminder 1 & Reminder 2, respectively, through e-mail in two consecutive weeks)

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

The above referenced project was approved by the IRB-IEC on __ __/__ __/__ __ __ __ and is due for continuing annual review by the IRB.

Kindly submit the continuing review application at the earliest.
Thanking you for your co-operation,

Yours truly,

Secretary,
Data Security & Monitoring Sub-Committee
Institutional Review Board, MCC

ANX3-VER1/SOP 05/VER1

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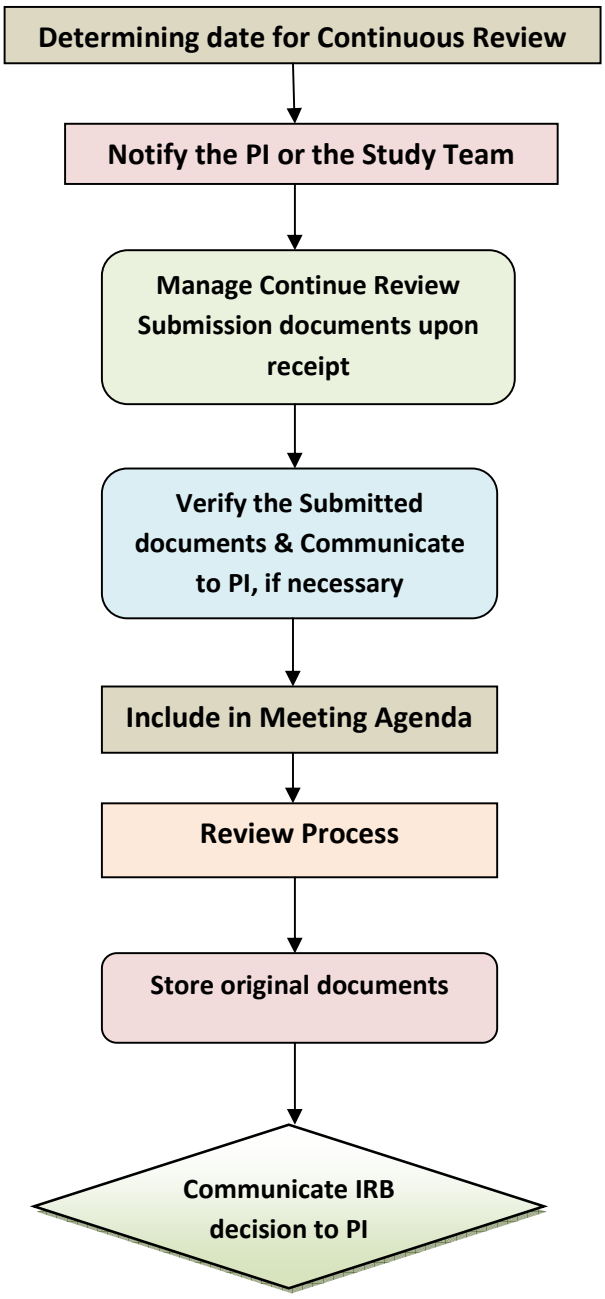
Determining date for Continuous Review
Notify the PI or the Study Team
Manage Continue Review Submission documents upon receipt
Verify the Submitted documents & Communicate to PI, if necessary
Include in Meeting Agenda
Review Process
Store original documents
Communicate IRB decision to PI

CHAPTER 6

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

SOP 06/ VER1

CHAPTER 6

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

6.1 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

6.2 SCOPE

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

6.3 RESPONSIBILITY

1. Office of IRB is responsible for receiving deviations /violations/waiver reports as per (*ANX1–VER1/SOP06/VER1*) 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.

6.4 DETAILED INSTRUCTIONS

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

6.4.1.(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

6.4.1 (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

6.4.1.(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.

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

6.4.1(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.

6.4.2 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.

6.4.3 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

6.4.4 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.

6.4.5 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.
- Maintains a file that identifies investigators who are found to be non-compliant with national / international regulations or who fail to follow protocol approval stipulations or fail to respond to the IRB-IEC request for information/action

References

1. World Health Organization, Operational Guidelines for Ethics Committees that Review
   Biomedical Research, (Geneva 2000) www.who.int/tdr/publications/publications
2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996- http://www.ich.org/LOB/media/MEDIA482.pdf

GLOSSARY

***Deviation / on-compliance / Violation*:** The Institutional Ethics Committee (IEC) of IRB, MCC, monitors whether investigators do not perform the study in compliance with the approved protocol, ICH GCP, FDA regulations and/or fail to respond to the IEC request for information/action.

Waiver: Protocol Waiver is analogous to a Protocol Deviation, except that prior IRB approval must be obtained before implementing the necessary departures from the protocol.

ANX1-VER1/SOP06/VER1

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:

☐ Minor ☐ Major ☐ Other (Tick whichever applicable)

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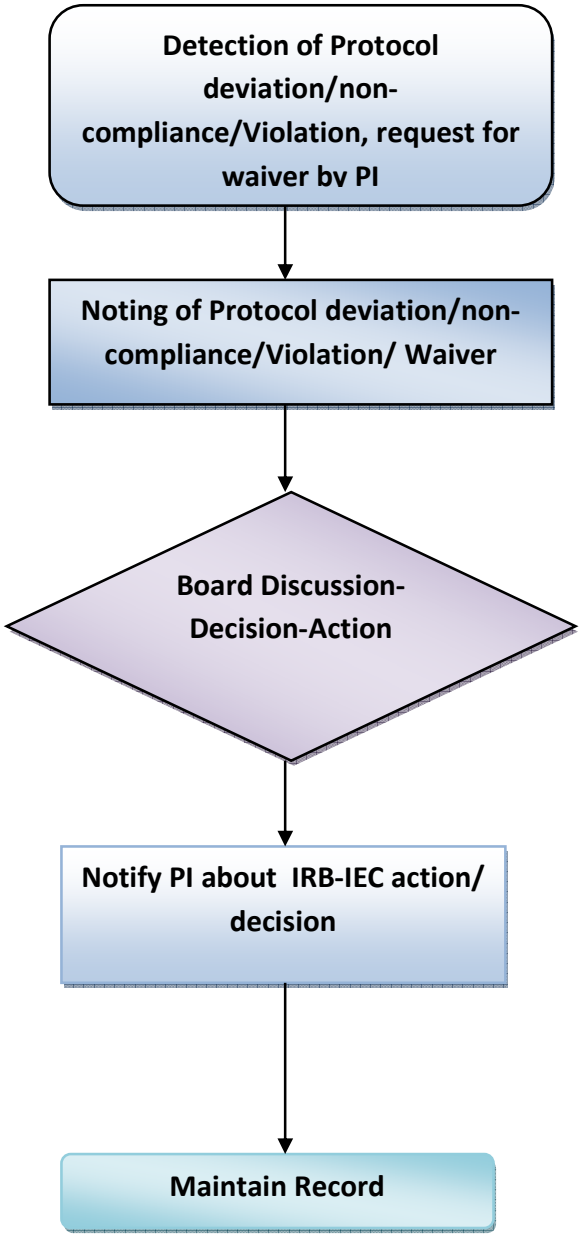
Detection of Protocol deviation/non-compliance/Violation, request for waiver bv PI
Noting of Protocol deviation/non-compliance/Violation/ Waiver
Board Discussion-Decision-Action
Notify PI about IRB-IEC action/ decision
Maintain Record

CHAPTER 7

Review of Reports on Serious Adverse Events (SAEs)

SOP 07/ VER1

CHAPTER 7

Review of Reports on Serious Adverse Events (SAEs)

7.1 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.

7.2 SCOPE

This SOP applies to the IRB review of SAE and unexpected events reports, onsite and offsite, including follow up reports submitted by investigators or researchers. The detailed instructions regarding on site and off site SAE review are described in the following section 7.4.

7.3 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.

7.4. DETAILED INSTRUCTIONS

(A) On site SAEs

7.4.1 Instructions for PI

- ✓ PI shall report all SAE to the any two members of IRB (either SRC or IEC) that accorded approval to the study protocol within 7 working days of their occurrence.
- ✓ If the outcome of an SAE is 'Death' the DSMB should be notified within 24 hours of the knowledge of the PI. If a delay is expected then the same should be initially notified by email. A comment will be made on the SAE form regarding the receipt of the information by Office of IRB.
- ✓ In case the event is Death due to progressive disease the event should be notified in the SAE reporting format unless specified in the protocol.
- ✓ If the patient is out of trial and on survival follow up the event should be notified unless specified in the protocol.
- ✓ 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.

7.4.2 SAE related activities before conducting IEC meeting

- ✓ SAEs are received at the DSMB office as original and two photo copies and a soft copy of the SAE.
- ✓ The Office of IRB will verify that the reports are complete, signed and dated by the PI/CoPI/CoI and are checked for dates and typo errors in the SAE event description, SAE event term and CTCAE grading .
- ✓ In case the Office of IRB notes that the report is incomplete, the report will be reverted back to PI by the consent of Member Secretary, DSMB.
- ✓ The Office of IRB should receive the reports of SAEs occurred for IRB approved studies within 7 days of the occurrence of the SAE.
- ✓ If the outcome of an SAE is 'Death', the Office of IRB should receive the SAE reporting form (*ANX1-VER1/SOP 07/VER1*) within 24 hours of the knowledge of the PI.

- ✓ In case of Death reporting, the hard copy is reviewed by DSMB & Office of IRB else the soft copy is sent to DSMB secretary and Office of iRB for comments within 24hrs of SAE reporting.
- ✓ The SAE reported for death will be stamped "DEATH" on the right corner of the 1st page of SAE form for easy / immediate identification.

7.4.3 Actions to be taken by Member Secretary, IEC

- The Member Secretary, IEC, will review the SAE Report, write comments and forward it to the Secretary, Data Safety & Management Sub-Committee (DSMB), immediately.
- If the outcome of any SAE reported is 'death', the Member Secretary, IEC, will review the SAE report and forward it to Member Secretary, DSMB within 1 working day for immediate action either as the hard copy or via email. If deemed necessary, Member Secretary of IEC and Member Secretary, DSMB will review the SAE, death, either in person, by e-mail or telephone and inform the Chairperson, IEC.
- Any queries raised are emailed to the PI for action
- In case of urgency or if a particular significant trend in serious unexpected and related or unrelated events is observed on any trial a meeting may be held based on comments and action suggested by the DSMB/Office of IRB.
- SAE received in every month, scheduled to be discussed in the subsequent DSMB meeting.
- Two Lead discussants are assigned by Secretary, 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, DSMB for finalization and signature.
- The original signed hard copy of agenda is filed. The meeting agenda and SAEs are sent to DSMB members.

7.4.4 After the DSMB review of SAE

- ➢ After meeting, the Minutes are finalized by the Secretary, DSMB.
- ➢ The Office of IRB will send a formal letter signed by DSMB Secretary to the investigator/s with instructions for specific actions as per the DSMB decision.
- ➢ In case a PI fails to respond to the DSMB letter, the matter will be discussed at the next full board IRB meeting and a decision will be taken for specific action by simple majority. The IRB secretariat will send the letter 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 '***DSMB AGENDA and MINUTES file***'
- ➢ Minutes are ratified in the next DSMB meeting. The reply to DSMB queries from PI are reviewed by Secretary DSMB, These replies are discussed in the meeting next scheduled DSMB meeting and may be forwarded to IRB in case further opinion is required. (Decision Pending)

- The Member Secretary will table the DSMB minutes which includes SAE review, at the next scheduled IRB full board meeting.

7.4.5 During the IRB meeting

On site SAEs

- The Secretary, DSMB will inform all the IRB members about the SAEs and actions taken. The minutes of DSMB meeting will be discussed.

- If appropriate, specific action or combination of actions will be taken, based on the consensus decision of the IRB discussion. 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 per recommendation
  - 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
  - Suspend enrolment of new research participants
  - 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

7.4.6 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 Off site SAE Classification form – *ANX2-VER1/SOP09/VER1*) 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 Off site SAE Classification form – *ANX2-VER1/SOP07/VER1*) 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 "Off site 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.

7.5 Off site SAEs

The Line listings submitted by PI on a monthly/quarterly/biannual 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

7.6 DCGI Query on Serious Adverse Events

1) Principal Investigator informs the DSMB about SAE query raised by Drugs Controller General India (DCGI) requesting IRB opinion for a SAE

2) DCGI queries on SAEs which are already discussed in DSMB and ratified in a previous IEC meeting will be answered based on the opinion and findings of the DSMB and IEC at that time. IEC discussion or opinion at that time will be conveyed to DCGI and Principal Investigator. This will be notified in the full board meeting.

3) In potentially contentious issues, Member Secretary, IEC will inform Chairperson, IEC and Chairperson may use his/her discretion to bring it to the full board IRB meeting. The reply to DCGI is sent with a copy of same to Principal Investigator.

References

1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, (Geneva 2000)- *www.who.int/tdr/publications/publications/*
2. International Conference on Harmonization, Guidance on Good Clinical Practice, (ICH GCP) 1996 - http://www.ich.org/LOB/media/MEDIA482.pdf
3. Schedule Y (Drugs and Cosmetic Act 1940; amendment 20th January 2005) Retrieved from- *http://www.cdsco.nic.in/html/Schedule-Y 20 (Amended 20Version- 2005)*
4. "Adverse Event Terminology" by Norman M. Goldfarb, Journal of Clinical Research Best Practices, Vol. 8, No. 7, July 2012.

GLOSSARY

Adverse Event (AE)
Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product (see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

Adverse Drug Reaction (ADR)
In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase ―responses to a medicinal product‖ means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.

Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (SADR)
Any untoward medical occurrence that at any dose: 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.

Investigational New Drugs (IND)
Investigational New Drugs means substances with potential therapeutic actions during the process of scientific studies in human in order to verify their potential effects and safety for human use and to get approval for marketing.

ANX1-VER1/SOP07/VER1

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 (Dechallenge &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 Date

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-VER1/SOP07/VER1

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-VER1/SOP07/VER1

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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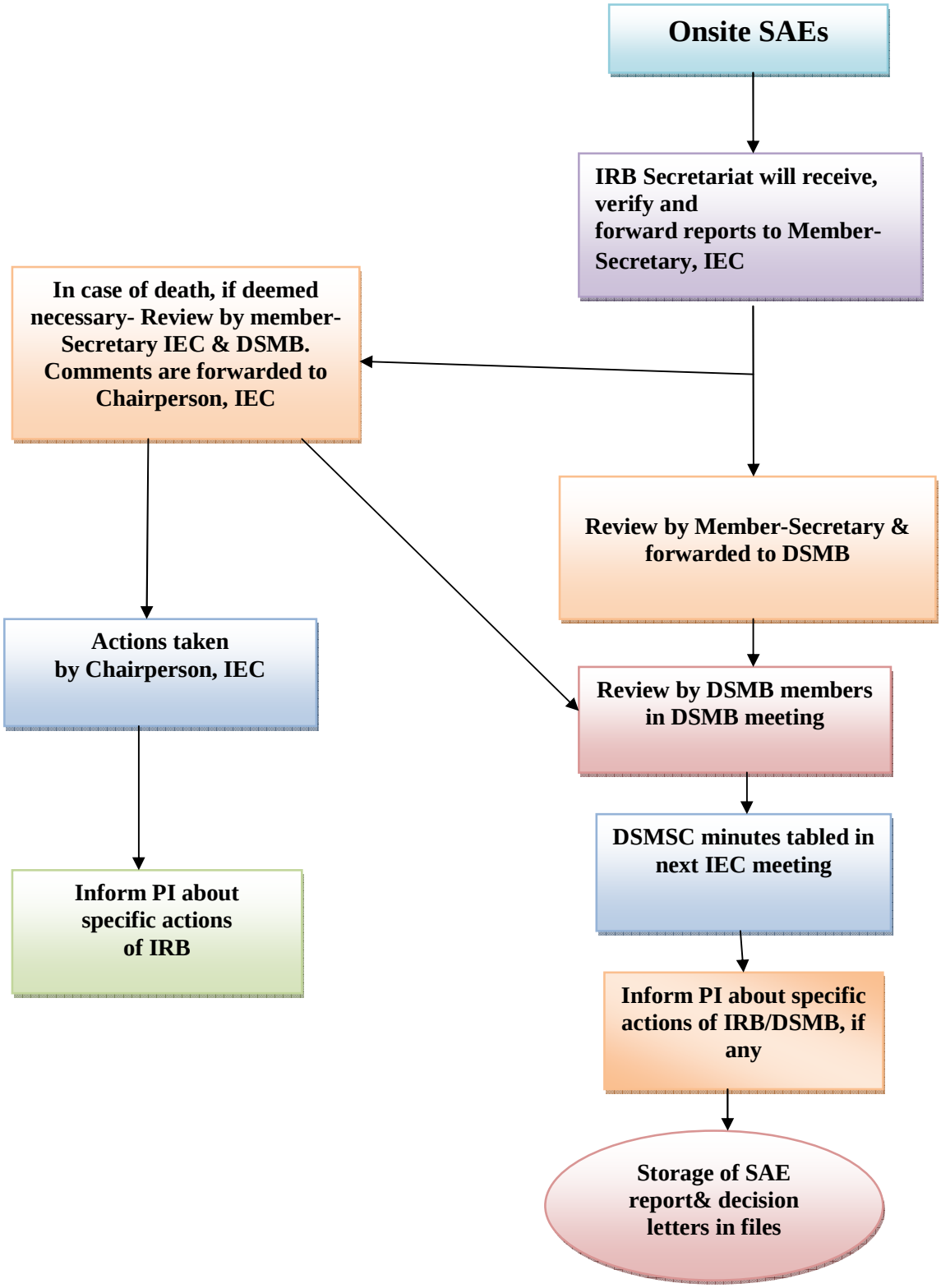

Onsite SAEs
IRB Secretariat will receive, verify and forward reports to Member-Secretary, IEC
In case of death, if deemed necessary- Review by member-Secretary IEC & DSMB. Comments are forwarded to Chairperson, IEC
Review by Member-Secretary & forwarded to DSMB
Actions taken by Chairperson, IEC
Review by DSMB members in DSMB meeting
DSMSC minutes tabled in next IEC meeting
Inform PI about specific actions of IRB
Inform PI about specific actions of IRB/DSMB, if any
Storage of SAE report& decision letters in files

CHAPTER 8

Maintenance of Active project Files, Disposal/Archival of Closed project, Documents Retrieval

SOP 08/ VER1

CHAPTER 8

Maintenance of Active Project files, Disposal/ Archival of Closed Projects, Documents Retrieval

8.1 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.

8.2 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.

8.3 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).

8.4 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 recorded in 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.

8.5 DIS[OSAL 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.

8.6 ACCEESSIBILITY/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 –VER1/SOP 08/VER1*). 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.

8.7 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- VER1/SOP 08/VER1*) will be maintained,

providing details of the documents being written off / disposed off after notification to the Member-Secretary, IEC, MCC.

……

GLOSSERY

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

***Closed Study File*:** Any approved protocol, supporting documents, records containing communications and reports that correspond to a study which is completed or terminated or discontinued or suspended

.

ANX1 –VER1/SOP08/VER1

DOCUMENT REQUEST FORM
Institutional Review Board (IRB)
Malabar Cancer Centre (MCC), Thalassery- 670 103

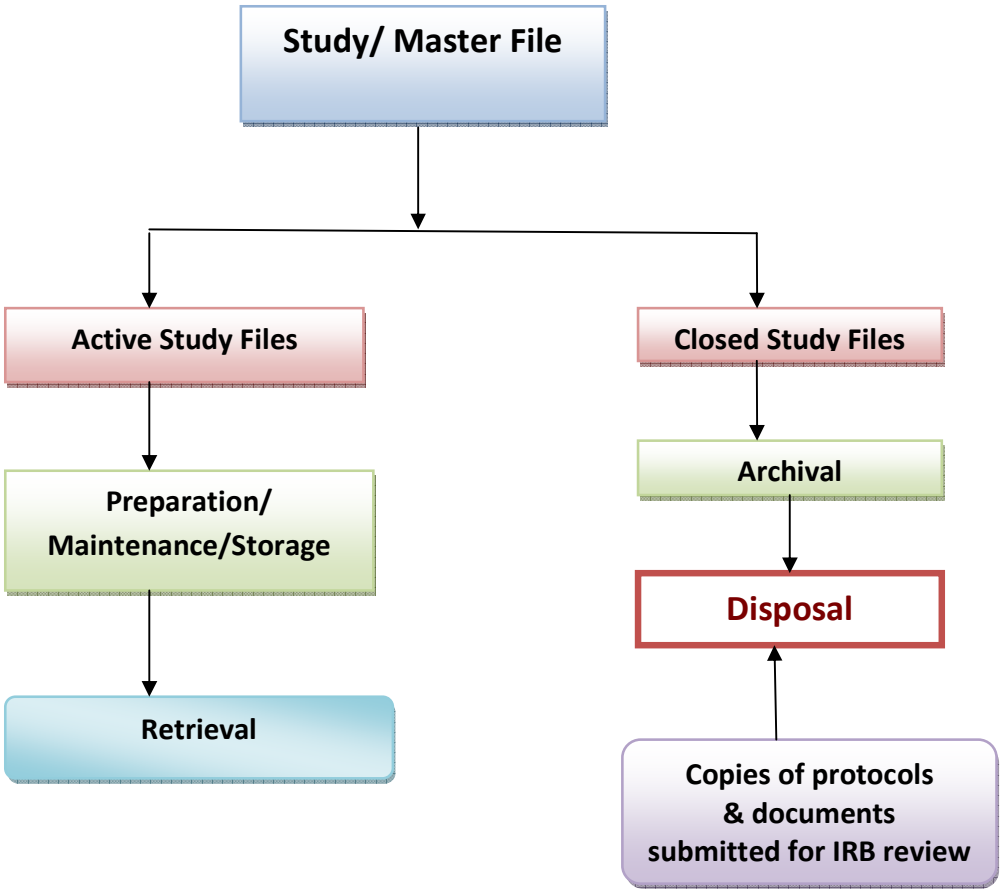
Name of the Principal Investigator/Requesting person:	Date:
Documents requested: Purpose of request:	
Principal Investigator / Requesting person's sign & date	
(For IRB Office use only) IRB Office Decision/Remark: Permission Status: Yes/ No Signature with date of In-Charge, IRB Office	

ANX2 –VER1/SOP08/VER1

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 review

CHAPTER 9

Documentation of IRB Activities

SOP 09/ VER1

CHAPTER 9

Documentation of IRB Activities

9.1 PURPOSE

To describe the procedures for documenting the IRB activities.

9.2 SCOPE

This SOP will apply to all research activity involving human subjects, irrespective of source and nature of funding.

9.3 RESPONSIBILITY

It is the responsibility of the staff members of IRB office to maintain the IRB files at the IRB office.

9.4 DETAILED PROCEDURES

9.4.1 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

9.4.2 Access to IRB records

IRB records will be made available for inspection to authorized representatives of regulatory authorities based on written request.

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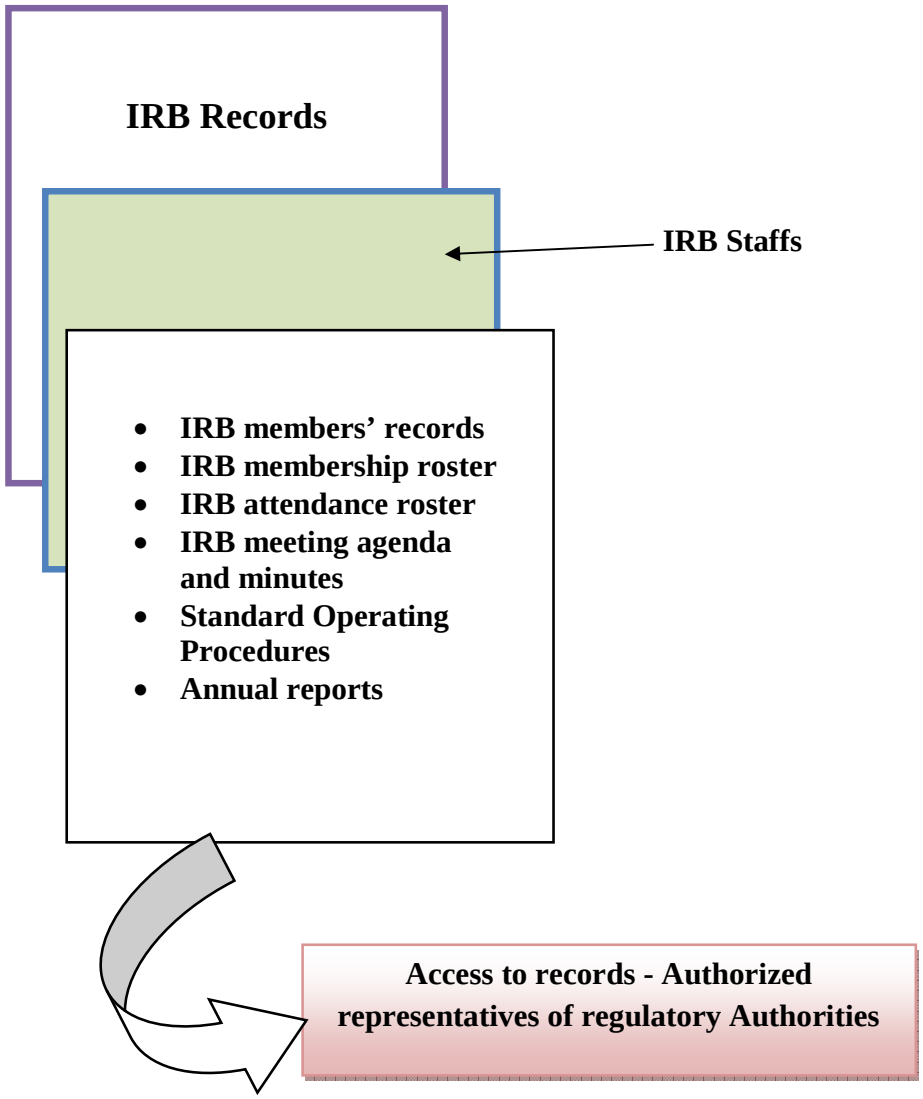
IRB Records
IRB Staffs
IRB members' records
IRB membership roster
IRB attendance roster
IRB meeting agenda and minutes
Standard Operating Procedures
Annual reports
Access to records - Authorized representatives of regulatory Authorities

CHAPTER 10

Study Completion Report Review

SOP 10/ VER1

CHAPTER 10

Study Completion Report Review

10.1 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.

10.2 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-VER1/SOP10/VER1*) 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.

10.3 RESPONSIBILITY

It is the responsibility of the IRB members to review the SCR and notify it or request for further information, if necessary.

10.4 DETAILED INSTRUCTIONS

10.4.1 Before each board meeting

- The Office of IRB will receive 20 hard copies or 5 hard copies + soft copy of Study Completion Reports from the PI.

- The IRB Office will follow instructions as in *SOP03/VER1* (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/VER1*)

10.4.2 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.

10.4.3 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 08/VER1* and the report for a period of 3 years from the date of completion of the project, if the report is accepted.

References

1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, (Geneva 2000)- *www.who.int/tdr/publications/publications/*
2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996- *http://www.ich.org/LOB/media/MEDIA482.pdf*

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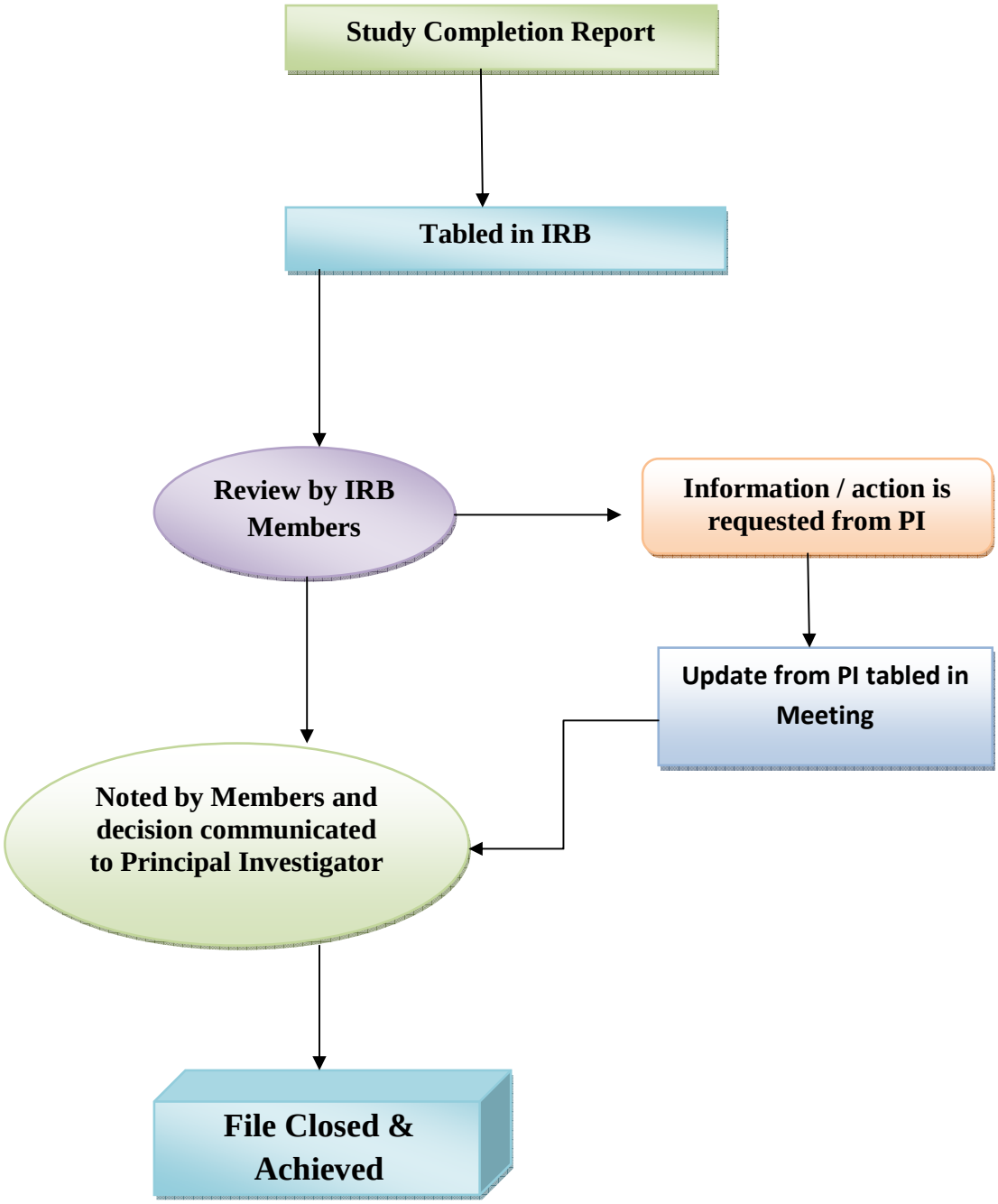
Study Completion Report
Tabled in IRB
Review by IRB Members
Information / action is requested from PI
Update from PI tabled in Meeting
Noted by Members and decision communicated to Principal Investigator
File Closed & Achieved

ANX1- VER1/SOP10/VER1

Study Completion Report (SCR) Form
Institutional Review Board (IRB)
Malabar Cancer Centre (MCC), Thalassery- 670 103

MCC Project No.:

Study Title:

Principal Investigator:

Co-PIs:

Sponsor(s):

Duration of the Study (in Months):

Study Start Date:

Study End Date:

Summary of Protocol participants:

o Target accrual of trial (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: _____
o Any Impaired participants

- None _____
- Physically _____
- Cognitively _____
- Both _____

MCC case no. & Reason for withdrawal
Objectives:
No. of Study arms:
Results (brief) (use extra blank sheets, if more space is required):
Presentation/ Publication on the data generated in this research :
SAEs at MCC (Total number and type) :
Whether all SAEs were intimated to the IRB (Yes/No) : If No, indicate Reason ……
Protocol deviations/violations (Number and nature)
Conclusion
Please specify if the raw data was submitted to Office of IRB, MCC (applicable only for investigator initiated studies supported by intramural funding):
Signature of PI: Date: Place:

CHAPTER 11

Management of Premature Termination/ Discontinuation/ Suspension of the Studies

SOP 11/ VER1

CHAPTER 11

Management of Premature Termination/ Discontinuation/ Suspension of the Studies

11.1 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.

11.2 SCOPE

This SOP applies to any study approved by IRB that is being recommended for termination/suspension/discontinuation before its scheduled completion.

11.3 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.

11.4 DETAILED INSTRUCTIONS

11.4 (A) Receive recommendation for study termination / suspension / discontinuation

- The IRB Office will receive recommendation and comments from DSMB, PI, Sponsors or other authorized bodies for premature termination of study.

- The IRB members/Chairperson, IEC, can prematurely terminate the study if protocol non-compliance/ violation is detected and IRB decision is to terminate the study due to any reason, e.g.- Frequent SAEs occurring at trial site may require the study to be terminated prematurely for the safety & security of the patients.
- The IRB Office will inform the PI to prepare and submit a Premature Termination Report (PTR)
- The IRB Office will receive the study protocol termination prepared and submitted by the PI and verify the contents of the report for inclusion of:

i. Premature Termination Report/ suspension/ discontinuation (*ANX1- VER1/SOP11/VER1*) signed and dated by the PI and/or other material (letter from PI/sponsor etc.)
ii. The Office of IRB will check the completeness of the information
iii. The Office of IRB will receive and acknowledge the reports.

11.4 (B) Review and discuss the Termination / suspension/discontinuation report

- IRB will review the termination report suspension/discontinuation at regular full board meeting or expedited review meeting.
- The Member-Secretary, IEC, MCC, in the meeting will inform of the premature termination suspension/ discontinuation of the project and the IRB members will review the Premature Termination Report (*ANX1- VER1/SOP11/VER1*) along with relevant SAE report/DSMB reports

- If the Premature Termination Report suspension/discontinuation is unclear/more information is required from the PI, the Office of IRB is instructed to send a query to the PI.

11.4 (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 forthcoming full board meeting /expedited review meeting and steps in **11.4 (B)** will be performed by the IRB secretariat.

11.4 (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.

……

References

……

1. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996 - *http://www.ich.org/LOB/media/MEDIA482.pdf*

2. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, (Geneva 2000)- w*ww.who.int/tdr/publications/publications/*

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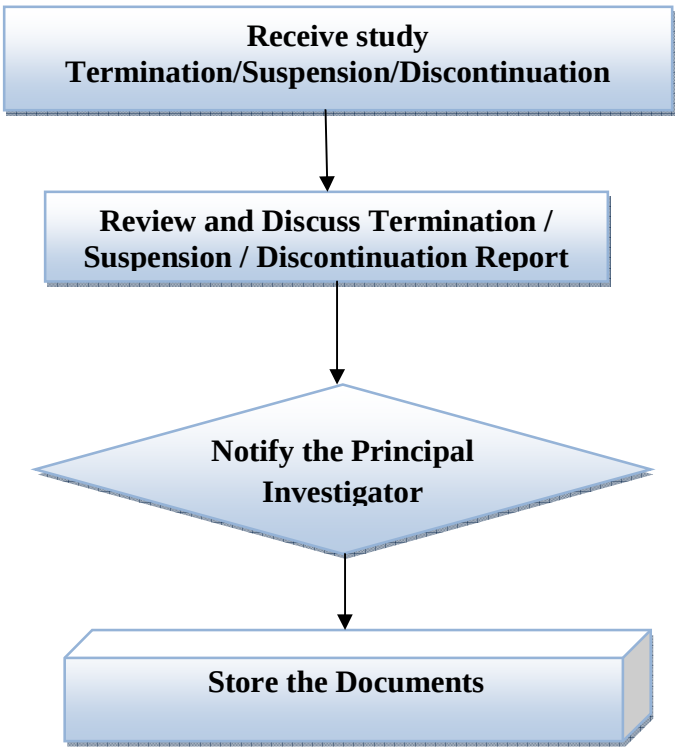

ANX1- VER1/SOP11/VER1

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: _____

<table>
<tr><td colspan="2">o Patients lost to follow up: _____

o Any other: _____</td></tr>
<tr><td colspan="2">Any Impaired participants

▪ None _____
▪ Physically _____
▪ Cognitively _____
▪ Both _____</td></tr>
<tr><td>SAE (Total No.)*:</td><td>SAE Event*:</td></tr>
<tr><td colspan="2">Reason(s) for Termination/Suspension/Discontinuation*:</td></tr>
<tr><td colspan="2">Summary of Results:</td></tr>
<tr><td>PI Signature</td><td>Date</td></tr>
</table>

***Mandatory fields**

CHAPTER 12

Review of Request for waiver of Written Informed Consent

SOP 12/ VER1

CHAPTER 12

Review of Request for Waiver of Written Informed Consent

12.1 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-VER1/SOP 12/VER1 is* designed to standardize the process of applying for consent waiver.

12.2 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.

12.3 RESPONSIBILITY

It is the responsibility of the Principal Investigator of a study to ask for a request directly to the Member Secretary of IEC, MCC, of Chairperson, SRC, (as the case may be) for tabling the request along with the project proposal for expedited or full board review.

12.4 DETAILED INSTRUCTIONS

When a request for waiver of consent is submitted by the Principal Investigator along with the study documents to the IRB Office, in the given format *ANX1-VER1/SOP 12/VER1* stating the reasons for the consent waiver; the following steps are taken:

- The IRB Office will check if the concerned documents are filled completely and the required list of documents is 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 methods described in the protocol for protection of the identity of the research participants and maintaining confidentiality of the study data. This is absolutely 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 whether to grant the waiver is taken during expedited or full board review.
- The decision regarding approval/disapproval of waiver is informed to the Principal Investigator in writing. If the waiver is not granted, the IRB must provide suitable reasons for the same.

12.5 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.

1. The proposed research presents no more than minimal risk to subjects. (ICMR guidelines, 45CFR 46) e.g. a retrospective review of patient case records to determine the incidence of disease/ recurrence of disease.
2. [***Minimal risk*** *would be defined as that which may be anticipated as harm or discomfort not greater than that encountered in routine daily life activities of 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 undergoing these interventions since it would be undertaken as part of current everyday life*].
3. Projects involving Theoretical developments of Techniques, e.g., Biostatistical/ Mathematical Model Building methods, Diagnosis Quality improvement Techniques etc. & Short term (*Max of 6 Months length*) academic projects in the area of Theoretical Developments of different Science streams related to onlocology. It is to be noted that these types of projects will not include any prospective data related to patient in any form of existence.

4. 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. (*ICMR 2006 guidelines*) *e.g. conducting interviews with citizens about their religious beliefs/ people with HIV and AIDS/conducting phone interviews with homosexuals.*
5. 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. [*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) <u>The following documents need to be submitted for the IRB review</u>

- ✓ 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 (questions to be asked???) 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, investigator(s) 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 specific number 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.

6. 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. (*ICMR 2006 guidelines*)
7. Research on anonymised biological samples from deceased individuals, left over samples after clinical investigation, cell lines or cell free derivatives like viral isolates, DNA or RNA from recognized institutions or qualified investigators, samples or data from repositories or registries etc. (*ICMR 2006 guidelines*)
8. In emergency situations when no surrogate consents can be taken. (ICMR 2006 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.

9. 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.

10. 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:
11. The research involves no more than minimal risk to the subjects;
12. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
13. 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.
14. The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.
15. 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 federal, state, or local law.
16. 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

17. 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. An IRB may waive the requirement for the investigator to obtain signed consent form for some or all subjects if it finds either:

    (I) 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

    (II) 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.
    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.

……

References:

1. Ethical Guidelines for Biomedical research on Human Participants, ICMR (2006)
2. 45CFR Title 45 Public Welfare (45 CFR 46) Protection of human subjects, Department of Health and Human Services, revised June 23, 2005. http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html; accessed on 6th May'2013

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ANX1-VER1/SOP 12/VER1

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:

3. Project Title:

4. 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 2006 Guidelines- http://www.icmr.nic.in/ethical_guidelines.pdf) ☐
   d) Any other (please specify)

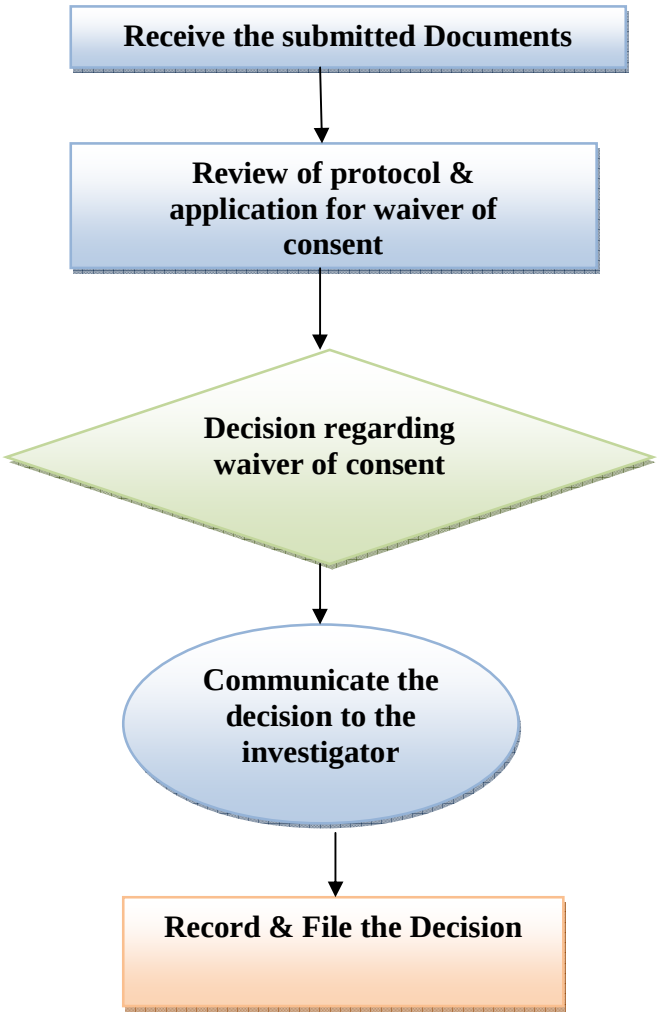
- Statement assuring that the rights of the participants are not violated

_____

- 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 13

Site Monitoring

SOP 13/ VER1

CHAPTER 13

Site Monitoring

13.1 PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to provide the procedures to select a site for monitoring and how the site will be monitored.

13.2 SCOPE

This SOP applies to any visit and/or monitoring of any study sites of IRB approved study protocols.

13.3 RESPOSIBILITY

The Secretary of Data Safety & Monitoring Board (DSMB) assigns the reviewers /monitors to monitor the investigator initiated trials.
The IRB members or IRB Office in consultation with the Chairperson, IEC, may initiate an onsite Evaluation of a study site for cause.

13.4 DETAILED INSTRUCTIONS

13.4.1 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:

i. *for high number of protocol violations*
ii. *too many studies carried out by Principal Investigator*

iii. high number of SAE reports
iv. high recruitment rate
v. non-compliance or suspicious conduct
vi. any other cause as decided by IRB, MCC

13.4.2 Before the visit

- For cause/routine monitoring of the project, the IEC 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.
  - 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-VER1/SOP13/VER1*).

13.4.3 During the visit

The monitor will

- Review the informed consent document to make sure that the site is using the current approved version
- Review randomly the subject's source files for proper informed consent documentation. Observe the informed consent process, if possible,
- Observe laboratory and other facilities necessary for the study at the site, if possible.
- Review the study files to ensure that 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 subjects.
- 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, the protocol, the IEC, the sponsor, and the applicable regulatory requirement(s).

- Collect views of the study participants, if possible.
- Fill the Site Monitoring Visit Report Form *ANX1-VER1/SOP13/VER1*and write the comments.

13.4.4 After the visit

- The monitor will complete the report (use the form *ANX1-VER1/SOP13/VER1***) within *2 weeks*** describing the findings of the monitoring visit and submit the same to the DSMB. After the form is received at IRB office, it is checked for completeness.
- Form is reviewed by DSMB secretary, queries if any, are sent to PI and the form is Forwarded to IEC for action
- In case of minor findings letter is sent to PI else the IRB office in-charge will decide whether to table the monitoring visit report in the next IRB full board meeting
- In-charge of IRB Office/DSMB member representative/lead discussant for the project can present the monitoring visit findings in the full board meeting.
- The Office of IRB 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 ***2 weeks*** **of the meeting**.

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GLOSSARY

Monitor

Many IRBs rarely find time to perform monitoring visit themselves. They may ask outside experts or the IRB member to perform the tasks on their behalf and later report their findings to IRB.

Monitoring Visit

An action that IRB or its representatives visit study sites to assess how well the investigators are conducting researches, taking care of subjects, recording data and reporting their observations, especially serious adverse events found during the studies. Normally monitoring visit will be arranged in advance with the principal investigators.

Monitoring Report

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

ANX1-VER1/SOP13/VER1

SITE MONITORING VISIT REPORT
Institutional Review Board (IRB)
Malabar Cancer Centre (MCC), Thalassery- 670 103

1) MCC Project No:

2) Study Title:

3) Principal Investigator:

4) Institute:

5) Type of study: □ Investigator initiated □Pharma □Thesis □Intramural □Extramural

6) Date of IEC approval:

7) Start Date of study:

8) Duration of study:

9) Date of monitoring visit:

10) **Reason for monitoring**:
□ Routine □For Cause (State reason)
□ Protocol Violations/Deviations □ SAE reporting
□ Recruitment rate
□ Other _____

11) **Last Monitoring done**:
□ Yes Date of last monitoring _____
□ No

12) **Project Status**
1) □ Ongoing 2) □ Completed 3) □ Accrual Completed 4) □ Follow-up 5) □ Suspended 6) □ Terminated 7) □ Closed 8) □ Closed Prematurely
In case of the response to the above question is option 5, 6, or 8 kindly provide reason:

13) **Recruitment Status**:

□ Total patients to be recruited -_____
□ Screened: _____
□ Screen failures: _____
□ Enrolled: _____
□ Withdrawn: _____ Reason: _____
□ Discontinued: _____ Reason: _____
□ Completed: _____
□ Active: _____

14) **Is the recruitment on schedule**?
1) □ Yes
2) □ No
If 'No' is it acceptable? □ Yes □ No
If 'No' State reasons/Steps taken by PI to improve recruitment:

15) **Protocol**
Have there been any amendments to the Protocol? □ Yes □ No
If Yes then state changes leading to amendment:
c) Is the Protocol version approved by IRB? □ Yes □ No
d) Is the latest version of the protocol being used for the study? □ Yes □ No

16) **Informed Consent**
a) Is Informed consent obtained from all enrolled participants? □ Yes □ No
c) Is the Informed consent form version approved by IRB? □ Yes □ No
d) Is the latest version of the ICF being used for the study? □ Yes □ No

17) Any Protocol Deviations/Violations noted? □ Yes □ No □ NA
If 'Yes' Kindly state:
Minor Violations: _____
Major Violations: _____
Minor Deviations: _____
Major Deviations: _____
Have all the deviations/violations notified to IRB? □ Yes □ No
Comments (If Any)

18) Have the eligibility, inclusion exclusion criteria been adhered to? □ Yes □ No
19) Are all the Case report forms complete? □ Yes □ No □ NA
20) Have there been any AE/SAE on the study? □ Yes □ No □ NA If 'Yes' a) No. of Adverse events:_____ b) No. of Serious adverse events: _____ c) No. of deaths reported: _____ □ Deaths unrelated to participation in the trial: _____ □ Deaths possibly related to participation in the trial: _____ □ Deaths related to participation in the trial: _____ d) Were all the SAE reports notified and submitted to DSMB within 7 working days and deaths within 24hrs of the knowledge of PI? □ Yes □ No □ NA Comments (If Any)
21) Any are there any changes to the study personnel? □ Yes □ No □ NA If 'Yes' kindly state the same: _____ _____ Is the change notified to IRB? □ Yes □ No □ NA
22) No of patients monitored during this visit: _____
23) Duration of the visit: _____
24) Any outstanding tasks/action items from the visit?

Monitoring visit conducted by:

Name of DSMB member_____ Signature and Date

Name of DSMB member_____ Signature and Date

Name of study team member present: _____ Signature and Date:

CHAPTER 14

Dealing with Patients'/ Study participants' Requests or Complaints

SOP 14/ VER1

CHAPTER 14

Dealing with Patients'/ Study Participants' Requests or Complaints

14.1 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 IEC inform the study participant that queries regarding their rights as a participant in the study may be addressed to the Member-Secretary, IEC 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.

14.2 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.

14.3 RESPONSIBILITY

It is the responsibility of the Member-Secretary, IEC, through a *Clinical Research Coordinator* (*CRC*) / *Clinical Research Manager* (*CRM*) or through a *Clinical Research Nurse (CRN)* 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 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.

14.4 DETAILED INSTRUCTIONS

When IRB member/ CRC/Research Nurse/Investigator/ administrative staff receive an inquiry or request from a research participant/ research participant's representatives/patient:

- The request and information will be recorded in the request record form (Form *ANX1- VER1/SOP 14/VER1*)
- The Member Secretary, IRB-IEC will inform the Chairperson, IRB-IEC about the query/complaint received.
- The Member-Secretary / Members designated by the Chairperson will provide the information required by the research participant.
- In case of a complaint received from a research participant, the Member-Secretary, IEC will initiate a process to identify and address any injustice that may have occurred.
- The Member Secretary will consider the matter for discussion at a full board meeting or to call an emergency meeting of 2 or more IEC members for discussion or to appoint a subcommittee of 2 or more SRC members for enquiry in order to resolve the matter on an urgent basis.

- The Chairperson/ Member Secretary/ designated IRB-IEC 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 research participant by the Secretariat.
- The information including any action taken or follow-up will be recorded in the form
  ANX1- VER1/SOP 14/VER1 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-SRC & IRB-IEC meetings.

14.5 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.

……

Reference

1. Kathleen J. Motil, Janet Allen and Addison Taylor, "When a Research Subject Calls with a Complaint, What Will the Institutional Review Board do?" *IRB: Ethics and Human Research* 26, no.1(January –February 2004):pp 9-13

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GLOSSARY

***Clinical Research Coordinator (CRC)* :** The Clinical Research Coordinator (CRC) is a specialized research professional working with and under the direction of the clinical Principal Investigator (PI). While the Principal Investigator is primarily responsible for the overall design, conduct, and management of the clinical trial, the CRC supports, facilitates and coordinates the daily clinical trial activities and plays a critical role in the conduct of the study. By performing these duties, the CRC works with the PI, department, sponsor, and institution to support and provide guidance on the administration of the compliance, financial, personnel and other related aspects of the clinical study. The clinical research coordinator reports primarily to the Principal Investigator with associated responsibilities to the department head, division administrator or program administrator.

Clinical Research Manager (CRM): A Clinical Research Manager (CRM) for a study assumes overall responsibility for the preparation of protocols and Case Report Forms, finalization of monitoring and data management options (either in-house or contracted to a Contract Research Organization), Ethics committee approval, development of recruitment strategies to increase patient randomization into the trial, the provision of clinical trial materials, and management of the trial. A CRM coordinates the smooth monitoring of trials by identifying and managing qualified staff, establishing audit procedures and ensuring that cleaned data is entered into the database in a timely fashion.

Clinical Research Nurse (CRN) : A Clinical Research Nurse works in a study team to assist team member in research projects. To coordinate the evaluation of subjects eligible for enrolment and to work with nurses, doctors and sponsoring companies and their delegates regarding matters pertaining to the studies ; coordinates with PI regarding giving doses of medicines/study drugs. Specifically to promote, coordinate, assist in study subject enrolment, and complete monitoring documentation and its database entry.

ANX1-VER1/SOP14/VER1

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:

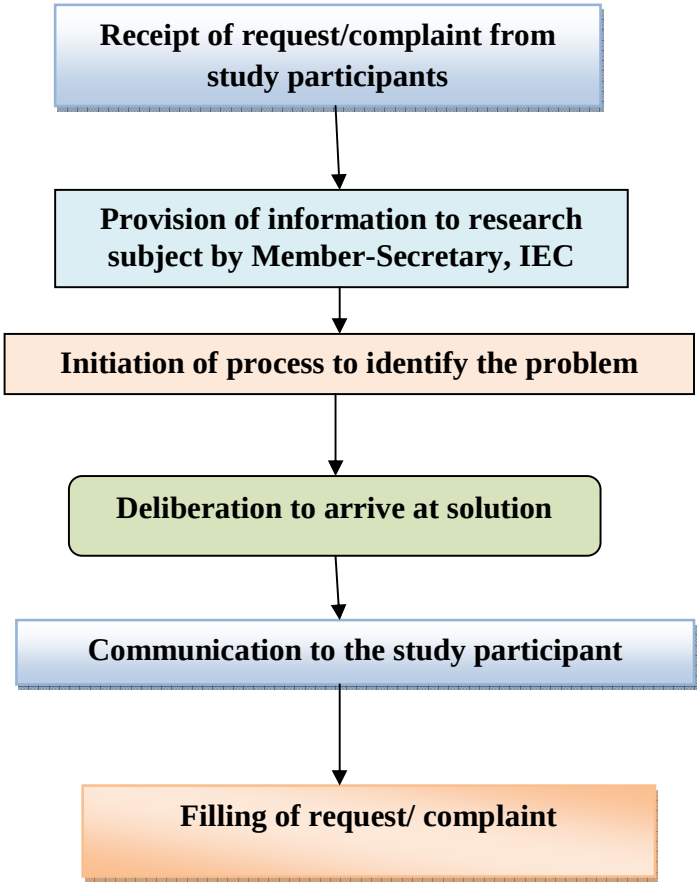
Request :

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 15

Protection of Vulnerable Population in Clinical Research

SOP 15/ VER1

CHAPTER 15

Protection of Vulnerable Population in Clinical Research

15.1. PURPOSE

The purpose of this SOP is to describe the policies and procedures for reviewing research involving vulnerable population such as children, prisoners, fetuses/neonates, pregnant women and individual with consent capacity impairment.

15.2. SCOPE

This guideline is applicable to all members of Institutional Ethics Committee (IEC) of Malabar Cancer Centre, involved in review of clinical trials proposals that include the vulnerable population.

15.3. INTRODUCTION

The Institutional Ethics Committee (IEC) of Malabar Cancer Centre takes special consideration in protecting the welfare considers protecting the welfare of vulnerable subjects such as children, prisoners, fetuses/neonates, pregnant women, and individuals with consent capacity impairment.
The IEC carefully considers group characteristics, such as economic, social, physical, and environmental conditions, to ensure that the research incorporates additional safeguards measures for vulnerable subjects.

The IEC may require additional safeguard measures to protect potentially vulnerable population. For instance, the IEC may require that the investigator submit each signed informed consent form to the IEC, that someone from the IEC oversee the consent process, or that a waiting period be established between initial contact and enrollment to allow time to allow the subject time for family discussion and query resolution, family discussion and questions.

IEC expects to follow the principals laid down in the *ICMR-Ethical Guidelines for Biomedical Research on Human Participant*.

15.4. RESPONSIBILITY

It is the responsibility of the Chairperson and Member-Secretary of IEC to implement, amend and give training to other members of IRB of this SOP.

15.5. PROTOCOL REVIEW PROCESS: DETAILED INSTRUCTION

15.5.1. For Pregnant Women, Foetuse

- Research involving pregnant women and fetuses should involve the least possible risk. The IEC will document specific findings to minimize the potential for risk or harm to the fetus, and additional attention must be given to the conditions for obtaining informed consent.
- The IEC will ensure that women are not encouraged to discontinue nursing for the sake of participation in research except in the cases where breast-feeding is harmful to the infant. IEC will also ensure that compensation in terms of supplying supplementary food such a milk formula will be considered in such circumstances.
- In the event of research related to pre-natal diagnostic techniques, IEC will ensure that such research is limited to detect foetal abnormalities or genetic disorders and not for sex determination.

15.5.2. Research involving Prisoners

- Prisoners may have a limited ability to make truly voluntary and un-coerced decisions about whether or not to participate as research subject.

15.5.3. Children involved as subjects/ participants in Research

- IEC requires special protections for research involving children. Under the regulations, children are persons who have not attained the legal age for consent to treatments or procedures involved in the research under the applicable conducted.

The proposed clinical research must fall within one of the four following categories:

a. Clinical Trial/ Research not involving Minimal Risk.
b. Clinical Trial/ Research involving greater than minimal risk, but presenting the prospect of direct benefits to the individual subjects.
c. Clinical Trial involving greater than minimal risk, yield knowledge that can be generalized about subject's disorder or condition.

- Clinical Trial not otherwise approvable, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health and welfare of children.

- Each category has specific conditions that must be included in their organization Standard Operating Procedures (SOPs) if the institution is involved in human research where children are in the subject population.

- **Parental/Legally acceptable representative Permission**:

    - The IEC require that adequate provisions are made for solicit the permission of each child's parents or guardian/legally acceptable representative.
    - Where parental permission is to be obtained, the IEC will determine whether permission of one parent is sufficient or whether permission must be obtained from both parents in order for the research to be conducted.

- **Assent of the Child**:

  (a) Provisions must also be made in the protocol to obtain the child's assent when the child is capable of giving assent.
  (b) IEC may determine that the assent of the child is not necessary if and only if all three of the following conditions are satisfied:
  (i) The research offers the child the possibility of direct benefit.
  (ii) The benefit is important to the health or well being of the child.
  (iii) The benefit is available only in the context of the research.

- IEC will take great care in approving research where the child is suffering from a life-threatening illness with little real chance of therapeutic benefit from the research.

- IEC will respect the child's refusal to participate in the research and will be cautious in allowing parents/ legally accepted representatives to overrule.

- IEC requires assent form is tailored for the child, with respect to his or her level of understanding. For young children, especially, the assent form should be designed as per the guidelines provided in the annexure of SOP 03/VER1 (*ANX3-VER1/SOP03/VER1*).

15.5.4. Clinical trial involving Decisionally Impaired Subjects

- IEC will consider selection issues, privacy and confidentiality, coercion and undue influence, and risk-benefit analysis. Additional safeguards must be considered by the IEC to protect these subjects.

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References

1. Schedule Y (Drugs and Cosmetic Act 1940; amendment 20th January 2005) Retrieved from *http://www.cdsco.nic.in/html/Schedule-Y 20 (Amended 20Version- 2005)*
2. WHO Operational Guidelines for Ethical Review Committee that Review Biomedical Research (Geneva 2000) Retrieved from - *www.who.int/tdr/publications/publications*
3. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) (1996) Retrieved form - *http://www.ich.org/LOB/media/MEDIA482.pdf*
4. ICMR Ethical Guidelines for Biomedical research on Human Participants, ICMR (2006) Retrieved from - *http://www.icmr.nic.in/ethical guidelines.pdf*

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GLOSSARY

Children: A young human being below the age of full physical development or below the legal age of majority.

Foetus : Means the product of conception from implantation until delivery.

Neonate : Means a newborn.

Pregnancy: This encompasses the period from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

Decisionally-impaired Individuals: Decisionally-impaired individuals are those who have a diminished capacity for judgment and reasoning due to psychiatric, organic, developmental, or other disorder that affects cognitive or emotional functions. Other individuals, who may be considered decisionally impaired, with limited decision-making ability, are individuals under the influence or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps.

List of Members & Addresses

of

Institutional Ethics Committee

Malabar Cancer Centre

List of Members-Institutional Ethics Committee (IEC)-MCC

Sr. No.	Name & Qualifications	Designation with Address, e-mail ID & Contact Number	Position in the IEC
1.	**Dr. T. N. Babu Ravindran,** B.Sc, MBBS, MD	Senior Medical Consultant Indira Gandhi Co-Operative Hospital Manjodi, Thalassery, Dist.: Kannur, Kerala, India PIN- 670 103 Phone: 0490-2341150 Mobile : (+91) 9447541909 e-mail ID:*baburavindran@yahoo.co.in*	**Chairperson** & Basic Medical Scientist
2.	**Dr. Satheesan Balasubramanian** M.B.B.S, MS(General Surgery) DNB, MCh (Surgical Oncology)	Director, Malabar Cancer Centre, Thalassery, Kerala, India. PIN 670 103 Phone : 0490-2355881, 2355981/2357881/2357981. Mobile: (+91) 9895848300 Fax: 0490-2355880 e-mail ID: *directormcctly@gmail.com*	**Member Secretary**
3.	**Dr. D.Vijay Kumar** M.Pharm. Ph.D (Pharmaceutical Sciences)	Principal, College of Pharmacy, Anjarakandy Integrated Campus Anjarakandy PO, Kannur - 670612 Kerala, India. Phone: (+91) 9656158500 e-mail ID: *vdaroji@gmail.com*	Member Scientist (Pharmacology)
4.	**Dr. Rajaram Kizhakkekkandiyil,** MBBS	Superintendent, Thalassery General Hospital, Thalassery. P.O. Thalassery Kannur, Kerala, India. PIN- 670101 Mobile: (+91) 9846005646 Phone:0490-2322150 e-mail ID:*drrajaramkk@gmail.com*	Member Clinician

List of Members-Institutional Ethics Committee (IEC)-MCC

(Contd.)

Sr. No.	Name & Qualifications	Designation with Address, e-mail ID & Contact Number	Position in the IEC
5.	**Prof. Vineetha Menon** M.A, Ph.D (Social Anthropology)	Professor & Head, Department of Anthropology, Kannur University,Thalassery Campus, P.O. Palayad, Kerala, India PIN-– 670 661 Mobile: (+91) 9447552469 e-mail ID: *menon.vineetha@gmail.com*	Member Social Scientist
6.	**Mrs. Kavitha Balakrishnan** B.Sc,LL.B., LL.M ,UGC-NET	Assistant Professor, Head of the Department, Department of Law School or Legal Studies, Kannur University,Thalassery Campus, P.O. Palayad, Kerala, India PIN-– 670 661 Mobile: (+91) 9495908478 e-mail ID: *kavithabalkrishnan@gmail.com*	Member Legal Expert
7.	**Fr Thomas Thengumpally** Doctorate in Canon Law	Judicial Vicar, Arch Bishop House, Thalassery, PB No. 70 Kerala, India. PIN -670101. Mobile: (+91) 9446889444 e-mail ID: *frsajan@gmail.com*	Member Theologist
8.	**Prof. A. N.P. Ummerkutty** M.Sc.(Fisheries), Ph.D (Marine Biology)	Former Vice-Chancellor, University of Calicut, " *Jameelath*", Acharath Road, Templegate P.O., Thalassery, Kerala, India. PIN 670 102. Mobile: (+91) 9495108832 e-mail ID: *ummerkutty.anp@gmail.com*	Member Scientist

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9.	**Prof. Richard Hay** M.Com, Master degree in College Teaching	Former Deputy Director of Collegiate Education, Hays Manor, Nr. Arch Bishop's House, Thalassery, Kerala, India. PIN-- 670 101. Mobile: (+91) 8089729327 e-mail ID:*profhay@gmail.com*	Member Lay Person
10.	**Mrs. Chinnammu Sivadas,** M.A(Sociology), MSW (Social Work)	Managing Trustee, *Salil Sivadas* Foundation, "Salil Bhavan", P.O. Sivapuram, Dist. Kannur, Kerala, India. PIN 670 702. Phone: 0490-2477483 Mobile: (+91) 9447481183 e-mail ID: *csivadas2000@yahoo.com*	Member Social Scientist
11.	**Dr. K. R. Vasudevan** M.B.B.S, MD(General Medicine)	Consultant Physician "*ARCHANA*", Kovilakam Road, Nilambur (P.O),Malappuram, Kerala, India. PIN- 679329 Mobile: (+91) 9447738684 e-mail ID: *krvasudevan50@yahoo.com*	Member Clinician