Tata Memorial Centre

Institutional Ethics Committee

Standard Operating Procedure (SOP)

April 2016

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Preparing Standard Operating Procedures (SOPs): Writing, Reviewing, Distributing & Amending SOPs for the Institutional Ethics Committee (IEC), TMC

SOP Code: SOP 01/V4 Date: 01/04/2016 Pages: 1 to 13

1.1 Purpose

This SOP defines the process for writing, reviewing, distributing, and amending SOPs within the IEC, TMC.

The SOPs will provide clear, unambiguous instructions to conduct activities of the IEC 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), Code Federal Regulations Title 21

1.2 Scope

This SOP covers the procedures of writing, reviewing, distributing, and amending SOPs within the IEC, TMC

1.3 Responsibility

It is the responsibility of Chairperson of the IEC to appoint the SOP Team to formulate the SOPs. SOP team will prepare the draft SOPs. The draft SOPs will be reviewed and approved by the IEC members. SOP team will be responsible to amend the SOPs as and when required.

SOPs will be reviewed by the members of IECs. The Chairpersons of IECs will approve the SOPs. The SOPs will then be signed by Director, TMC as these are Institutional Ethics Committees for Research Review.

SOP team will consist of Member Secretaries of IEC, administrative staff and one or two other IEC members. The team will-

- Assess the request(s) for SOP revision in consultation with the Secretariat and Chairperson
- Propose a new, or modification in existing SOPs as needed
- Select the format and coding system for the SOPs
- Draft the SOP
- Review the draft SOP
- Submit the draft for approval to Chairperson

Chairperson of the IEC

- Appoint one or more SOP Teams
- Reviews and approves the SOPs
- Signs and dates the approved SOPs

IEC members

- Review and sign and date SOPs
- Return all out-of date SOPs to IEC office

Secretariat of IEC

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

1.4 Detailed instructions

1.4.1 Identify the need for new or amendment to the SOP

Any member of the IEC, secretariat or administrative staff or investigators or administration 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, can put forth his / her request by using the Request Form for Formulation of new SOP/ Revision of an SOP Form (AX5-V4/SOP01/V4). This Formulation of new SOP/ Revision of an SOP Form (AX5-V4/SOP01/V4) is submitted to the Chairperson, IEC. The Chairperson will inform all IEC members about this request in a regular full board meeting.

If IEC members agree to the request, the Chairperson will appoint an appropriate SOP team comprising of Member Secretaries of both committees. The Chairperson may also appoint one or two committee members as members of SOP team, if necessary. This designated team will proceed with the task of revision / formulation process of the SOP.
If IEC members do not agree to the request, no further action will be taken.

The Chairperson will inform the person/ IEC member who made the request for modification of the SOP in writing about the decision.

1.4.2 Appoint the SOP team

The Chairperson will constitute a SOP team consisting of the Member-Secretaries administrative staff and one or two other IEC members who have a thorough understanding of the scientific and ethical review process. The SOP writing team will carry out the subsequent steps. (1.4.3-1.4.7)

1.4.3 List of relevant SOPs

- Write down step by step all the procedures of the IEC
- Organize, devise and name each process
- Make a list of SOPs with coding format (e.g. AX1-V4/SOP01/V4)

1.4.4 Design a format and layout

Each SOP should be given a number and a title that is self-explanatory and is easily understood

A unique code number with the format **SOP xx / Vy** will be assigned to each SOP. xx is a two-digit number assigned to a specific SOP. "V" refers to version of the SOP and "y" is a number identifying the version e.g. SOP01/V4 is SOP number 01 with V=version no.04

Each Annexure (AX) is unique code with format AXn–Vp/SOP xx/Vy. **e.g.** AX1–V4/SOP01/V4 indicates AX is Annexure, 4 is Annexure no. , V4 is version 4, belonging to the SOP 01/V4

Each SOP will be prepared according to the template for Standard Operating Procedures (AX2 – V4/SOP01/V4). 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 Head of the Institution.

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, the IEC members who have reviewed the SOPs, IEC Chairperson and Director, TMC

1.4.5 Write, Review and Approve SOP

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

1.4.6 Review by Consultation

- The draft SOP will be discussed with members of IECs and all administrative staff.
- The final version will be forwarded to the Chairperson for review and approval

1.4.7 Preparation and submission of final draft

- All the members of IEC may review the draft / revised SOP
- During respective IEC meetings, members can put forth their suggestions / comments on the draft / revised SOP
- The suggestions agreed upon unanimously by all IEC members will be incorporated and the final draft SOP will be formulated

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

1.4.8 Final Approval of new/revised SOP

- The final version will be presented to the Chairpersons of committees for review and approval. The Chairpersons will sign and date the SOP on the first page of the SOP document.
- This approved document will then be submitted to the Director, TMC for acceptance. This date of approval is declared as the effective date for implementing the SOP.

1.4.9 Implementation, distribution and filing of SOPs

- Approved SOPs will be implemented from the effective date.
- The Member Secretary will discuss the approved SOPs with the administrative staff and instruct them to implement the SOP accordingly.
- Approved SOPs will be distributed to IEC members and IEC staff according to the distribution list (AX4 –V4/SOP 01/V4)
- 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 IEC Secretariat and maintained in the IEC Office.
- A copy of the SOP master file will be maintained in the individual offices of IEC and DSMSC.
- 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 (AX6 –V4/SOP 01/V4)

1.4.10 Review and request for revision of an existing SOP

- Any member of the IEC, secretariat or administrative staff or investigators or administration who notices that current SOPs have some lacunae or have any suggestions to improve a procedure should make a written request, using a form (AX5-V4/SOP 01/V4)
- If IEC agrees with the request, the Chairperson will appoint an appropriate team for the revision process. If the committee does not agree, the Chairperson will inform the concerned individual who made the request for revision. Revised SOPs will be reviewed and approved as per Section 1.4
- The Member Secretary initializing the review and the Secretariat assists the Member Secretary of the SOP at least once every 2 years and records the dates of review in the SOP master file.

1.4.11 Manage and archive old SOPs

Old SOPs should be retained and clearly marked “superseded” and archived in a file by the secretariat. The process of evolution of previous SOPs of the IEC will be documented in a defined format (AX3 –V4/SOP01/V4).

References

1. Schedule Y (Drugs and Cosmetic Act 1940; amendment 20th January 2005) Amendment 2013)
2. ICMR Ethical Guidelines for Biomedical research on Human Participants, ICMR (2006)
3. WHO Operational Guidelines for Ethical Review Committee that Review Biomedical Research (Geneva 2000)
4. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) (1996)
5. Code Federal Regulation Title 21

Glossary

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

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

Master SOP files: An official collection of the Standard Operating Procedures SOP) of IEC, TMC accessible to all staff, IEC members, auditors and government inspectors as a paper copy with approval signatures

Previous SOPs of the IEC: 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 1) IEC members 2) Non-IEC members i.e. investigators/sponsors

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

SOP Team: A team of members selected from the IEC, TMC including the Member Secretary, administrative staff, and any other member of IEC as identified by the chairperson who oversee the creation, preparation, review and periodic revision of the IEC, TMC SOPs

AX1-V4/SOP 01/V4

List of SOPs of Institutional Ethics Committee

Sr. No.	SOP TITLE		SOP CODE	Page Nos.
1	Preparing Standard Operating Procedures (SOPs): Writing, Reviewing, Distributing & Amending SOPs for the Institutional Ethics Committee (IEC), TMC		01/V4	
2	Constitution of Institutional Ethics Committee, TMC		02/V4	
3	Management of Research Study Submissions		03/V4	
4	4a	Full board Review of Submitted Protocol	04a/V4	
	4b	Expedited Review of Submitted Protocol/Documents	04b/V4	
	4c	Exemption from the Review for Research Projects	04c/V4	
5	Agenda Preparation, Meeting Procedures and Recording of Minutes		05/V4	
6	Review of Amended protocol/ Protocol related documents		06/V4	
7	Continuing review of study Protocols		07/V4	
8	Review of Protocol Deviation/ Violation / Non-Compliance/ Waiver		08/V4	
9	Review of Serious Adverse Events (SAE) Reports		09/V4	
10	Maintenance of Active Project Files, Archival/Disposal of closed files and Retrieval of documents		10/V4	
11	Documentation of the IEC activities		11/V4	
12	Review of study completion reports		12/V4	
13	Management of Premature Termination / Suspension / Discontinuation of the study/ Withdrawal of study before site initiation		13/V4	
14	Review of Request for Waiver of Written Informed Consent		14/V4	
15	Study Monitoring		15/V4	
16	Dealing with participants/patients requests and complaints		16/V4	
17	Reviewing Research Protocols Involving Vulnerable Populations		17/V4	

AX2- V4/*SOP01/V4*

Template for Standard Operating Procedures

Institutional Ethics Committee	
Title: *Title which is self-explanatory and is easily understood*	
SOP No: *SOPxx/Vy*	Page: a of b
SOP Code: SOP xx/Vy **Effective date**: DD/MM/YYYY **Authors**: xxxxxxxxx **Reviewed by**: xxxxxxxx **Approved by**: xxxxxxxxx	

AX3-V4/SOP01/V4

Document History of the SOP

Name of the author	Version	Effective date (dd-mm-yy)

Details of superseded SOP

Name of the Team	Version	Type (draft/final)	Date (dd-mm-yy)	Describe the main change

AX 4-V4/SOP01/V4

Log of the IEC members receiving SOPs

No.	Name of Recipients	Designation	SOP code number	No. of Copies	Signature	Date
1	XXXX	Chairperson				
2	XXXX	Member Secretary				
3	XXXX	Member				
4	XXXX	Member				
5	XXXX	Member				
6	XXXX	Member				

AX5-V4/SOP01/V4

Request for Formulation of new SOP/ Revision of SOP

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

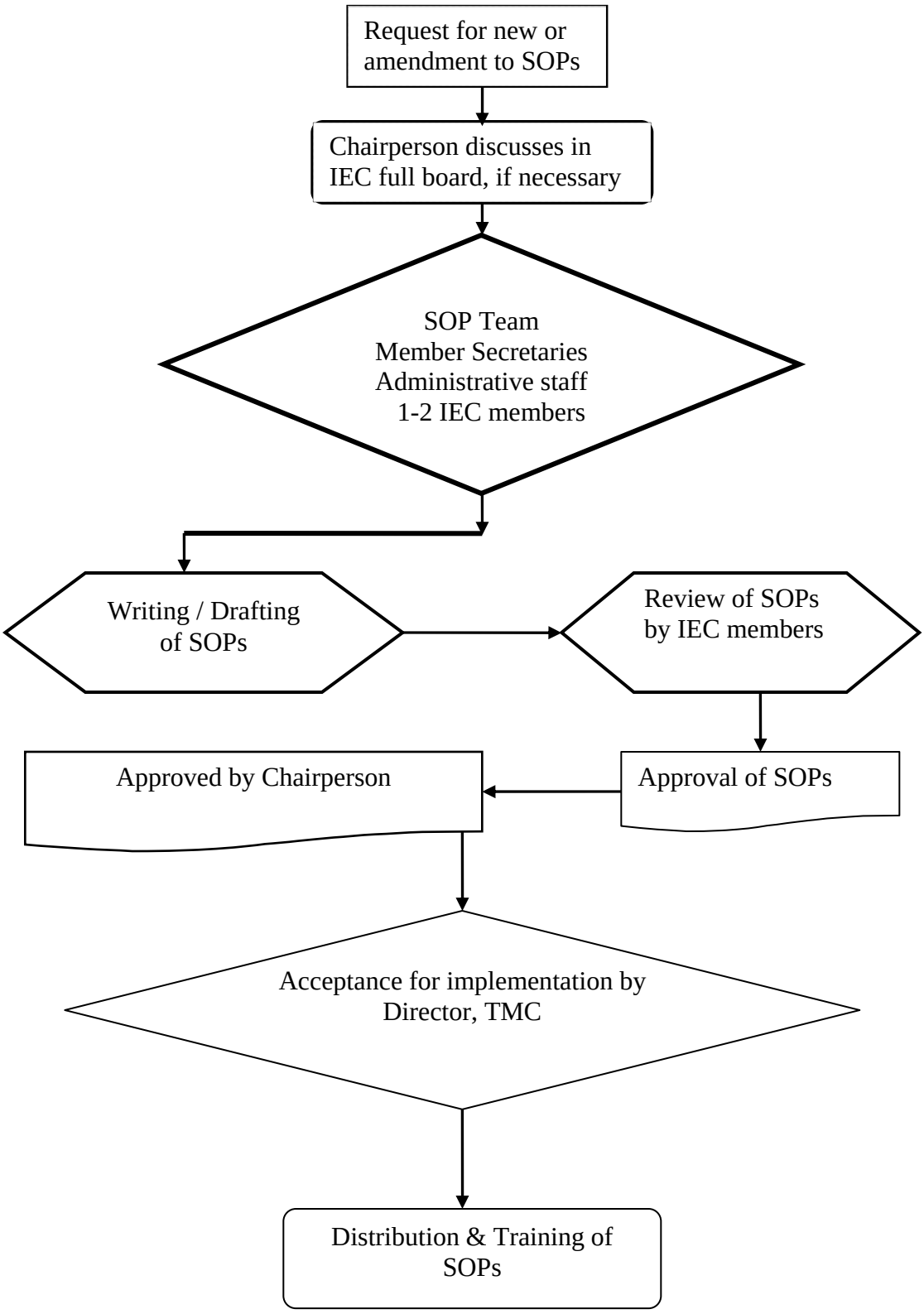
SOP No.	
Title:	
Details of problems or deficiency in the existing SOP	
Need to formulate an entirely new SOP (i.e. SOP not existing previously)	
Identified by:	Date (DD/MM/YYYY):
Discussed in IEC Meeting held on :-	
SOP revision required: ☐Yes	☐No
New SOP to be formulated: ☐Yes	☐No
If yes, to be carried out by whom?	
If no, why not?	
Date SOP revised:	
Date SOP approved:	
Date SOP becomes effective:	

AX6-V4/SOP01/V4

Log of SOP recipients

No.	Name of the Recipients	Designation	SOP code number	No. of Copies	Date
1.	XXXX	XXXX			
2.	XXXX	XXXX			
3.	XXXX	XXXX			
4.	XXXX	XXXX			
5.	XXXX	XXXX			
6.	XXXX	XXXX			

Flow Chart


Request for new or amendment to SOPs
Chairperson discusses in IEC full board, if necessary
SOP Team
Member Secretaries
Administrative staff
1-2 IEC members
Writing / Drafting of SOPs
Review of SOPs by IEC members
Approved by Chairperson
Approval of SOPs
Acceptance for implementation by Director, TMC
Distribution & Training of SOPs

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Constitution of Institutional Ethics Committee (IEC), TMC

SOP Code: SOP 02/V4 Date : 01/04/2016 Pages: 14 to 42

TMC being a premier cancer institute in the country, it has become a hub for oncology based trials. Over the years its scientific rigor and research culture led to a significant increase in the number of clinical trials being conducted. This gave rise to the need for impeccable and efficient management of its clinical trials to ensure the protection of human rights as mandated by Indian law (Schedule Y), and to satisfy public scrutiny.

In lieu of the above, the Hospital Ethics Committee of TMC was established in the year 1996. All research proposals after scientific evaluation and approval by the Scientific Review Committee were subjected to ethical review by Hospital Ethics Committee. Timely review and the safeguarding of high ethical standards formed the basis of the IRB review process. These are essential for clinical research including student research, investigator initiated research, extramural, intramural funded research and multi-centric multinational research.

In view of the tremendous growth of clinical research in the institution, the Director, TMC in the year 2008, constituted two Ethics Committees to function with the same purpose and SOPs, to expedite the review process. All research proposals were scientifically evaluated and approved by Scientific Review Committee before ethical review was taken up. These two committees were renamed as Human Ethics Committee I and II.

However, as per the decision of the TMC-Research Administrative Council (TRAC), in order to manage the review process more efficiently, the TMC Scientific Review Committee and the Human Ethics Committees viz HEC-I and HEC-II, were merged to form the Institutional Review Board. In view of the large number of projects to be reviewed, two Institutional Review Boards (IRBs) were instituted and designated as IRB I and IRB II at TMH. Each IRB reviews both, the scientific and ethical aspects of the study. The IRBs became functional in February 2012. IRB-III located at ACTREC was established in Dec 2009.

The Data Safety Monitoring Subcommittee (DSMSC) is a subcommittee of the IEC, and is essentially responsible 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.

Tata Memorial Centre- IRBs are registered with Drug Controller General India. As the DCGI registration dated May 2013 is in name of Institutional Ethics Committee (IEC), Institutional Review Boards (IRBs) were renamed as Institutional Ethics Committees (IEC-I,II,III).

- IEC-I has Ethics Committee Registration No. ECR/170/Inst/MH/2013 issued under Rule 122DD of the Drugs & Cosmetic Rules 1945
- IEC-II Ethics Committee Registration No. ECR/414/Inst/MH/2013 issued under Rule 122DD of the Drugs & Cosmetic Rules 1945.
- IEC-III Ethics Committee Registration No. ECR/149/Inst/MH/2013 issued under Rule 122DD of the Drugs & Cosmetic Rules 1945.

Name and Address of the IECI &II:

Institutional Ethics Committee,
Main Building, 3rd Floor,
Tata Memorial Hospital,
Dr. Ernest Borges Marg,
Parel, Mumbai 400 012
Phone: +91-22-24177262/ extn-4268
Email- tmhethics@gmail.com

Name and Address of the IECIII:

Tata Memorial Centre- Advanced Centre for Treatment, Research & Education in Cancer, Institutional Ethics Committee (TMC- IEC III),
Room no 128, Paymaster Shodhika, First floor,
ACTREC, Kharghar,
Sector 22 Navi Mumbai 410210
Phone: +91-22-27405154
Email- irb@actrec.gov.in

Institutional Ethics Committees function with the same purpose and SOPs.

The Institutional Ethics Committees (IECs) are constituted by the Director, Tata Memorial Centre (TMC) under authority vested by the Governing Council of the TMC. This refers to all Institutional Ethics Committees (IECs) constituted under TMC. Currently TMC has 3 IECs. In case the numbers of IECs increase or reduce, this IEC SOPs applies to all IECs.

Institution has a Federal Wide Assurance (FWA) with the Department of Health and Human Services (DHHS) through the Office for Human Research Protections (OHRP). The assurance number is **FWA00006143**. This is periodically renewed as required.

IECs are also registered with HHS and have IORG Nos. IRB00003414, IRB00007802, IRB00009642 for IEC-I, IEC-II & IEC-III respectively. This is periodically renewed as required.

WHO/The Strategic Initiative for Developing Capacity in Ethical Review (SIDCER) in collaboration with the Forum for Ethical Review Committees in Asia and the Western Pacific Region Forum for Ethical Review Committees in Asia and the Western Pacific Region (FERCAP) have awarded recognition to the Tata Memorial Centre Human Ethics Committees-I & II (TMC-HEC) in November 2009. The recognition of IRBs-I & II was renewed in Nov 2012.

Tata Memorial Centre was awarded accreditation by the Association for the Accreditation of Human Research Protection Programs (AAHRPP) in June 2014.

2.1 Purpose

The IEC was established to formalize and specify Institution's commitment to the promotion of high scientific and ethical standards in patient care, professional education, clinical research, and community interests.

2.2 Mandate

The IEC through its delegated sub-committees functions independently for maintaining a consistent scientific and ethical framework for patient care and research, and for integrating ethical values into practice, policy relationships, and organizational activities.

- The purpose of the IEC is to cultivate a pluralistic and democratic exchange of scientific and ethical values and concerns, and to critically analyze them while looking for opportunities to enhance the scientific and ethical integrity of Institution.
- The mandate of the IEC essentially is to promote patient care through a scientific and ethical approach to research and education.

The terms of reference for the IEC are as follows:

1. Ensure the highest scientific and ethical standards of research at TMC
2. Review and approve, proposals for clinical, basic or translational research projects (Intra and Extra mural) for scientific and ethical content
3. Improve ethical standards and issue guidelines on ethical dilemmas related to patient care services
4. To function as a forum to advise the administration in case of any ethical issues that may arise from patients, families or public
5. To maintain our leadership as a national standard of reference in all fields
6. To issue and periodically, update and revise SOPs and guidelines for effective functioning of IEC as and when necessary
7. Continuing education in clinical research bioethics and ethical aspects of clinical practice by seminars, workshops and interactive discussions for all categories of staff members including nursing and paramedical staff
8. To initiate and commission research studies on ethical aspects of practice in TMC

    - The IEC endeavors to provide guidance on a broad range of topics such as disclosures of diagnosis, diagnosis of brain death, indications for stopping resuscitation, true informed consent, etc.
    - The committee does not address or interfere in matters of administration, nor does the committee function as a grievance cell for staff members.

2.3 Scope

The SOP applies to the formation of the IEC.

2.4 Responsibility

The IEC 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 in compliance with the appropriate laws, and welfare of participants.
- 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 IECs (SOPs).
- Initiate research studies in ethics.
- Continuing education and training programs to ensure that IEC members are qualified 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 IEC 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 IEC is aware of the diversity of laws, cultures and practices governing research and medical practices in various countries around the world
- The IEC 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 IEC is guided in its reflection, advice and decision by the Ethical principles expressed in the Declaration of Helsinki (Adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964, and amended by the 29th World Medical Assembly, Tokyo, Japan, October 1975; 35th World Medical Assembly, Venice, Italy, October 1983; 41st World Medical Assembly, Hong Kong, September 1989; 48th World Medical Assembly, Somerset West, Republic of South Africa, October 1996; and the 52nd World Medical Assembly, Edinburgh, Scotland, October 2000; Note of Clarification on Paragraph 29 added by the World Medical Assembly, Washington 2002; Note of Clarification on Paragraph 30 added by the World Medical Assembly, Tokyo 2004, 59th WMA general Assembly, Seoul, October 2008)
- It makes further reference to the International Ethical Guidelines for e.g. The Nuremburg Code (1945), the Council of International Organizations of Medical Sciences (CIOMS), the Belmont Report 1979, the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Geneva 2002), and the European Convention on Human Rights and Biomedicine 1977
- The IEC establishes its own Standard Operating Procedures 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)

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

2.6 Composition

- IEC will be multidisciplinary and multisectorial in composition.
- IEC is composed of a minimum of 7, and maximum of 15 members. The members are selected so as to have an equitable representation of all specialties in TMC. 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 Committees will comprise of a Chairperson, Co-Chairperson, a Member Secretary, and other active members who represent an appropriate balance of professional, ethical, legal, cultural, educational, and community interests.

  As far as possible, based on the requirement of research area such as HIV, genetic disorder, etc., specific patient group may also be represented in the Ethics Committee.
- 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 TMC.

Composition of IEC

The composition should be as follows:-

1. Chairperson (not – affiliated to TMC)
2. Co-Chairperson (not – affiliated to TMC)
3. Member secretary (TMC Staff member)
4. 1-2 clinicians (not affiliated to TMC)
5. 4 clinicians (TMC staff members)
6. DSMSC Member Secretary
7. Basic medical scientist
8. Clinical Pharmacologist
9. One legal expert or retired judge or medico-legal expert
10. One social scientist / representative of non-governmental voluntary agency/ philosopher / ethicist / theologian
11. One lay person from the community

2.6.1 Membership

The Director, TMC appoints the Chairperson, IEC and the Member Secretaries. All members will be appointed by the Director, TMC in consultation with the Chairperson and Member Secretaries. The licensing authority shall be informed in writing about the constitution of the Ethics Committee or in case of any change in the membership.

Criteria for selection of members:

- Members are selected in their personal capacities, based on their interest, ethical and/or scientific knowledge and expertise, experience in the domain field and profile.
- The members representing medical scientist and clinicians should have post graduate qualification & adequate experience in their respective fields
- Conflict of interest will be avoided while making appointments, but where unavoidable, there will be transparency with regard to such interests.
- Directors, Head of Institution, Superintendents, Administrative officers who are responsible for business development will not serve as members or ex-officio members.
- 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.

The following qualities are sought in IEC members:

- experience and education
- interest and motivation
- commitment and availability
- respect for divergent opinions
- integrity and diplomacy

2.6.2 Terms of Appointment

2.6.2. a Duration

- The members of the IEC, TMC will be appointed for duration of 2 years.
- The appointment procedure for membership will be followed so that it allows for continuity, development and maintenance of expertise within the IEC, and the regular input of fresh ideas and 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 IECs.
- To ensure an appropriate quorum is maintained, all IEC-I, II, III members will be alternate members for each other. Alternate members will serve in the same representative capacity as the member for whom they substitute. The IEC minutes will document when an alternate member replaces a primary member. When an alternate member substitutes for a primary member, the alternate member will receive and review the same material that the primary member would have received and reviewed.

- In case of the resignation/discontinuation of a Member Secretary, Chairperson or member, a replacement may be newly appointed by the Director, TMC before the completion of the tenure of the existing appointed committee. This appointment will be effective for the remaining tenure of the existing Committee

2.6.2. b Renewal

- The membership will be renewed after the stated term of 2 years.
- The process of renewal will be as follows :

  Selection of Member Secretary and other members should be done at least 3 months and 1 month in advance respectively. Member secretary designate should be inducted into the IEC as an observer before he/she takes on the mantle in the new IEC. Other members designate may attend the board meeting as observers before starting their tenure as IEC members.

  Designated members of the IEC who wish to attend IEC meetings as observers should read, understand, accept and sign the agreement contained in the Confidentiality / Conflict of Interest form (AX2 – V4/SOP02/V4) at the beginning of the IEC meeting and/or before scientific and ethical review tasks of the IEC commence
- If a regular member resigns, or ceases to be a member due to disqualification, or death, a new member will be appointed for the remaining term as per the Conditions of appointment stated below – section 2.6.3

2.6.2. c Resignation / Replacement procedure

The members who have resigned may be replaced at the discretion of the Director, TMC. IEC members who decide to resign must provide the Director, TMC, 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, TMC 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 the Member Secretary and /or Chairperson.

2.6.2. 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 IEC
- Inability to participate in the meetings on any grounds
- Failure to attend more than 3 consecutive meetings of the IEC and subsequent to review of the membership by the IEC; if deemed necessary, the IEC may decide to terminate the membership and the Chairperson, IEC may make a recommendation to the Director, TMC, for necessary action.
- Relocation to another city or any such matter.

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

2.6.3 Conditions of Appointment

- Name, gender, profession, and affiliation of IEC members will be publicized.
- Members must accept the appointment in writing.
- Members must submit a one page CV and training certificates in Ethics and/ or GCP.
- Conflict of interest, if any, must be disclosed.
- Members must apprise themselves of the Schedule Y, GCP for clinical trials in India, ICH GCP guidelines and the ICMR guidelines and IEC TMC SOPs.
- Members are required to sign the Confidentiality / Conflict of Interest Agreement (AX1-V4/SOP 02/V4) and Financial Disclosure at the start of their term. The confidentiality agreement protects the privacy and confidentiality of all parties whose information may be disclosed to the IEC in the course of its work. All IEC members shall disclose in writing to the IEC all conflicts of interest for themselves and their spouses/domestic partners and dependent children. For purposes of this policy, a conflict of interest may be identified as either financial in nature (such as when an IEC member holds an economic interest in the research) or non-financial in nature (such as when an IEC member or consultant participates in the research or will be included as a co-author on a publication from the research), either of which could affect or appear to affect the design, conduct, oversight, or reporting of the research project. Financial interests that require disclosure include but are not limited to:
- Ownership interest, stock options, or other economic interest related to the research, Board, scientific officer, or executive relationship related to the research, regardless of compensation for that position.

Non-financial interests that require disclosure include but are not limited to:

a. Participation in the research project as key personnel (PI, Co-PI, sub-investigator);
b. Co-Author on a publication of the research project's results;
c. Other relationships which may influence judgment of the IEC member in reviewing the research project:
    i. is a direct supervisor or trainee of the researcher(s)
    ii. is related to a researcher whose protocol is under consideration
    iii. has a prominent role in a directly competing research team or product
    iv. has a close personal relationship with a researcher or for other reasons feels unable to render a fair and unbiased review.

An investigator can be a member of the IEC. 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

- IEC members are prohibited from participating in the review of a research protocol or plan in which they have a conflict of interest, except to provide information requested by the IEC.

2.6.4 Independent Consultants

- The IEC may call upon, or establish a standing list of, independent consultants who may provide special expertise to the IEC on proposed research protocols, when the Chairperson / Member secretary or the IEC members determine that a study will involve procedures or information that is not within the area of expertise of the IEC members. These consultants may be specialists in ethical or legal aspects, specific diseases or methodologies (e.g. genetic disorders, stem cell research, medical statistics etc.), or they may be representatives of communities, patients, or special interest groups. These consultants must sign the confidentiality agreement (AX2-V4/SOP02/V4) regarding meeting, deliberations, and related matters. These consultants or subject experts cannot vote for a decision.
- Directors, Head of Institution, Superintendents, Administrative officers who are responsible for business development will not be appointed as independent consultants.

2.7 Office Bearers

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

2.7.1 Chairperson

The IEC Chairperson should be a highly respected individual from outside TMC, fully capable of managing the IEC and the matters brought before it, with fairness and impartiality. The task of making the IEC a respected part of the institutional community will fall primarily on the shoulders of this individual. The IEC must be perceived to be fair and impartial, immune from pressure either by TMC'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 IEC members, especially the contributions of the non-scientists, and must have the ability to foster such respect among the IEC members

Co-Chairperson

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

2.7.2 Member Secretary

The Member Secretary will be a staff member of TMC, 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 member-secretary of other IEC will function as acting Secretary for routine IEC work.

In the absence of a Member Secretary of IEC for scheduled IEC meeting, another member of the IEC will be nominated by the Chairperson for that meeting to coordinate and manage the activities of the IEC for that meeting.

Member Secretary/ IEC Chair shall review disclosures to determine whether a conflict of interest exists and to determine appropriate management of the conflict of interest.

2.7.3 Secretariat

The Secretariat is composed of the Member Secretary, IEC, and the administrative supporting staff. The supporting staff consists of staff members of TMC appointed by the Director, TMC.

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 IEC meetings. .
- Preparation of the agenda and the minutes of the meetings,
- Maintenance of the IEC records and archives.
- Communication with IEC members and PIs.
- Arrangement of training for personnel and IEC members.
- Provision of the necessary administrative support for IEC related activities to the Member Secretary, IEC.
- Receipt of IEC processing fees for pharma-funded projects and the issue of official receipts for the same.

The IEC Administrative Staff: Working Rules

1. There will be administrative officer/s and attendant/s /helper/s who will help the IEC Chairperson and Member Secretary in executing functions of the IEC. Additional staff may be appointed and duties assigned as and when deemed necessary by the IEC. 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 IEC members during regular IEC meeting and will be recorded in minutes. These will be forwarded to the Director, TMC.
2. The administrative staff will be appointed by conducting formal interviews as per TMC policy.

   Duties of the administrative officer/s/staff:

   - Organizing an effective and efficient tracking procedure for each proposal received.
   - Preparing, maintaining and distributing study files.
   - Organizing IEC meetings regularly
   - Preparing the agenda and minutes of the meetings

- Maintaining IEC records and archives.
- Communicating with IEC members and PIs.
- Arranging training for personnel and IEC members
- Providing necessary administrative support for IEC related activities to the Member Secretary, IEC.
- Receiving IEC processing fees and issuing official receipts for the same.
- Corresponding with the IEC members, external experts and investigators.
- Making the pre and post arrangements of IEC meetings.
- Preparing the agenda and minutes of the IEC meetings.
- Answering queries of the investigators.
- Filing study related documents.
- Archiving and maintaining the study files.
- Preparation for accreditation, audits
- Training for investigators, key study personnel, IEC members, and IEC staff.
- Participate in the development and subsequent implementation of SOPs
- Developing an effective and efficient tracking procedure

3. Duties of the attendant/s /helper/s
    a. Assisting the secretariat in arranging the IEC meetings.
    b. Dispatching sets of study documents to IEC members and external experts.
    c. Receiving the study related documents from and dispatching the IEC letters to the investigators.
    d. Filing study related documents.
    e. Archiving and maintaining the study files
    f. Corresponding with the IEC members and external experts.

The IEC staff will report to the Member Secretary and/or Chairperson. The office timings for the IEC staff will be as per TMC rules and regulations. The staff will avail leave as per TMC norms.

2.8 Roles and Responsibilities of the IEC 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 participants.

- Participate in the IEC 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 IEC meetings.
- Declare conflict of interest, if any - IEC members shall disclose to the IEC all conflicts of the IEC member, their spouse/domestic partner, and their dependent children with

regard to a research project involving human participants. Such disclosure shall be sufficiently detailed and timely to allow the IEC Administration to transfer the project to another IEC member or allow time for an alternate member to attend the IEC meeting to meet quorum. The IEC member/consultant shall evaluate whether a conflict of interest exists, and he/she shall disclose any identified conflicts to the IEC at the next IEC meeting. If an IEC member discovers that he/she has a conflict of interest during the conduct of a study over which the IEC provides oversight, the IEC member/consultant shall report the conflict to the IEC. IEC members shall cooperate with the IEC and other officials in their review of the conflicts of interest issues and shall comply with all requirements of the IEC.

- Carry out work delegated by the Chairperson, Co-Chairperson and/or Member Secretary.
- 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 IEC secretariat.

Directors, Head of Institution, Superintendents, Administrative officers who are responsible for business development will not be involved in the review process.

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

2.9 Quorum Requirements

- All research projects for approval by the full board of the IEC shall be reviewed at convened meetings at which a majority of the members of the IEC are present. 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 meeting cannot be convened and a decision regarding the project cannot 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 representative of non-governmental voluntary agency or philosopher or ethicist or theologian or similar person;
  e) lay person from the community;

In addition to the above , the quorum must fulfill following criteria-

i. 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 TMC/research site and has no immediate family member affiliated to TMC.
ii. No quorum should consist entirely of members of one profession or one gender.

iii. When an alternate member attends a meeting as a substitute for a regular member, the alternate member's participation counts toward the quorum requirements. Alternate members will serve in the same representative capacity as the member for whom they substitute.

2.10 Quorum Requirements

- Decisions will be arrived at through consensus/unanimous or majority opinion amongst the voting members of IEC. The decision-making is thus concerned with the process of deliberating and finalizing a decision. When a consensus is not possible, the IEC will vote.
- Voting may be in the form of voice vote, show of hands, or by secret ballot, as determined by the Chairperson, IEC.
- All members are entitled to one vote. However, in case of a tie, the Chairperson will vote to break the tie.
- The IEC minutes will document each alternate member's status, vote, and attendance as they relate to IEC actions and quorum requirements.
- Opinions of absent members that are transmitted by mail or telephone or fax may be considered by the attending members during discussion. But absent member cannot be counted as voting member or quorum member for formally convened full board meetings.
- Any committee member with a conflicting interest in a proposal will abstain from deliberations and in the decision making process on that proposal, except to provide information as requested by the Committee. Such abstentions will be recorded in the minutes.
- An IEC member or consultant with either a financial or non-financial conflict of interest in a research project involving human participants may not participate in the IEC review of that research. The IEC shall not approve a research protocol where a conflict of interest is not eliminated, and it has the final authority to determine whether a conflict of interest has been eliminated appropriately.

2.11 Education for IEC Members

IEC members have a need for initial and continued education regarding the science and ethics of biomedical research.

All IEC members must be conversant with ICMR Guidelines for Research involving Human Subjects 2006, Schedule Y of Drugs and Cosmetics Act and ICH-GCP guidelines.

IEC members will receive introductory training material in IEC SOPs and research bioethics and will be exposed to ongoing opportunities for enhancing their capacity for ethical review.

Training of the IEC members in Research Bioethics:

- A new member will be inducted 1 month prior to his/her appointment and will be requested to be an 'Observer' for the first board meeting. An introductory training will be imparted by the Member Secretary.

- The IEC members will be encouraged to receive ongoing training by attending workshops at least once every year.
- The IEC will conduct workshops from time to time to impart training to the IEC members and Institutional faculty members.
- The training programs should be scheduled and spread over the year.

2.12 Annual activity report

The Member Secretary in Consultation with the Chairperson shall prepare an annual activity report of the IEC for submission to the Director, TMC and SIDCER. This shall include:

- A quantitative evaluation of the activities of the Committee in a year.
- List of the research proposals reviewed in a year.

2.13 Honorarium

All external non-TMC members are given honorarium as per TRAC recommendations.

2.14 Annual Evaluation of IEC Chair / Co-Chairperson / Members / Member Secretary / IEC Staff

Annual Self Evaluation of Chairperson will be done. (AX4-V4/SOP02/V4)

Annual Evaluation of IEC members/Member Secretary will be done by Chairperson **(**AX5 -V4/SOP02/V4). The individual feedback will be provided by email to the members.

Annual Evaluation of IEC staff will be done by Member Secretary (AX6-V4/SOP02/V4). The individual feedback will be provided to the staff.

References

1.	Schedule Y (Drugs and Cosmetic Act 1940) amendment 2013
2.	ICMR Ethical Guidelines for Biomedical research on Human Participants, ICMR (2006)
3.	European Convention on Human rights and Biomedicine (1997).
4.	International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996.
5.	World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000. (Geneva 2000)
6.	CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects
7.	Code of Federal Regulations 45 CFR 46.108

Glossary

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

Institutional Ethics Committee (IEC): 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 participants. It is an independent body whose responsibility is to ensure the protection of the rights, safety and well-being of human participants involved in a clinical trial and to provide public assurance of that protection.

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 TMC.

AX1-V4/SOP02/V4

Confidentiality and Conflict of Interest Agreement form / Financial Disclosure for IEC Members

In recognition of the fact, that I, Dr……. herein referred to as the "Undersigned", have been appointed as a member of the Institutional Ethics Committee and would be asked to assess research studies involving human participants 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 IEC 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 IEC member is to independently review research protocols involving human participants and make a determination and the best possible objective recommendations, based on the merits of the submissions under review;

Whereas, the IEC 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 participants;

The undersigned, as a member of the IEC 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 IEC. 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 IEC.

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 TMC'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 IEC and its Chairperson to manage the conflict issues so that the ultimate outcome is the protection of human participants.

In accordance of the policy of the 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 IEC.

The Undersigned will immediately disclose to the Chairperson of the 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.

The Undersigned will immediately disclose to the Chairperson of the IEC all conflicts of interest for themselves and their spouses/domestic partners and dependent children.

Agreement on Confidentiality and Conflict of Interest

In the course of my activities as a member of the IEC, 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 IEC'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.

Whenever I have a conflict of interest, I shall immediately inform the committee and recuse myself from discussion and /or voting on the issue and leave the room while the discussion is ongoing”

Whenever I have a conflict of interest, I shall immediately inform the committee all conflicts of interest for myself and my spouses/domestic partners and dependent children.

Name of the spouses/domestic partners (if applicable) - _____

Name of the dependent children (if applicable) - _____

I, Dr. ……. have read and I accept the aforementioned terms and conditions as explained in this Agreement.

_____ _____

Undersigned Signature Date

_____ _____

Director of the TMC Date

Tata Memorial Centre
Financial Disclosure Form

1. Employment or Leadership Position

   Check yes if you or an immediate family member currently holds any full-time or part-time employment or service as an officer or board member for an entity having an investment, licensing, or other commercial interest in the research study under consideration

   Yes No If yes, amount received in last 12 months in Rs. _____

2. Consultant or Advisory Role

   Check yes if you or an immediate family member holds or has held any consultant or advisory arrangements with an entity having an investment, licensing, or other commercial interest in the research study under consideration,

   Yes No If yes, amount received in last 12 months in Rs. _____

3. Stock Ownership

   Check yes if you or an immediate family member currently holds any ownership interest in any company (publicly traded or privately held) that has an investment, licensing, or other commercial interest in the research study under consideration

   Yes No If yes, amount received in last 12 months in Rs. _____

4. Honoraria

   Check yes if you or an immediate family member has been paid directly any honoraria (reasonable payments for specific speeches, seminar presentations, or appearances) from an entity that has an investment, licensing, or other commercial interest in the research study under consideration

   Yes No If yes, amount received in last 12 months in Rs. _____

5. Research Funding

   Check yes if you or an immediate family member currently conducts any clinical research project(s) funded, in whole or in part, or has received any post study awards by an entity that has an investment, licensing, or other commercial interest in the research study under consideration

   Yes No If yes, amount received in last 12 months in Rs. _____

6. Patent or Royalty interests

   Check yes if you or an immediate family member has received any patent or royalty from an entity having an investment, licensing, or other commercial interest in the research study under consideration

   Yes No If yes, amount received in last 12 months in Rs. _____

7. Other Remuneration

   Check yes if you or an immediate family member has received any trips, travel, gifts, or other in-kind payments at any point from an entity having an investment, licensing, or other commercial interest in the research study under consideration

   Yes No If yes, amount received in last 12 months in Rs. _____

I hereby agree to recuse myself from any deliberations and actions involved in the approval or re-approval of a protocol for which I have a real or apparent conflict of interest, and from discussions of these matters unless my presence for discussions is requested by the IEC Chair.

_____ _____

Signature **Date**

AX2-V4/SOP02/V4

Confidentiality Agreement Form for Independent Consultants

I, _____ (Name and Designation) as a non-member of IEC understand that the copy (ies) given to me by the IEC is (are) confidential. I shall use the information only for the indicated purpose as described to the IEC and shall not duplicate, give or distribute these documents to any person(s) without permission from the IEC.

Upon signing this form, I agree to take reasonable measures and full responsibility to keep the information as confidential.

_____ _____
Undersigned Signature Date

_____ _____
Chairperson of IEC Date

I, _____ (Enter name) acknowledge that I have received a copy of this Agreement signed by Chairperson, IEC and me.

_____ _____
Signature of the recipient Date

AX3-V4/SOP02/V4

Confidentiality Agreement Form for Observer Attendees

I, _____, understand that I am allowed to observe IEC activities and attend the IEC meeting/ scheduled on _____ at _____am/ pm as an Observer.

The meeting will be conducted in the IEC Meeting room, 3rd Floor Main Building, TMH.

In the course of the observership / meeting of the IEC 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/Chairperson of IEC

_____
Date

I, _____ (Enter name) acknowledge that I have received a copy of this Agreement signed by Member Secretary/Chairperson, IEC and me.

_____ _____
Undersigned Signature Date

AX4-V4/SOP02/V4

IEC Evaluation Form of Chairs & Co- chairs

1. Mention (✔) the individual who is performing the evaluation:
   Self – evaluation : ☐
   Supervisor or other administrator : ☐
   Member secretary IEC : ☐
   IEC members or other chairs or vice- chairs : ☐
2. Name of the person who is evaluated :
   _____
3. Number of Meeting attended out of total meetings : ☐/☐
4. Number of exempt determination made : ☐
5. Number of protocol reviewed by the expedited procedure : ☐
6. Number of protocol reviewed that went to the convened IEC : ☐
7. Number of reviews completed as the primary reviewer : ☐
8. Completion of educational requirements : ☐ Yes ☐ No
9. Attendance at educational sessions (Make tick (✔) in the column)
   Regular : ☐
   Irregular : ☐
10. Number of educational sessions conducted : ☐

Evaluation of Chairs & Co- chairs

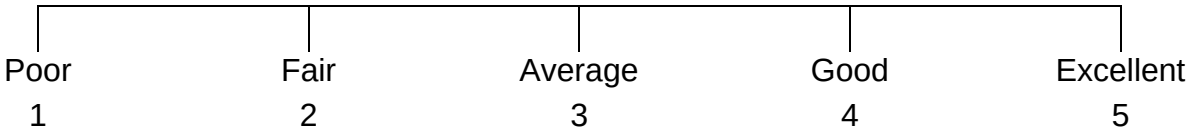
Person performing the evaluation – _____

Name of the person who is evaluated- _____

Period –

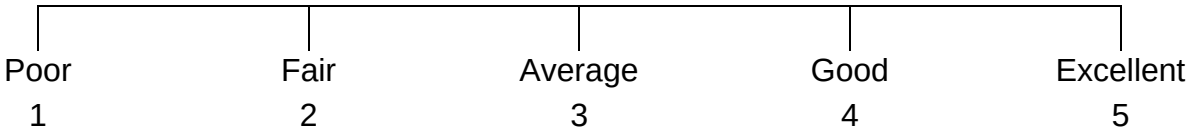
i) Preparedness for meetings

Scale



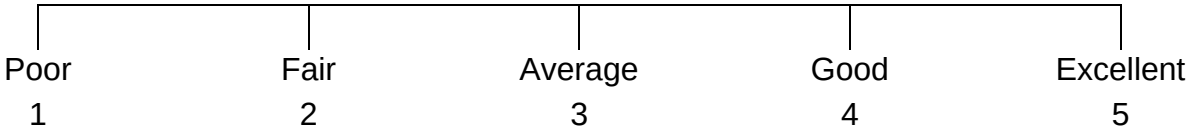
ii) Contribution to IRB meetings

Scale



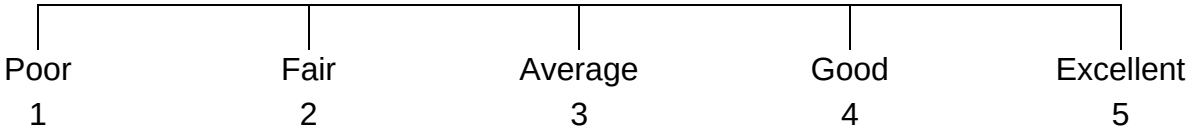
iii) Quality of reviews

Scale



iv) Communication with IRB staff

Scale



Feedback- _____

Signature:
Date:

AX5-V4/SOP02/V4

IEC Evaluation Form of IEC Member Secretary/Members

1. Mention (✔) the individual who is performing the evaluation:
   Self – evaluation : ☐
   Supervisor or other administrator : ☐
   Member secretary IEC : ☐
   IEC members or other chairs or vice- chairs: ☐
2. Name of the person who is evaluated: _____
3. Number of Meeting attended out of total meetings : ☐/☐
4. Number of exempt determination made : ☐
5. Number of protocol reviewed by the expedited procedure : ☐
6. Number of protocol reviewed that went to the convened IEC : ☐
7. Number of reviews completed as the primary reviewer : ☐
8. Completion of required checklist : (Make tick (✔) in the column)
   Yes: ☐ No: ☐
9. Completion of educational requirement : (Make tick (✔) in the column)
   Yes: ☐ No: ☐
10. Attendance at educational sessions : (Make tick (✔) in the column)
    Regular: ☐ Irregular: ☐
11. Number of educational sessions conducted: ☐
12. Preparedness for meetings : (Make tick (✔) in the column)
    Good: ☐ Average: ☐ Poor: ☐
13. Contribution to IEC meetings: (Make tick (✔) in the column)
    Good: ☐ Average: ☐ Poor: ☐
14. Quality of Reviews : (Make tick (✔) in the column)
    Good: ☐ Average: ☐ Poor: ☐
15. Communication with IEC staff : (Make tick (✔) in the column)
    Good: ☐ Average: ☐ Poor: ☐

IEC Evaluation Form of IEC Member Secretary/Members

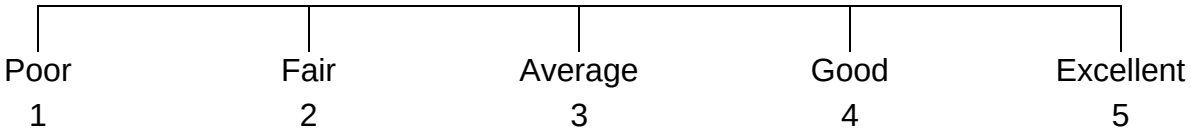
Person performing the evaluation – _____

Name of the person who is evaluated- _____

Period –

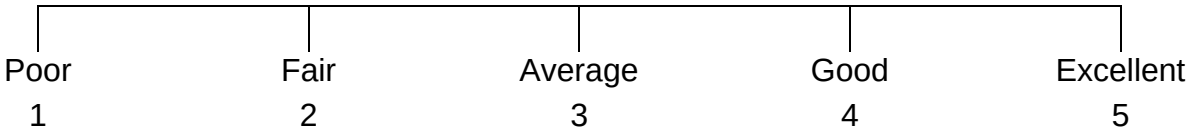
i) Preparedness for meetings

Scale



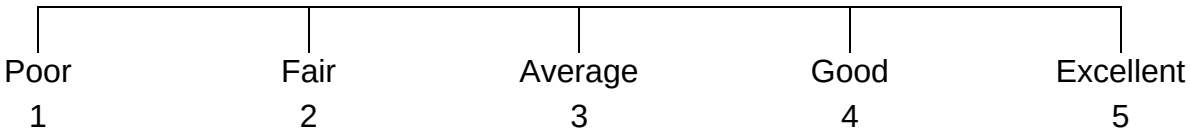
ii) Contribution to IRB meetings

Scale



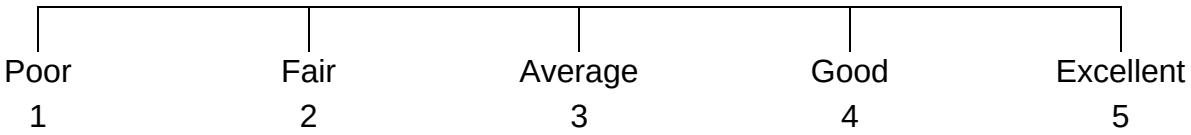
iii) Quality of reviews

Scale



iv) Communication with IRB staff

Scale



Feedback- _____

Signature:
Date:

AX6-V4/SOP02/V4

IEC Evaluation Form of Staff

1. Mention (✔) the individual who is performing the evaluation:
   Self – evaluation :
   Member secretary IEC :
   Name of the person who is evaluated :
   _____

2. Handles workload efficiently : (Make tick (✔) in the column)
   Yes: ☐ No: ☐

3. Number of protocol processed that were reviewed by the expedited procedure : ☐

4. Number of protocols processed that went to the convened IEC : ☐

5. Completion of required checklists and documentation : (Make tick (✔) in the column)
   Yes: ☐ No: ☐

6. Maintains paper files efficiently and correctly : (Make tick (✔) in the column)
   Yes: ☐ No: ☐

7. Prepares agenda and minutes in timely manner : (Make tick (✔) in the column)
   Yes: ☐ No: ☐

8. Maintain IEC rosters efficiently and correctly : (Make tick (✔) in the column)
   Yes: ☐ No: ☐

9. Prepare IEC records efficiently and correctly : (Make tick (✔) in the column)
   Yes: ☐ No: ☐

10. Completion of educational requirement : (Make tick (✔) in the column)
    Yes: ☐ No: ☐

11. Attendance at educational sessions : (Make tick (✔) in the column)
    Yes: ☐ No: ☐

12. Number of educational sessions conducted : ☐

13. Preparedness for meetings : (Make tick (✔)in the column)
    Good: ☐ Average: ☐ Poor: ☐

14. Quality of pre-reviews : (Make tick (✔) in the column)
    Good: ☐ Average: ☐ Poor: ☐

15. Communication with IEC chair and vice-chair : (Make tick (✔) in the column)
    Good: ☐ Average: ☐ Poor: ☐
16. Communication with supervisor: (Make tick (✔) in the column)
    Good: ☐ Average: ☐ Poor: ☐
17. Communication with investigators : (Make tick (✔) in the column)
    Good: ☐ Average: ☐ Poor: ☐
18. Ability to help investigator :
    Good: ☐ Average: ☐ Poor: ☐

Feedback- _____

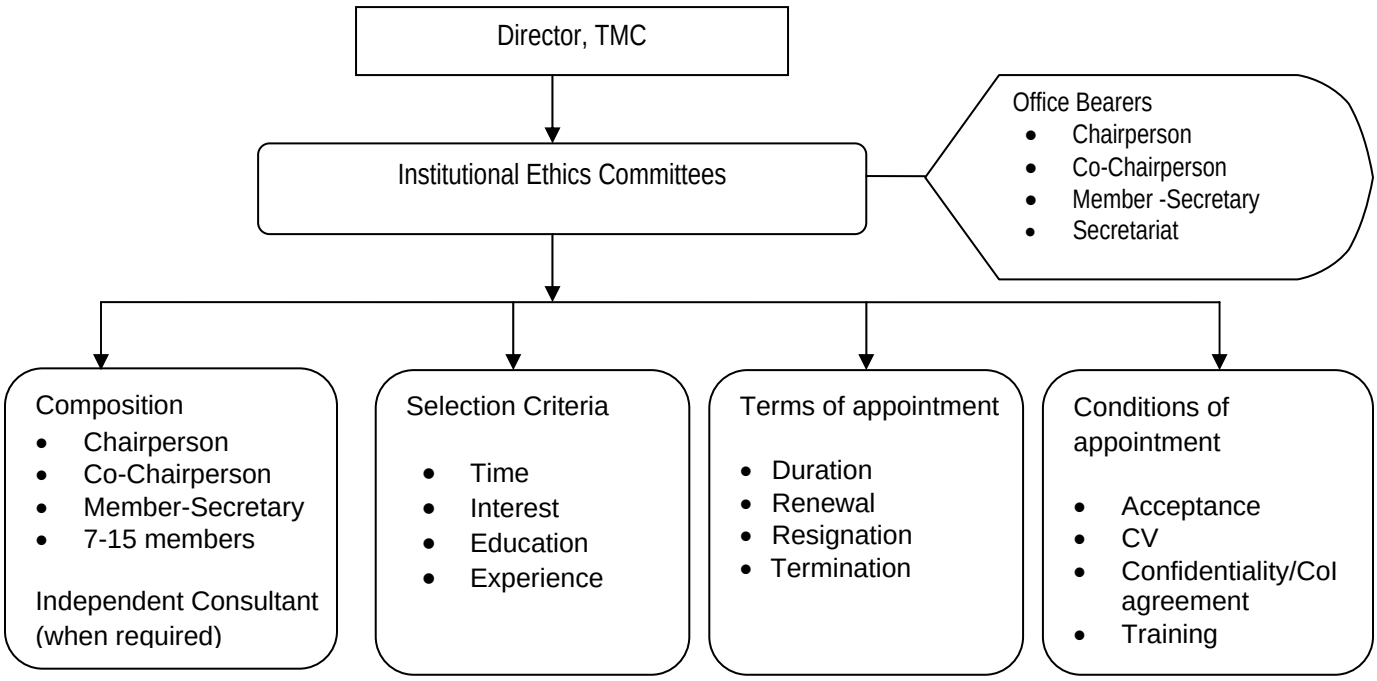
_____

_____

_____

Signature:
Date:

Flow Chart


Director, TMC
Institutional Ethics Committees
Office Bearers
Chairperson
Co-Chairperson
Member -Secretary
Secretariat
Composition
Chairperson
Co-Chairperson
Member-Secretary
7-15 members
Independent Consultant (when required)
Selection Criteria
Time
Interest
Education
Experience
Terms of appointment
Duration
Renewal
Resignation
Termination
Conditions of appointment
Acceptance
CV
Confidentiality/CoI agreement
Training

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Management of Research Study Submissions

SOP Code: SOP 03/V4 Date : 01/04/2016 Pages: 43 to 100

3.1 Purpose

This SOP is designed to describe and act as a guideline for the IEC Secretariat to manage research study submissions

3.2 Scope

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
- Any other documents

3.3 Responsibility

It is the responsibility of the IEC secretariat to receive record and distribute the study documents for IEC 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 IEC, no fewer than fourteen (14) days before the next scheduled meeting. The PI should submit research proposal to the IEC for review and approval under any of the 5 sections 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 IEC Secretariat:

- Check the submissions for initial review as per checklist, (AX2-V4/SOP 03/V4) to ensure that all mandatory forms and documents are submitted.
- Submission should include
  - Project submission Form (AX1-V4/SOP 03/V4)
  - Study protocol
  - Other related documents necessary for initial review (AX 2-V4/SOP 03/V4)

- 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 (AX 3-V4/SOP03/V4).
- Stamp, sign & date on the cover letter confirming receipt of the documents.
- Record the completeness of submission on document receipt form (AX 3-V4/SOP03/V4) and inform the investigators for necessary action
- Ensure payment of Institutional Ethics Committee processing fees for all sponsored clinical trials-
  - Initial protocol submission - Rs. 20,000/-
  - Protocol amendment (major) for ongoing study- Rs. 5,000/-

The fees will be accepted as cheque / demand draft drawn in favour of "Tata Memorial Centre".

- One hardcopy and soft copy of the proposal (Thesis Investigator-initiated studies, Pharma-sponsored studies) will be accepted
- The ICFs and questionnaires in vernacular versions in.pdf format should only be accepted
- Store the hard copies and soft copy of the research project. The hard copies will be stored under controlled access storage in IEC office.

  The soft copy of the study accepted will be stored electronically.
- The project details such as-
  - Type of Trial/DMG/Dept/Year/Serial Number/Continuous Number e.g. IM/THX/ DMO/2011/01/900 will indicate –
  - Intramural study (IM) from Thoracic DMG (THX) Department of Medical Oncology (DMO) of the Year (2011), serial number (01) project of the year 2011 and running project Number (900) is maintained. The running project number is for use in the IEC Secretariat
- Running project number, Study Title, Principal Investigator, Type of study, Duration will be labeled on each project file.
- All correspondence for the projects, should quote only the running project number i.e 900 (unique identity number)

3.5 Detailed description of Study Project Submission

The study protocol should be accompanied with the following relevant supporting documents for scientific and ethical review. These are –

Checklist (Refer AX 2-V4/SOP 03/V4)

1. **Project Submission Form**

   a. Grouping of Project
   b. Project Fact Sheet
   c. Investigator Declaration and Financial Agreement
   d. Project Submission Overview
   e. Budget Sheet for the Proposed Study

2. 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 English, Hindi and Marathi are mandatory and any other language if required [Refer (AX5-V4/SOP 03/V4)]. Back translations of Participant Information Sheet & Informed Consent Forms is required for other languages and not mandatory for English, Hindi and Marathi
b. Application for waiver of consent
c. Audio video informed consent (if applicable)
d. Investigator's Brochure (if applicable)
e. Package insert/product insert.
f. Case Record Form
g. Questionnaires (if applicable)
h. One page, recent, signed and dated curriculum vitae of the investigators indicating qualifications and relevant experience.
i. Agreement to comply with national and international GCP protocols for clinical trials
j. Regulatory clearance from appropriate regulatory authorities i.e. DCGI approval / ICMR /Health Ministry Screening Committee(HMSC) (if applicable)
k. For national/international collaborative study Draft/Final Memorandum Of Understanding between the collaborating institutes
l. Draft/Final Clinical Trial Agreement (if applicable)
m. Draft/Final Material Transfer Agreement(MTA) if applicable
n. Insurance/Indemnity policies, indicating who are covered (if applicable)
o. Any other important information relevant to the study
p. Decision of other Ethics Committees (If required / asked for)
q. Participant recruitment and enrollment procedures/advertisement (if any).
r. Good Clinical Practice Certificate/Training certificate in clinical research

3.6 Resubmission of study with corrections as per IEC suggestions

- For resubmission- the PI will submit 1 copy of the amended study related documents along with justification for amendment or modification, and clearly highlighted / demarcated sections which have undergone change.
- The IEC Secretariat will verify the completeness and reconfirm that the copies contains the modification highlighted with respect to the earlier submission
- The IEC Secretariat will perform the steps 3.4.2. The unchanged study related documents need not be submitted

3.7 Research Protocol Amendments and other study related documents

- The PI should submit 1 hard copy + soft copy of the amended documents
- The IEC Secretariat 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. This process is further elaborated in SOP 06/V4.

3.8 Annual Continuing Reviews of Approved Research studies

- The DSMSC will send reminders for annual report to Individual PI at least 60 days prior to lapse of approval.
- The DSMSC will receive a copy of Annual Status/ Continuing Review Report in the prescribed format and related documents (as per SOP 07/V4) for the approved research study
- The IEC Secretariat will verify the completeness of the Continuing Review Application Form (AX1-V4/SOP07/V4) Progress report. The IEC Secretariat will sign and date the documents.
- The progress or continuing review application will be discussed in the expedited review meeting or full board meeting of IEC

3.9 Research study Completion/termination

- The IEC will send reminders for annual status report to Individual Principal Investigators.
- The IEC will receive a copy of Study Completion Report / **termination** in the prescribed format (as per SOP 12/V4 & SOP13/V4).
- The IEC Secretariat will verify the completeness of the Study Completion / **termination** Report (SOP12/V4 & SOP 13/V4) filled by the PI.
- The study completion / **termination** report will be discussed in the expedited / full board meeting of IEC.

Reference

1. Schedule Y
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 guidelines 2006
4. http://www3.imperial.ac.uk

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

Investigational Product (IP): A pharmaceutical product (including the Comparator Product) being tested or used as reference in a clinical study. An Investigational Product may be an active chemical entity or a formulated dosage form.

Investigator Undertaking (IU): A formal written, commitment (submitted to regulatory authorities) by trial investigator(s) assuring their compliance with the study protocol and all the applicable regulatory requirements.

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

Material Transfer Agreement (MTA): A contract that governs the transfer of tangible research materials between two organizations when the recipient intends to use them for their own research purposes.

Memorandum of Understanding: A document intended to de scribe a bilateral or multilateral agreement between parties. It is often a preliminary document and is generally not intended to create a legal commitment between the parties but to set out the working principles of the relationship.

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

Tata Memorial Centre
(AX1-V4/SOP03/V4)

Project Submission Form for review by IEC

A. Grouping of Project

Project No.	(Will be allotted by IEC office)
Title:	
PI:	

Please complete the questionnaire for submitting the research proposal for TMC- IEC for review and approval

Study Group

(Please circle the applicable Y/N neatly)

	Group		Detail	Yes	No
			Controlled trials		
1.	A1	a	Is this a randomized controlled trial?	**Y**	**N**
2.	A1	b	Is this a non-randomized controlled trial?	**Y**	**N**
3.	A1	c	Is this a controlled trial that seeks new indication for establishing drug, process or a procedure?	**Y**	**N**
			Uncontrolled trials		
4.	A2	a	Is this a prospective trial testing new intervention, drug, or device on patients?	**Y**	**N**
5.	A2	b	Is this a prospective trial designed to test new (unproven) indication for established drug, process, procedure or device on patients?	**Y**	**N**
6.	A2	c	Is this a pilot trial on new intervention, drug, and device on patients?	**Y**	**N**
7.	A2	d	Is this a survey, QoL, psychosocial studies	**Y**	**N**
			Trial involve transfer of data/ material from TMC		
8.	A3	a	Is this a multi-centre trial?	**Y**	**N**
9.	A3	b	If multicentric, is TMC the co-coordinating centre?	**Y**	**N**
10.	A3	c	Is this trial involves transfer of patients' data to another site (including industry)?	**Y**	**N**
11.	A3	d	Is this trial involves transfer of patients' blood, serum, DNA, tissue to another site?	**Y**	**N**
			Intramural Funding		
12.	A4	a	Are you seeking intramural funding?	**Y**	**N**
13.	A4	b	Does this trial use additional resources of TMC beyond the usual patients' work-up (e.g. IHC, molecular profiling, MRI etc. which is not a routine part of work-up)?	**Y**	**N**

	Group	Detail	Yes	No
		Extramural Grants		
14.	A5 a	Are you submitting application for extra-mural grant for this trial?	**Y**	**N**
15.	A5 b	Is this trial partly or wholly supported by grants from sponsored industry?	**Y**	**N**
16.	A5 c	Is this a phase IV/ marketing trial undertaken on behalf of the industry?	**Y**	**N**
		Modification in approved trials		
17.	A6	Are you seeking modification/s in the TMC- IEC approved trial?	**Y**	**N**
		Patient to bear the cost of trial		
18.	A7 a	Are patient going to bear the cost of experimental intervention or drug therapy?	**Y**	**N**
19.	A7 b	Does patient has to undergo additional blood sample collection, biopsy, endoscopy, procedure etc.?	**Y**	**N**
20.	A7 c	Does patient has to bear the cost of complications arising from experimental treatment?	**Y**	**N**
21.	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 trials		
22.	A8 a	Will this trial be undertaken in the community?	**Y**	**N**
23.	A8 b	Will this trial involve the screening?	**Y**	**N**
		Trials involving Vulnerable Population		
24.	A9	Does this trial involve children, pregnant or nursing women, economically or socially disadvantaged group, mentally challenged/mentally differently abled group, participants with reduced autonomy, persons who are terminally ill, have incurable disease, mental illness	**Y**	**N**
		Trials involving genomics & proteomics		
25.	A10	Does this trial involve conducting genomics or proteomics studies on patients' specimens?	**Y**	**N**
		Trials with conflict of interest		
26.	A11	Will this trial involve development of a device, drug or test lead to profits or patent?	**Y**	**N**
27.	A12	Is this a prospective follow-up study (documentation of parameters only) of patients being offered standard treatment at TMC?	**Y**	**N**
28.	A13	Is this a phase II-IV trial restricted to standard intervention/	**Y**	**N**

	Group	Detail	Yes	No
		treatments published in EBM booklet?		
29.	A14	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 TMC?	**Y**	**N**
30.	A15 i)	Is this a retrospective analysis of charts and audit of procedures / tests / treatments?	**Y**	**N**
	ii)	Is this a prospective analysis of charts and audit of procedures / tests / treatments?	**Y**	**N**
31.	A16 i)	Is this a retrospective review of pathology specimen (may involve some additional staining techniques)?	**Y**	**N**
	ii)	Is this a prospective review of pathology specimen (may involve some additional staining techniques)?	**Y**	**N**
32.	A17 i)	Is this a retrospective review of radiology reports and their clinical correlation?	**Y**	**N**
	ii)	Is this a prospective review of radiology reports and their clinical correlation?	**Y**	**N**
33.	A18 i)	Is this a retrospective review of laboratory reports and their clinical correlation?	**Y**	**N**
	ii)	Is this a prospective review of laboratory reports and their clinical correlation?	**Y**	**N**
		Procedure / demonstration at workshops etc.		
34.	A19	Are you demonstrating an experimental procedure which is 'not established standards of care' at a workshop, or a public meeting?	**Y**	**N**
35.	A20	Are you performing a procedure in workshop at TMC by non-TMC staff member? (Please check other requirements also)	**Y**	**N**
	Signature of PI			
	Date of submission			

If you have any questions, concerns, suggestions regarding the Human Research Protection Program (HRPP), you can contact Ms. Rohini Hawaldar (HRPP contact person) telephone 022-24168601 or 24177000 extn 4265, email: hawaldarrw@tmc.gov.in / rwhawaldar@gmail.com

B. Project Fact Sheet

B1	Project No. (To be filled by the Secretariat)	
B2	Date of receipt by IEC	
B3	Project Title	
	Key Words title (2-4 options)	
B4	Principal Investigator Co-Principal Investigator Co-Investigator	
B5	Number of ongoing studies in which PI is involved? (as PI only)	
B6	Contact number Principal Investigator	
B7	Site/sites where study is to be conducted i.e. TMH / ACTREC /TMC/Any other(Please specify).	
B8	Tick the type of study (multiple options if applicable)	☐ Investigator Initiated study ☐ Pharmaceutical sponsored Study ☐ Thesis ☐ multicentric study- Tata Memorial Centre as co-ordinating centre ☐ multicentric study
B9	Funding Agency	
	* Sponsor	
B10	Total estimated budget in Rs.	
B11	Duration of the Project (months)	
B12	Total number of participants to be accrued in study (including TMC, if multi-institutional study)	
B13	Number of participants from TMC to be accrued	
B14	a) If this is a retrospective study, mention time frame from which data is collected b) The total number of participants whose data is being analyzed	
B15	Will biological products be sent out of the country?(Yes/No) If yes attached the copy of regulatory	Yes/No

	clearance obtained [DCGI/ ICMR /Health Ministry Screening Committee (HMSC)]	
	Signature of PI	
	Date of submission	

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

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

Investigators Declaration

01.	This research project (including collection of blood or tissues samples for research) will not be started until the final approval of the IEC has been obtained.
02.	We agree to undertake research proposal involving human subjects in accordance with the Schedule Y (Drugs & Cosmetics Act 1940), ICH-GCP and ICMR ethical guidelines, 2006. We will not modify the research protocol, consent, etc without prior approval by the IEC.
03.	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 IEC. Participants will receive an 'information sheet' which will detail the project design in simple understandable layperson's language.
04.	The investigators agree to report within a week all serious adverse events (SAE) associated with the trial in the SAE form to the IEC. In the event of a death of the trial subject, the Secretary, IEC and DSMSC, will be informed within 24 hours.
05	The investigators agree to submit status report atleast annually of the trial in the appropriate form. A final report will be submitted at the end of the trial.
06	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.
07	We understand that the IEC is concerned about transparent financial transactions during the trial. A report on how the trial funds were utilized will be presented to the EC along with the final project report at the end of the trial.
08	The investigators agree to transfer 10% of the total budget to TMC as service charges and Estimated Professional charges for clinical services. (15% at the end of the study on actuals). This will not apply to intramural projects, those projects co-sponsored by TMC/ CRI/ ACTREC/ DAE and ICMR/ DBT /DST/WHO/IAEA funded projects.
09	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 IEC. Thirty percent of the surplus grant if left over at the end of the study will be credited to TMC. 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 IEC.
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 will declare any financial gain from the commercial sponsor and any conflict of interest in the drug or product by way of consultations, shareholding, etc as detailed in the TMC Conflict of Interest Policy.
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. TMC, 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 Tata Memorial Centre or as per the Clinical Trial Agreement.
14.	The salaries to staff employed for the research project will be as shown in the budget sheet and at par with the prevailing TMC salary scales.
15.	The study documents will be made available to members of the IEC any time for random verification and monitoring. The study documents must ensure archived for 15 years post study close out or until the sponsor confirms that the records are no longer required; whichever is earlier.
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 TMC before they are released or presented elsewhere.
18.	The investigators will not issue any press release before the data and conclusions have been peer-reviewed by the TMC 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 cover any expenses for injury and/or compensation arising from the study as per the national regulations/institutional policies..
20.	The investigators will constantly inform the IEC 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 changes in the study protocol or conduct of the study will be carried out without prior approval of the IEC.
21.	The investigators realize that the IEC is particular that all aspects of the study are in accordance with the Schedule Y (Drugs & Cosmetics Act 1940), ICH-GCP and ICMR ethical guidelines, 2006. The investigators will comply with all policies and

	guidelines of the TMC 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 IEC 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 IEC

Study Team Undertaking with Duties & Delegation

Project Title-							
	CC No. if available	**Investigator Name**	**Email**	**Status** (PI, Co-PI, CI,)	***Role & responsibility**	**Conflict of Interest Yes/No If Yes Please specify**	**Sign & date**

- 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 IEC secretariat.

Financial Disclosure Form for Researchers

Project entitled: ……
Name of PI:

1. Employment or Leadership Position

Check yes if you or an immediate family member currently holds any full-time or part-time employment or service as an officer or board member for an entity having an investment, licensing, or other commercial interest in the research study under consideration.

☐ Yes ☐ No If yes, amount received in last 12 months in Rs. _____

2. Consultant or Advisory Role

Check yes if you or an immediate family member holds or has held any consultant or advisory arrangements with an entity having an investment, licensing, or other commercial interest in the research study under consideration.

☐ Yes ☐ No If yes, amount received in last 12 months in Rs. _____

3. Stock Ownership

Check yes if you or an immediate family member currently holds any ownership interest in any company (publicly traded or privately held) that has an investment, licensing, or other commercial interest in the research study under consideration.

☐ Yes ☐ No If yes, amount received in last 12 months in Rs. _____

4. Honoraria

Check yes if you or an immediate family member has been paid directly any honoraria (reasonable payments for specific speeches, seminar presentations, or appearances) from an entity that has an investment, licensing, or other commercial interest in the research study under consideration.

☐ Yes ☐ No If yes, amount received in last 12 months in Rs. _____

5. Research Funding

Check yes if you or an immediate family member currently conducts any clinical research project(s) funded, in whole or in part, or has received any post study awards by an entity that has an investment, licensing, or other commercial interest in the research study under consideration.

☐ Yes ☐ No If yes, amount received in last 12 months in Rs. _____

6. Patent or Royalty interests

Check yes if you or an immediate family member has received any patent or royalty from an entity having an investment, licensing, or other commercial interest in the research study under consideration.

☐ Yes ☐ No If yes, amount received in last 12 months in Rs. _____

7. Other Remuneration

Check yes if you or an immediate family member has received any trips, travel, gifts, or other in-kind payments at any point from an entity having an investment, licensing, or other commercial interest in the research study under consideration.

☐ Yes ☐ No If yes, amount received in last 12 months in Rs. _____

I hereby agree to recuse myself from any deliberations and actions involved in the approval or re-approval of a protocol for which I have a real or apparent conflict of interest, and from discussions of these matters unless my presence for discussions is requested by the IEC Chair.

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

☐ I have above conflict of interest:

_____ _____

Signature of PI **Date**

Consent of Head of the PI's Department

Date:…….

I have reviewed the project entitled " " submitted by …… Principal Investigator from my Department. I endorse the project and have 'no objection' for submission for consideration by Institutional Ethics Committee.

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

I have reviewed the financial and non financial disclosure

☐ Yes ☐ No

PI has conflict of interest

☐ Yes ☐ No

Signature & date	Name	Department

Consent from Disease Management Group(DMG) / Working Group Date:……. The project entitled "_____"submitted by …… ., Principal Investigator, has been discussed in the ……. working group on (date) and has been accepted to be submitted for submission for Institutional Ethics Committee consideration. The investigators / participants included in the study are acceptable to the members. I have reviewed the financial and non financial disclosure ☐ Yes ☐ No PI has conflict of interest ☐ Yes ☐ No	
Signature & date	Name (Convener or senior member of DMG/ working group)

C. Project Submission Overview

C.1	**Title**	
C.2	**Principal Investigator**	
C.3	**Introduction/ background** Give the background, including human or animal research relevant to the design of the proposed study. When new techniques or procedure are to be used, provide a description of preliminary work. When an investigation drug is to be used, animal data and phase I or II data on the drug should be included. A summary of how the study may help in the future should be included in the protocol.	
C.4	**Aims/ Objectives** Clearly state the aims or objectives of the study. Whenever possible	

	this should be in the form of a hypothesis.	
C.5	**Design of the Study (see study design enclosed)**	
C.5.1	**Treatment studies /Interventional Studies**	
	➢ Randomized controlled trial • Double-blind randomized trial • Single-blind randomized trial • Partial-Blind randomized trial • Open labeled ➢ Adaptive clinical trial ➢ Nonrandomized trial (quasi-experiment) ➢ Interrupted time series design Any other (please specify)	
C.5.2	Phase-I, Phase-II, Phase-III, Phase-IV, NA	
	Pharmacokinetics / Pharmacodynamics	Yes No NA
	Feasibility Study Pilot Pivotal	Yes No NA Yes No NA Yes No NA
C.5.3	Observational studies	
	➢ Prospective cohort ➢ Retrospective cohort ➢ Time series study ➢ Case-control study ➢ Nested case-control study ➢ Cross-sectional study ➢ Community survey (a type of cross-sectional study) ➢ Longitudinal study ➢ Others (please specify)	
C.6	**Study methodology** Explain, in sequence, the conduct of study and all data collection procedures. Describe the involvement of human subjects including initial evaluation procedures and screening tests, phases, medical/surgical procedures and sequence	

	of the study. Separate standard and experimental aspects of the study as much as possible. Give brief account of procedures for treatment, dose adjustments, etc. Describe the randomization procedure, if applicable. Specify if procedure involves banking of biological samples. Define stop points and criteria for withdrawing subjects from the study.	
C.6.1	**Eligibility** (Explain inclusion and exclusion criteria; To be stated clearly in the summary) (Explain inclusion of Normal / Healthy volunteer, Student, Staff of the institute in the study Does it involve vulnerable subjects	Yes No (If yes, tick the appropriate boxes) ☐ minors ☐ pregnant women ☐ elderly ☐ seriously/terminally ill ☐ neonates ☐ mentally challenged ☐ handicapped ☐ economically / socially backward ☐ institutional employees / students
C.6.2	How many subjects/samples will be screened? How many subjects/samples are likely to be accrued?	
C.6.3	Describe benefits to the subject/participant in this study. Also describe the benefits, if any, to the society.	
C.6.4	**Power estimates** Describe power calculations, if the study involves statistical comparisons between two or more groups. Mention evidence to support that adequate number of subjects can be enrolled during the study period by the investigators.	
C.6.5	**Variables to be estimated** (e.g. response, survival, toxicity, age, etc) Enumerate the variables, outcomes and end points that will	

	be measured. Try to separate variables as response and explanatory variables. Describe the type and frequency of tests, admissions, outpatient visits, etc used to obtain these variables or variables.	
C.6.6	**Analysis of the variables** Describe how the variables obtained during the study will be statistically analyzed. e.g. Univariate comparison or Cox- proportional hazards model, etc	
C.7	**Adverse Events**	
C.7.1	Have you defined adverse events in your study, and what rules you will use for stopping the study due to adverse events? (Please note that SAEs have to be reported to IEC as per national regulations and SOPs.)	
C.7.2	Describe all possible risks and discomfort for subjects due to use of intervention and /or data collection methods proposed. Describe expected degree and frequency of such risks, discomfort, side effects of drug etc.	
C.7.3	If the procedures in the trial are invasive or potentially harmful, describe what arrangements have been made for treatment of the complications arising from the trial?	
C.7.4	If some procedures in this trial are emotionally upsetting describe what arrangements have been made for psychological counseling?	
C.7.5	Who will bear the cost of treating the complications arising from this trial?	
C.7.6	Have you made provision for insuring trial subjects for any accidental unforeseen trial related injury?	
C.8	**Informed Consent**	
C.8.1	Describe (i) How, where, when and by whom the Informed Consent will be obtained. (ii) how much time the subject/participant will be given to consider participation and decide, (iii) describe additional plans/needs for informed consent	

	in case the study involves special population such as minors, pregnant mothers, neonates, etc. (iv) Describe how you will assess that information is correctly understood by the participant.	
C.8.2	In what way will you ensure the confidentiality and privacy of the subjects?	
C.8.3	Are your seeking waiver of consent Specify reasons	Yes [ ] No [ ]
C.9	**Drug/Sponsor details**	
C.9.1	Does your study involve testing of drug/s, device/s and/or biologics? If yes- 1) Please attach copy of DCGI permission. 2) If marketed drug, please attach copy of package insert/product insert.	Yes [ ] No [ ]
C.9.2	Are they already approved by the regulatory authorities and available in the market or are they new ones?	Already approved [ ] New one [ ]
C.9.3	Does your study involve modified or new claims, namely, indications, dosage forms (including sustained release dosage form) and route of administration of already approved drugs and combination of two or more drugs	Yes [ ] No [ ]
C.9.4	Who has prepared and /or is manufacturing the drug/s, device/s and biologics under investigation?	
C.9.4	Who holds the patent or IND/IDE of the drug/s, device/s and biologics under investigation?	
C.9.5	What are the reasonable possibilities of the availability after the study of the investigational drug(s), device(s) and biologics for the study participants/subjects if it is found to be effective?	
C.10	**Regulatory Permissions**	
C10.1	Does your study require permission from regulatory authorities?	Yes [ ] No [ ]

C10.2	If yes,	
	1. from the Director, TMC	Yes [ ] No [ ]
	2. from Health Ministry's Screening Committee(HMSC)	Yes [ ] No [ ]
	3. from DCGI	Yes [ ] No [ ] Please Specify
	4. Others, please specify	
C10.3	Does your study require you to send human biological material/data outside India?	Yes [ ] No [ ] NA [ ]
C10.4	If yes, have you obtained/sought permission :	
	1. from the Director, TMC	Yes [ ] No [ ] NA [ ]
	2. from Health Ministry's Screening Committee(HMSC)	Yes [ ] No [ ] NA [ ]
	3. from DCGI	Yes [ ] No [ ] NA [ ]
	4. Others, please specify	Yes [ ] No [ ] NA [ ]
C.10.5	Has TMC and the foreign party signed agreement/MOU for that? If yes, attach a copy of agreement/MOU	Yes [ ] No [ ]
C.10.6	If study will be conducted fully or partially outside the TMC, please describe the need for permission from institution(s), health centre(s),local government/administrative bodies, etc.	
C.10.7	Have you made provision for insuring yourself, and TMC against any legal action that may arise out of this project?	
C.11	**Trial Monitoring , Data Management and access**	
C.11.1	Does your study have provisions for monitoring the data to ensure the safety of participants?	Yes [ ] No [ ] NA [ ]
C.11.2	Who is responsible for monitoring and ensuring the safety of participants?	
C.11.3	Who will be maintaining the trial records and where? For how long will the data be stored? Give details of where they will be stored, who will access	
C.11.4	Post trial access will be provided If yes, describe briefly arrangements for post trial access.	Yes [ ] No [ ] NA [ ]
C.11.5	How is it intended, the results of the study	Please tick in the box

	will be reported and disseminated?	☐ Peer reviewed scientific journals ☐ Other publication ☐ Conference presentation ☐ Internal report ☐ Submission to regulatory authorities ☐ Access to raw data and right to publish freely by all the investigators in study or by independent steering committee on behalf of all investigators Other ……Please specify……..

D. Budget Sheet for the Proposed Study

1	Title of the Project:	
2	Principal Investigator	
3	Designation and address of the PI	
5	Source of funding	
	Intramural	
	Extramural	
	a) Government (please specify)	Central [ ], State [ ],Local [ ]
	b) Private Foundation: (please specify)	Indian [ ], Foreign [ ]
	c) Industry: (please specify)	Private [ ], Public [ ], Other [ ]
	d) Other:	
	Pharma sponsored	Indian [ ], Foreign [ ]
	Address, phone, fax. E-mail of sponsor with the name of the contact person	
	No funding required	
6	Total Budget for the entire project in Rs.	
7	Duration of the Project in months	
8	Proposed date of starting the project	
9	Direct payments to investigators, if any	

10	Any other benefits to the investigators		
11	Name of PI:	Signature:	Date:

Detailed Budget for the Proposed Study*

1. **Source of funding**	**Please specify**			
Items	1st Year	2nd Year	3rd Year	Total
2. **Salaries-personnel (Numbers)**				
Doctor / Post-Doc (Research Fellow)				
Research Nurse				
Data operator				
Any other specify				
1. Equipment and Hardware- kindly specify				
-				
-				
-				
-				
4. **Drugs and Consumables**				
-				
-				
-				
-				
5. **Clinical Investigations**				
-				
-				
-				
-				
6. **Hospitalization**				
-				

-				
-				
7.**Travel expenditure for investigators**				
-				
-				
8. **Travel expenditure for trial subject and one attendant**				
9. **Honorarium to doctors/technicians**				
10**. Insurance**				
i. for investigators				
ii. any unforeseen, accidental trial related injury				
11. **Any other expenditures**				
12.**Miscellaneous (<5% of budget)**				
13. **TMC Service Charge (10% of total applicable for pharma sponsored studies))** (TMC, DAE, ICMR, DBT, DST, IAEA, WHO, IARC etc. funded project are exempted)				
14**. Estimated** Professional charges for clinical services. **(15% at the end of the study on actual applicable for pharma sponsored studies)**				
15. Grand Total				
Name of PI:	**Signature:**			**Date:**

Note:

- PI should devise incremental budget whenever necessary.
- Please provide the complete break-up of item nos. 3, 4 & 5 on separate sheet.
- Please specify year-wise total in grand total column

Project No.	
Trial Register No.	
Project Title (To be filled by PI)	..
Revised Title if any (To be filled by IEC)	
Principal Investigator	..

Institutional Ethics Committee Approval

The members of the Institutional Ethics Committee met on ……. at Tata Memorial Centre and reviewed the above named project with all the documents submitted. The Institutional Ethics Committee after careful deliberations has granted final approval to the project. The above mentioned project/ study may now be undertaken at Tata Memorial Centre in accordance with the study protocol submitted by the investigators, subject to fulfilling local and other institutional regulations.

Member Secretary ……..…….	Chairperson…..……..
Name: ……..…	Name:……..
Date…….	Date……..

Instructions:

- This form must be printed and not handwritten.
- Fill the form completely (If there are any questions/queries, please contact the IEC office 022-24177262/ 022-27405154).
- Make sure to include the e-mail address and contact numbers of the PI, Co-investigators.
- Please submit the documents as per the checklist (AX2-V4/SOP03/V4) to ensure all requirements for submission are fulfilled for timely review by IEC.
- Submit the submission form (Part A,B,C,D)along with the supporting documents to the IEC office.

AX2-V4/SOP03/V4

Checklist of Documents

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

AX3-V4/SOP 03/V4

Tata Memorial Centre

Institutional Ethics Committee

Document Receipt Form

TMC Study Number : **Submitted date:**	
Type of Submission:	**Initial Review**
Protocol Title:	
Principal Investigator:	
Mode of submission: ☐ Post ☐ E-submission ☐ In Person	
Type of document:	

Checklist to assess the projects before they are submitted to IEC review

Item No.	Mandatory Documents	Yes	No	NA
1.	IEC processing fee **(applicable for pharma sponsored trials)**			
2.	Project Submission Form (both hard and soft copies) duly signed by the Principal Investigator			
	A. Grouping of Project			
	B. Project Fact Sheet Investigators Declaration Conflict of Interest Consent of Head of the PI's Department Consent from Working Group			
	C. Project Submission Overview			
	D. Budget Sheet for the Proposed Study Detailed Budget for the Proposed Study			
3	Study Protocol			

Item No.	Mandatory Documents	Yes	No	NA
4	Participant Information Sheet & Informed consent forms (ICFs) in English, Marathi & Hindi (and if required any other language)			
5	Back translations of ICFs (not mandatory for Hindi and Marathi)			
6	Waiver of ICFs			
7	Case Record Form			
	Questionnaire			
8	Investigator Brochure			
	Package insert/label			
9	Insurance policy			
10	DCGI submission letter			
11	DCGI approval letter			
	HMSC			
12	Appendix VII (Schedule Y)Undertaking By The Investigator			
13	Clinical Trial Agreement (CTA) **if applicable**			
14	Memorandum of Understanding (MOU) **if applicable**			
15	Material Transfer Agreement (MTA) **if applicable**			
16	Brief resume of Principal Investigators and Co-investigators (1 Page each)			
17	GCP Training certificate			

Documents submitted:

☐ Complete

☐ Incomplete will submit on……...

Comments:

Receiver Name, Sign & Date

(IEC Secretariat)

AX4-V4/SOP03/V4

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

Guideline for preparation of the informed consent document

While submitting your project to the IEC, ensure that you have included an informed consent document that is prepared as per the Schedule Y ICMR ethical guidelines 2006, , ICH- Good Clinical Practice (ICH – GCP) and the Declaration of Helsinki.

Kindly note:

- Informed consent documents in English, Marathi, and Hindi are mandatory and any Language if applicable
- Font: Arial and appropriate Hindi & Marathi eg. Shivaji
- Size: 12
- All the consent documents must have Version No, Date, Page no in the footer
- Separate documents should be prepared when minors (children) are study participants; assent form for the mature minors (age 7-17 years) and consent document for the parents

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

Template for a "Participant Information Sheet & Informed Consent Form"

(Include or exclude information, as applicable)

Participant Information Sheet & Informed Consent Form

[The simplified title of the project as per the project submission form with names of Principal Investigator and all other investigators.]

Name of the funding agency (if applicable)

Name of the sponsor (if applicable)

Address of Research Site

Introduction:

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

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 participant.

If this is a randomized trial, details of both arms of the trial must be explained.

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

Clearly state

i. The number of participants who will take part in the research
ii. Information concerning taping or filming (If applicable)
iii. For clinical studies which require regulatory approval - Please include
    a) A statement that there is a possibility of failure of investigational product to provide intended therapeutic effect
    b) A statement that in the case of placebo controlled trial, the placebo administered to the participants shall not have any therapeutic effect
iv. 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)

Biological sample study:

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

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

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

Alternative treatments:

Disclose appropriate alternative treatments available, if any.

Risks:

List the foreseeable risks and discomforts, 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 amount for expenses incurred, time spent and any inconvenience. State clearly the details for travel reimbursement for trial participants &/or attendant.

Emergency Medical Treatment

(If applicable, add here)

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

Describe available medical treatment in case of complications.

Benefits

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

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

Confidentiality

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

Compensation for study related Injury or death

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

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

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

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

Statement describing the financial compensation and medical management as under

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

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Contact

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

If you have any questions about the informed consent process or your rights as a participant, contact the Member Secretary, IEC [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."

Audio-video recording of the consent process (applicable for DCGI regulated studies in case of vulnerable participants in clinical trials of New Chemical Entity or New Molecular entity).

Your study doctor would video-tape the consenting process as per regulatory requirement. These recordings will be stored securely by the study doctor/study site that would adhere to the principles of confidentiality. A copy shall be provided to you on request. Your audio video recording may be made accessible only to the study sponsor, the clinical research organization involved in the study, independent auditors, the Ethics Committee or the regulatory authority or as required by applicable law. You would be included in the clinical trial only if you give consent for AV recording.

Storage

Audio-Video recording of informed consent process and other related documents will be preserved after the completion/termination of the study for at least a period of 5 years if it is not possible to maintain the same permanently.

Any other pertinent information

Consent

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

Study Title:

Study Number:

Participant' Initials:_____ Participant's Name:_____

Date of Birth / Age:_____

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

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

Participant's name (print):	
Participant's signature & date:	
Address : Qualification (please attach supporting documentation) (if applicable) _____ Occupation: Student / Self-Employed / Service / Housewife /Others (Please tick as appropriate) and attach supporting documentation (if applicable) Annual Income of the participant (please attach supporting documentation) (if applicable):_____	
Phone Nos.:	

Legal Acceptable Representative name	
Legal Acceptable Representative signature & date(if applicable)::	
Address (capital letters): Phone Nos.:	
Impartial Witness's name :	
Impartial Witness's signature & date (if applicable)::	
Address (capital letters): Phone Nos.:	
Name of PI or Co-PI/Co-I:	
PI or Co-PI/Co-I sign & date:	

Informed consent form to participate in a biological sample study

Study Title:

Study Number:

Participant' Initials:_____ Participant's Name:_____

Date of Birth / Age:_____

Do you consent to biological sample study?

☐ YES, I consent ☐ NO, I do not consent

1. I understand that I am being invited to take part in the research study. 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 the risks and potential benefits of this research study that were explained to me. I freely give my consent to take part in research study described in this form.
4. I understand that the Sponsor of the research study, others working on the Sponsor's behalf, IEC and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.
5. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

6. I agree to take part in the above study.

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

_____

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

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

- The prospective participant should be given Participant Information Sheet first.
- The participant should then be encouraged to read the Information Sheet and think over, preferably for a period of 24 hours. Following which, the participant should be served a questionnaire to ensure that he/she is aware of his/her own rights as a participant in the clinical trial. The informed consent form should be served to the participant only after ensuring that the participant is now prepared for informed decision making.
- The PIs are urged by the IEC to use the simple non-technical words or should add the glossary and follow the sample template of Participant Information Sheet & Informed Consent Form
- Use of alternative wording or different format may slow down the review process. The form should be written in second person ("You are invited..."). Use of first person ("I") can be interpreted as suggestive and coercive.
- The study participant should be explained all the details in a language she/he understands.
- The Informed Consent Document must have the name and Telephone No. of the Principal Investigator or of any other co-investigator in case of an emergency, or even to seek answers to their queries.
- The consent document must bear version no. & date.

A copy of the signed Informed Consent Document (ICD) must be given to prospective participant. A receipt of copy of ICF by the participant should be documented by the investigator in the source documents. Copies of the consent document must be available in English, Marathi and Hindi.

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

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

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

Please make provision for the assent of the child to the extent of the child's capabilities 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 document, 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)

†The investigator, or a suitably qualified and trained person designated by the investigator to conduct the informed consent process, must sign and date the form at the same time as the participant.

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

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

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

AX5-V4/SOP 03/V4

Child Information Sheet and Assent Form

Study title: "……"

Introduction- Background and Rationale would be more appropriate

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

We invite you to participate in this study.

What will you have to do?

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

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

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

Risks, discomforts & Side effects

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

Dr. **Phone:**

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

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

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

Costs:

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

Reimbursement for Participation

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

Emergency Medical Treatment

(If applicable, add here)

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

Describe available medical treatment in case of complications.

Benefits

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

Confidentiality

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

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

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

Right to refuse or withdraw

You do not have to be in this study, if you do not want to be. If you do not want to be in this study, we will tell you what other kinds of treatments there are for you. If you decide that you don't want to be in the study after we begin, that's OK too. Nobody will be angry or upset. We are discussing the study with your parents and you should talk to them about it too.

Whom to contact

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

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

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

<Name of Secretary of IEC > **Phone:** <Contact No.>

Your responsibilities

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

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

We expect your co-operation throughout the study.

Child Assent Form

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

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

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

_____

Name and Signature of the study participant Date:

_____

Name and Signature of Legally Acceptable Representative Date:

_____

Name and Signature of Impartial Witness Date:

_____

Name and Signature of the attending Physician Date:

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Parent Information sheet and Informed Consent Form

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

Introduction:

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

Purpose:

The purpose of this study is to ……

Participant selection

Voluntary Participation

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

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

Information on the Trial Drug

Procedures and Protocol

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

Duration

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

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

Side Effects

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

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

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

Risks

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

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

Discomforts

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

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

Costs:

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

Reimbursement for Participation

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

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

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

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

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

Confidentiality

Explain how the research team will maintain the confidentiality of data, especially with respect to the information about the participant, which would otherwise be known only to the physician but would now be available to the entire research team. Because something out of the ordinary is being done through research, any individual taking part in the research is likely to be more easily identified by members of the community and is therefore more likely to be stigmatized.

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

anyone except [name who will have access to the information, such as research sponsors, DSMB board, your clinician, etc].

Sharing of the results

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

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

Right to Refuse or Withdraw

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

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

protected from harm. If you have any queries regarding your rights as a study participant, you may contact, the Member Secretary, of the Institutional Ethics committee, Dr. Phone:

Consent

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

_____ _____

Signature of Parent/Guardian Date

_____ _____

Signature of Subject (when appropriate) Date

_____ _____

Signature of Person Obtaining Consent/Authorization Date

_____ _____

Signature of Impartial Witness Date

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Short consent for prospective audit/observational study

Participant Consent for Participation in the study

I understand that a study “Titled _” conducted by “Dr.”_ (name, phone no.) involves the analysis of my medical data that has been collected as part of my routine medical care.

I understand that there will not be any additional medical procedures over and above those which I would encounter during standard treatment.

I understand that this study has been approved by the Institutional Ethics Committee, Tata Memorial Centre and does not pose any additional risk to me beyond that which I would encounter while undergoing routine physical or psychological examinations or tests and/or which I would encounter in routine daily life activities. I further understand that confidentiality with regard to my medical data will be ensured, and that the results published will not in any way be linked to me. I understand that the Principal Investigator (name) would be willing to provide me with any additional information that I would want to know regarding the study.

I understand that if I decline to participate in this study or withdraw my consent at any stage of the study my medical treatment will not be affected.

I am willing to allow the use of my data for the study.

Name and Sign/Thumb impression of the participant
Date

Name and Sign of the Principal Investigator
Date

AX8-V4/SOP 03/V4

Short consent for prospective audit/observational study

Parental/LAR consent

I understand that a study “Titled _” conducted by “Dr.”_ (name, phone no.) involves the analysis of my ward’s medical data that has been collected as part of his/her routine medical care.

I understand that there will not be any additional medical procedures over and above those which my ward would encounter during standard treatment.

I understand that this study has been approved by the Institutional Ethics Committee, Tata Memorial Centre and does not pose any additional risk to my ward beyond that which he/she would encounter while undergoing routine physical or psychological examinations or tests and/or which he/she would encounter in routine daily life activities. I understand that the Principal Investigator (name) would be willing to provide me/my ward with any additional information that I/my ward would want to know regarding the study.

I further understand that confidentiality with regard to my ward’s medical data will be ensured, that his/her privacy would be maintained and that the results published will not in any way be linked to him/her.

I understand that if I decline to give consent for my ward’s participation in this study or withdraw my consent at any stage of the study his/her medical treatment will not be affected.

I am willing to allow the use of my ward’s data for this study.

Name and Sign/ Thumb impression of the Guardian/Parent /LAR

Date

Name and Sign of the Principal Investigator

Date

AX9-V4/SOP 03/V4

Short assent for prospective audit/observational study

Assent for Participation in the study

I understand that a study “Titled _” conducted by “Dr.”_ (name, phone no.) involves the analysis of my medical data that has been collected as part of my routine medical care.

I understand that there will not be any additional medical procedures over and above those which I would encounter during standard treatment.

I understand that this study has been approved by the Institutional Ethics Committee, Tata Memorial Centre and does not pose any additional risk to me beyond that which I would encounter while undergoing routine physical or psychological examinations or tests and/or which I would encounter in routine daily life activities. I further understand that confidentiality with regard to my medical data will be ensured, and that the results published will not in any way be linked to me. I understand that the Principal Investigator (name) would be willing to provide me with any additional information that I would want to know regarding the study.

I understand that if I decline to participate in this study or withdraw my consent at any stage of the study my medical treatment will not be affected.

I am willing to allow the use of my data for the study.

Name and Sign / Thumb impression of the minor
Date
Name and Sign of the Guardian/Parent /LAR
Date
Name and Sign of the Principal Investigator
Date

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Instructions for Submission of Project for Institutional Ethics Committee Approval

The latest version of IEC documents can be accessed ONLINE @TMC website- **tmc.gov.in, actrec.gov.in**

- Kindly refer to the checklist of documents to be submitted to IEC. All documents listed may not be applicable to your project
- A brief description of study designs is provided along with the document checklist for your assistance.
- The checklist of documents, Study design and this instruction page is for your reference and should not be submitted at the time of IEC submission of your study.

Initial Review of Projects

Instructions for filling the IEC submission form.

1. IEC submission form has 4 sections- A, B, C and D
2. All sections should be completely filled.
3. Questions not relevant to your study should be filled as NA.
4. **Do not alter or remove the version no and date reflecting in header of IEC submission form.**
5. Do not make any formatting changes in the IEC submission form.
6. **The title of the study should be same in all four sections of the Project Submission Form.**
7. All 4 sections should be signed and dated by the Principal Investigator.
8. The signatures of your DMG Convener (if applicable) and Head of Department should be obtained before IEC submission.

After initial review of projects

After review of project by IEC, your study may attain any one of the following status

- **Approved-** Your study is scientifically and ethically sound and you may initiate the study subject to terms indicated in the final approval letter.
- **Approved subject to modification-** This is a conditional approval only. Implies that your study may be approved once all the queries/recommendations of IEC are addressed satisfactorily. The revisions will not be taken up for full board and would be reviewed by Member Secretary the respective lead discussant on behalf of the full board. The revised proposals will not be taken up for the full board review
- **Resubmit-** The study design and/or ethical aspect of the study is not satisfactory and would require extensive revision and would be re reviewed during full board Ethics Committee Meeting.
- **Not Approved-** The study is not approved in its current form. A negative decision on an application will be supported by clearly stated reasons. If the investigator wishes to

appeal to the decision, he/she may do so by contacting the IEC Secretariat within 20 working days

If your project, after initial review falls into the category of **approved subject to modification /resubmission**, the following documents are to be submitted to IEC:

1) IEC form for re-review of projects **AX11-V4/SOP 03/V4**
2) Response letter, if applicable
3) Supporting documents such as modified protocols, CRFs, ICFs and any other documents if applicable and any other documents

You do not have to submit the IEC PROJECT SUBMISSION FORM which was submitted at the time of initial review.

The checklist of document provided to you lists out the mandatory documents to be submitted at the time of initial review. Instruction/template to develop them is provided below

General information

- Protocol, CRF, ICF, should bear Project title, page number, **version no. & date** (not to be confused with the version no. and date present in the TMC-IEC submission form.
- **The vernacular versions of ICF (Hindi, Marathi and any other language) should be submitted in .pdf format.**
- The ICF template provided by IEC is a reference document to assist in developing an effective informed consent document. However, the Principal Investigator may develop a customized ICF to suit the protocol requirement while addressing all key points.
- Kindly ensure that the study rationale and procedures described in the ICF is not a mere replica of the protocol. The ICFs should be written in a simple, non-technical style keeping in mind the educational and socio-economic background of the TMC patient population. Similarly, the child information sheet should be simple. It should be developed keeping in mind, the age group being addressed. Parent Information Sheet and consent form should be submitted in case of minors.
- In case of collaborative studies, kindly provide a draft MOU, CTA, MTA whichever is applicable.
- Find below a brief definition of the study designs presented in the IEC Project Submission Form. In case, your study is based on a study design which is not mentioned in Section C of the IEC form, please specify the same while filling up the IEC Submission Form.

Appendix-Study Designs

Randomized Controlled Trial:

In a **randomized controlled trial**, participants are assigned to treatment conditions at random (i.e., they have an equal probability of being assigned to any group). Procedures are controlled to ensure that all participants in all study groups are treated the same except for the factor that is unique to their group. The unique factor is the type of intervention they receive. The **primary goal** of conducting an RCT is to test whether an intervention works by comparing it to a control condition, usually either no intervention or an alternative intervention. **Secondary goals** may include: identify factors that influence the effects of the intervention (i.e., moderators), understand the processes through which an intervention influences change (i.e., mediators or change mechanisms that bring about the intervention effect)

In double-blinding, neither the participants nor the investigator know the participants' treatment assignment. In placebo-controlled trials, Masking can be improved by using an active placebo that has the same side effects as the drug but lacks its therapeutic effects.

Partial Blinding: Double-blinding is rarely possible in trials of behavioral treatment. It is usually obvious to participants which treatment they are receiving. Also, the treatment assignment is known by any research staff who delivers the treatment. However, the staff that assesses the study outcome can and should be kept blind to the patient's treatment condition. Special care is needed to prevent staff and study participants from unblinding the outcome assessor.

Single-blind: Term used to describe a study in which either the investigator or the participant, but not both of them, is unaware of the nature of the treatment the participant is receiving.

Non-blinded trial or Open-label trial: is a type of clinical trial in which both the researchers and participants know which treatment is being administered.

Adaptive design is a trial design that allows modifications to some aspects of the trial after its initiation without undermining the validity and integrity of the trial. Adaptive design makes it possible to discover and rectify inappropriate assumptions in trial designs, lower development costs and reduce the time to market. An adaptive clinical trial evaluates patients' reactions to a drug beginning early in a clinical trial and modifies the trial in accord with those findings. The adaptation process continues throughout the trial. Modifications may include dosage, sample size, drug undergoing trial, patient selection criteria etc. In some cases, trials have become an ongoing process that regularly adds and drops therapies and patient groups as more information is gained. The aim is to more quickly identify drugs that have a therapeutic effect and to zero in on patient populations for whom the drug is appropriate. A key modification is to adjust dosing levels.

Quasi-experiment or Nonrandomized clinical trials arise from situations in which it is impossible or difficult to assign subjects to treatment by chance. A quasi-experiment is an empirical study used to estimate the causal impact of an intervention on its target population. Quasi-experimental research shares similarities with or randomized controlled trial, but they specifically lack the element of random assignment to treatment or control.

Interrupted time series study a study that uses observations at multiple time points before and after an intervention (the 'interruption'). The design attempts to detect whether the intervention has had an effect significantly greater than any underlying trend over time.

Cohort study: For research purposes, a cohort is any group of people who are linked in some way and followed over time. Researchers observe what happens to one group that's been exposed to a particular variable — for example, the effect of company downsizing on the health of office workers. This group is then compared to a similar group that hasn't been exposed to the variable.

Prospective cohort study: A prospective study watches for outcomes, such as the development of a disease, during the study period and relates this to other factors such as suspected risk or protection factor(s). The study usually involves taking a cohort of subjects and watching them over a long period. Prospective studies are carried out from the present time into the future. Because prospective studies are designed with specific data collection methods, it has the advantage of being tailored to collect specific exposure data and may be more complete. The disadvantage of a prospective cohort study may be the long follow-up period while waiting for events or diseases to occur. Thus, this study design is inefficient for investigating diseases with long latency periods and is vulnerable to a high loss to follow-up rate.

Retrospective cohort study: Retrospective cohort studies, also known as historical cohort studies, are carried out at the present time and look to the past to examine medical events or outcomes. In other words, a cohort of subjects selected based on exposure status is chosen at the present time, and outcome data (i.e. disease status, event status), which was measured in the past, are reconstructed for analysis. The primary disadvantage of this study design is the limited control the investigator has over data collection. The existing data may be incomplete, inaccurate, or inconsistently measured between subjects.2 However, because of the immediate availability of the data, this study design is comparatively less costly and shorter than prospective cohort studies.

Case control study: Here researchers use existing records to identify people with a certain health problem ("cases") and a similar group without the problem ("controls"). Example: To learn whether a certain drug causes birth defects, one might collect data about children with defects (cases) and about those without defects (controls). The data are compared to see whether cases are more likely than controls to have mothers who took the drug during pregnancy.

Nested Case control study: A nested-case control study depends on the pre-existence of a cohort that has been followed over time. This cohort, at its inception or during the course of follow-up, has had exposure information and/or biospecimens collected of interest to the investigator. The investigator identifies cases of disease that occurred in the cohort during the follow-up period. The investigator also identifies disease-free individuals within the cohort to serve as controls. Using previously collected data and obtaining additional measurements of exposures from available biospecimens the investigator compares the exposure frequencies in cases and controls as in a non-nested case-control study. Nested case-control studies are carried out when it is either too costly or not feasible to perform additional biospecimen analyses on an entire cohort.

Cross-sectional study -examines the relationship between diseases (or other health related state) and other variables of interest as they exist in a defined population at a single point in time or over a short period of time (e.g. calendar year).Cross-sectional studies can be thought of as providing a snapshot of the frequency of a disease or other health related characteristics (e.g. exposure variables) in a population at a given point in time. Cross-sectional studies may be descriptive or analytical in nature.

1. **Descriptive Cross-sectional study** -A cross-sectional survey may be purely descriptive and used to assess the burden of a particular disease in a defined population.
2. **Analytical cross-sectional surveys** - Used to investigate the association between a putative risk factor and a health outcome In a cross-sectional survey the risk factors and outcome are measured simultaneously, and therefore it may be difficult to determine whether the exposure proceeded or followed the disease.

A longitudinal survey is an epidemiologic study that follows a population forward over time, evaluating the effects of one or more variables on a process. is a correlation research study that involves repeated observations of the same variables over long periods of time.

Feasibility study:

Feasibility studies are pieces of research done before a main study in order to answer the question “Can this study be done?” They are used to estimate important parameters that are needed to design the main study. For instance:

1. Standard deviation of the outcome measure, which is needed in some cases to estimate sample size;
2. Willingness of participants to be randomised;
3. Willingness of clinicians to recruit participants;
4. Number of eligible patients; carers or other appropriate participants;
5. Characteristics of the proposed outcome measure and in some cases feasibility studies might involve designing a suitable outcome measure;
6. Follow-up rates, response rates to questionnaires, adherence/compliance rates, ICCs in cluster trials, etc. o availability of data needed or the usefulness and limitations of a particular database; and
7. Time needed to collect and analyse data.

Pilot Study- is a version of the main study that is run in miniature to test whether the components of the main study can all work together. It is focused on the processes of the main study, for example to ensure recruitment, randomization, treatment, and follow-up assessments all run smoothly. It will therefore resemble the main study in many respects, including an assessment of the primary outcome. In some cases this will be the first phase of the substantive study and data from the pilot phase may contribute to the final analysis; this can be referred to as an internal pilot. Or at the end of the pilot study the data may be analysed and set aside, a so-called external pilot. Also referred to as exploratory trials.

Pivotal Study- Usually a phase III study which presents the data that the FDA uses to decide whether or not to approve a drug. A pivotal study will generally be well-controlled, randomized, of adequate size, and whenever possible, double-blind. Also referred to as confirmatory trials.

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Revised Submission Template

Project No.
Title:
Principal Investigator :

Section A-Grouping of project

Mention the section in *PSF to which IEC query was raised.	**Revision / Amendment made in the Section / Subsection** **(Mention NA if no changes required)**
	Original:
	Amendment:

Section B- Project Fact Sheet

Mention the section in *PSF to which IEC query was raised.	**Revision /Amendment made in the Section/Subsection** **(Mention NA if no changes required)**
	Original:
	Amendment:

Section C- Project Submission Overview

Mention the section in *PSF to which IEC query was raised.	**Revision /Amendment made in the Section/Subsection** **(Mention NA if no changes required)**
	Original:
	Amendment:

Section D**- Budget Sheet for the Proposed Study

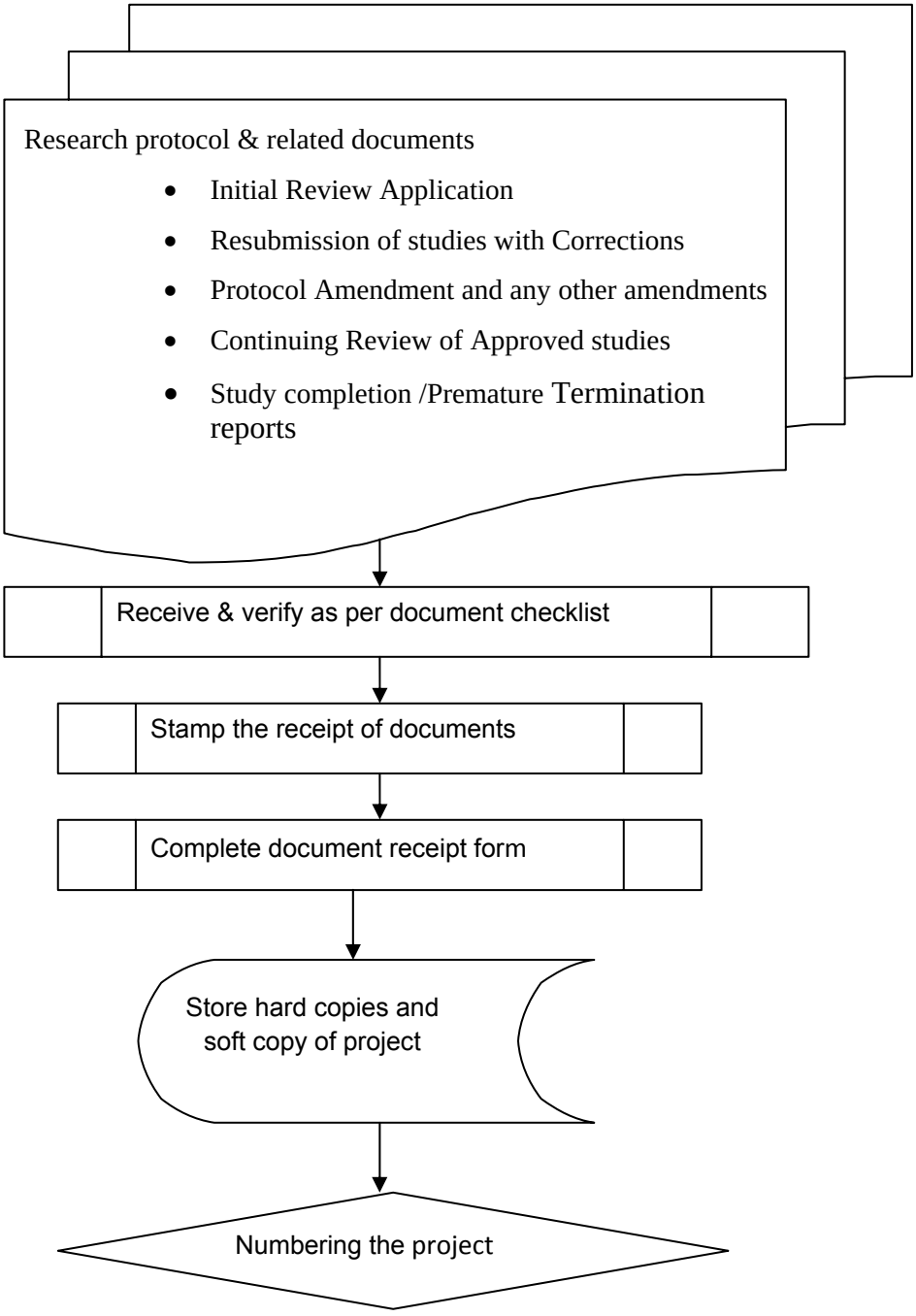
Mention the section in *PSF to which IEC query was raised.	**Revision /Amendment made in the Section/Subsection** **(Mention NA if no changes required)**
	Original:
	Amendment:

Sign & Date of Principal Investigator	

***PSF-Project Submission Form**

****In case of revision in budget sheet, the signed detailed budget sheet has to be attached**

Flow Chart


Research protocol & related documents
Initial Review Application
Resubmission of studies with Corrections
Protocol Amendment and any other amendments
Continuing Review of Approved studies
Study completion /Premature Termination reports
Receive & verify as per document checklist
Stamp the receipt of documents
Complete document receipt form
Store hard copies and soft copy of project
Numbering the project

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Full Board Review of Submitted Protocol

SOP Code: SOP 04a/V4 Date: 01/04/2016 Pages: 101 to 121

4a.1 Purpose

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

The purpose of this Standard Operating Procedure (SOP) is to describe how the IEC members will review an initial submission of the research study for approval using the Assessment Form. The Assessment Form AX1-V4SOP04a/V4 is designed to standardize the review process and to facilitate reporting, recommendations and comments offered to each study.

4a.2 Scope

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

4a.3 Categorization of protocols

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

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

An investigator may categorize his/her protocol in to the above three types, providing justification for the same, and after filling up Standard Request Forms for Expedited Review AX1-V4/SOP04b/V4 (SOP 04b/V4) / Exemption from review AX1-V4/SOP04c/V4 (SOP 04c/V4). However the decision to accept the request for Exemption from review / Expedited Review will be made by the Member Secretary, IEC.

This SOP describes the process of initial review.

4a.4 Full board Review

All research involving more than minimal risk, proposals/ protocols which do not qualify for exempted or expedited review and projects that involve vulnerable population and special groups shall be subjected to a full board review by all the members.

While reviewing the proposals, the following situations may be considered as minimal risk and should be carefully assessed against the existing facilities at the research site for determining risk/benefit analysis.

a. Collection of blood samples by finger prick, heel prick, ear prick, or venipuncture:
   I. From healthy adults and non-pregnant women who weigh normal for their age and not more than 500 ml blood is drawn in an 8 week period and frequency of collection is not more than 2 times per week;
   II. From other adults and children, where the age, weight, and health of the participants, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected has been considered and not more than 50 ml or 3 ml per kg, whichever is lesser is drawn in an 8 week period and not more than 2 times per week;
   III. From neonates depending on the haemodynamics, body weight of the baby and other purposes not more than 10% of blood is drawn within 48 – 72 hours. If more than this amount is to be drawn it becomes a risky condition requiring infusion/blood transfusion;
   IV. Prospective collection of biological specimens for research purposes by noninvasive means. For instance:
      1. Skin appendages like hair and nail clippings in a non-disfiguring manner;
      2. Dental procedures - deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction of permanent teeth; supraand subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth;
      3. Excreta and external secretions (including sweat);
      4. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum or by applying a dilute citric solution to the tongue;
      5. Placenta removed at delivery;
      6. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
      7. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
      8. Sputum collected after saline mist nebulization and bronchial lavages.

b. Collection of data through non-invasive procedures routinely employed in clinical practice. Where medical devices are employed, they must be cleared/approved for marketing, for instance -
   I. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the participant or an invasion of the participant's privacy;
   II. Weighing or testing sensory acuity;
   III. Magnetic resonance imaging;
   IV. Electrocardiography, echocardiography; electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow,

V. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

c. Research involving clinical materials (data, documents, records, or specimens) that will be collected solely for non-research (clinical) purposes.

d. Collection of data from voice, video, digital, or image recordings made for research purposes.

e. Research on individual or group characteristics or behavior not limited to research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

4a.5 Full board Review

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

The following will be considered as applicable:

4a.5.1 Scientific Design and Conduct of the Study

- Is the project original and innovative? e.g. Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this area?
- Is this an attempt to validate, prove or disapprove the validity of existing knowledge?
- Appropriateness of study design, work plan and structure to achieve the stated objectives: Are the conceptual or clinical framework, design, methods and analyses adequately developed, well integrated, well reasoned and appropriate to the aims of the project?
- Relevance of the work in the context of contemporary translation or clinical cancer research:
  - ❖ Does this study address an important research question or is it a predominantly service proposal?
  - ❖ If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced?
  - ❖ What will be effect of these studies on the concepts, methods, technologies, treatments, services, or preventive interventions that drive this field?
- Appropriateness of the study design in relation to the objectives of the study;
- The statistical methodology (including sample size calculation), and the potential for reaching sound conclusions with the smallest number of research participants;

- The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants and the concerned communities;
- The justification for the use of control arms;
- Potential of the work that would be conducted to lead into a larger and high impact study;
- Criteria for prematurely withdrawing research participants, and criteria for suspending or terminating the research as a whole;
- The adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a Data Safety Monitoring Board;
- Investigator's capability, availability of infrastructure and scientific environment to conduct the study within the time frame and carry it forward;
- The adequacy of the site, including the support staff, available facilities, and emergency procedures;
- Study Reporting and publication of the research.
- Regulatory permission for conduct of the study, HMSC clearance for international collaborative studies, MOU and MTA for national and international collaborative research.

4a.5.2 Care and Protection of Research Participants

- Required qualifications and experience of the investigators' for the proposed study;
- Any plans to withdraw or withhold standard therapies for the purpose of the research, and the justification for such action;
- Plans to withdraw subjects from the study by the investigator ;
- Medical care to be provided to research participants during and after the course of the research;
- Adequacy of medical supervision and psycho-social support for the research participants;
- Steps to be taken if research participants voluntarily withdraw during the course of the research;
- Criteria for extended access to, the emergency use of, and/or the compassionate use of study products;
- Arrangements, if appropriate, for informing the research participant's general practitioner or family doctor, including procedures for seeking the participant's consent to do so;
- Description of any plans to make the study product available to the research participants following the research and description of any financial costs to research participants
- Rewards and compensations for research participants (including money, services, and/or gifts);
- Provisions for compensation/treatment in the case of the injury/disability/death of a research participant attributable to participation in the research (as per institutional policy/ICMR guidelines/existing national legislation (CDSCO, DCGI).

- Insurance and indemnity arrangements.

4a.5.3 Protection of Research Participant Confidentiality

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

4a.5.4 Informed Consent/ Consent Process

- Essential Elements :
  1. Statement that the study involves research and explanation of the purpose of the research
  2. Statement that the study is approved by IEC
  3. Expected duration of the Subject's participation and total number of subjects that will be accrued on the study.
  4. Description of the procedures to be followed, including all invasive procedures
  5. Description of any reasonably foreseeable risks or discomforts to the Subject
  6. Description of any benefits to the Subject or others reasonably expected from research. If no benefit is expected Subject should be made aware of this.
  7. Disclosure of specific appropriate alternative procedures or therapies available to the Subject.
  8. Statement describing the extent to which confidentiality of records identifying the Subject will be maintained and who will have access to Subject's medical records
  9. Trial treatment schedule(s) and the probability for random assignment to each treatment (for randomized trials)
  10. Compensation and/or treatment(s) available to the Subject in the event of a trial-related injury
  11. An explanation about whom to contact for trial related queries in the event of any injury and rights of Subjects
  12. The anticipated prorated payment, if any, to the Subject for participating in the trial. In particular IEC review payments to determine that:
      - The amount of payment and the proposed method and timing of disbursement neither is coercive nor presents undue influence.
      - In case any amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
      - A description of acceptable and unacceptable payment arrangements for the sponsor, organization, researcher, and those referring research participants, if applicable:
        - Address the acceptability of payments in exchange for referrals of prospective participants ("finder's fees" or "referral fees").

- Address payments designed to accelerate recruitment that are tied to the rate or timing of enrollment (“bonus payments”).

13. Subject's responsibilities on participation in the trial \
14. Statement that participation is voluntary, that the subject can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the Subject is otherwise entitled
15. Any other pertinent information

- Additional elements, which may be required
  a. Statement of foreseeable circumstances under which the Subject's participation may be terminated by the Investigator without the Subject's consent.
  b. Additional costs to the Subject that may result from participation in the study.
  c. The consequences of a Subject’s decision to withdraw from the research and procedures for orderly termination of participation by Subject.
  d. Statement that the Subject or Subject's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect the Subject's willingness to continue participation will be provided.
  e. A statement that the particular treatment or procedure may involve risks to the Subject (or to the embryo or foetus, if the Subject is or may become pregnant), which are currently unforeseeable.

- A full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent
- Adequacy, completeness and comprehension of written and oral information to be given to the research participants, and, when appropriate, their Legally Acceptable Representative(s) (LAR) and/or Impartial witness (if applicable)
- Clear justification for the intention to include research participants who cannot consent, and a full account of arrangements made to obtain their consent /authorisation/consent of LAR and/or Impartial witness (if applicable)
- Assurances that research participants will receive information that becomes available during the course of the research relevant to their participation including their rights, safety, and well-being;
- Provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project.

4a.5.5 Community Considerations

- Impact and relevance of the research to the local community and the concerned communities from which the research participants are drawn;
- Steps taken to consult with the concerned communities during the course of designing the research;
- Influence of the community on the consent of individuals;
- Proposed community consultation during the course of the research;

- Extent to which the research contributes to capacity building, such as the enhancement of local healthcare, research, and the ability to respond to public health needs;
- A description of the availability and affordability of any successful study product to the concerned communities following the research;
- The manner in which the results of the research will be made available to the research participants and the concerned communities.

4a.5.6 Recruitment of Research Participants

- The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status, and ethnicity)
- The means by which initial contact and recruitment is to be conducted;
- The means by which full information is to be conveyed to potential research participants or their representatives;
- Inclusion criteria for research participants;
- Exclusion criteria for research participants;
- Students or staff recruitment in research.
- Healthy volunteers.
- Information contained in the advertisement and mode of its communication.
- Final copy of printed advertisements.
- Final audio or video taped advertisements.

4a.5.7 Advertisements

The IEC reviews advertising to ensure that advertisements do not:

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

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

- The name and address of the researcher or research facility.
- The purpose of the research or the condition under study.
- In summary form, the criteria that will be used to determine eligibility for the study.
- A brief list of benefits to participants, if any.
- The time or other commitment required of the participants.
- The location of the research and the person or office to contact for further information.

4a.6 Responsibility

The IEC Secretariat is responsible for receiving, verifying, and managing the hard copies of the received submission. In addition, the Secretariat should create a study specific file, distribute the packages and study assessment forms to the IEC members for review, and communicate the review results to the investigators.

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

4a.7 Detailed instructions

Only investigator initiated trials/studies seeking intramural grants if required may be sent prior to the meeting for external review otherwise these projects will be reviewed and scored in the respective full board IEC meeting. Project is scored by the reviewer (Reviewer Assessment Form AX2-V4/SOP04a/V4). The external scores will be considered for granting intramural funds. The external reviewer comments if received on time will be considered during the IEC discussion. However pharma-sponsored studies and investigator initiated studies requiring no intramural funds/extramural studies will be tabled in the IEC meeting without any prior external review.

Distribution of the project documents

- The distribution of the project documents for IEC review will be as follows:
- A hard copy of the Agenda and Study Assessment forms would be dispatched to all IEC members.
- Soft copies of protocols and other study related documents under discussion will be sent on email preferably 7 days in advance of the scheduled meeting

Assigning Lead discussants

- The Member Secretary, IEC will assign lead discussants to each research study for scientific, ethical and statistical review. The lead discussants will be members of the IEC and will have to present a detailed relevant review of the assigned study.
- The lead discussants/Primary Reviewers will present the research study at a regular full board or expedited review subcommittee or special meeting of the IEC.
- The Investigator may be called for any questions or clarification required by the board members.
    - The lead discussant is informed no less than 7 days prior to the meeting through the agenda. In case the lead discussant is not in a position to review due to some reason, he/she should inform the Member Secretary, IEC at the earliest, so that the research study can be assigned to another member.
    - In the event of his/her absence, a lead discussant can send written comments on the research protocols to the Member Secretary, which will be tabled and discussed during the meeting. However, a final decision on the research protocol will be arrived at, by a broad consensus at the end of discussion among attending members and not solely based on written comments.

  - It is the responsibility of the assigned lead discussant/s to review the research protocols assigned to them thoroughly and communicate their observations, comments and decisions to the IEC during the meeting. The lead discussant/s should return the research protocols and relevant documents to the secretariat on the day of the meeting.
- The Member Secretary can invite an independent consultant (if necessary) for comments during the full board meeting.

Responsibilities of IEC members

- Check the contents of the packages.
- Sign and date an acknowledgement form / receipt upon receiving the packages.
- Return the acknowledgement form / receipt back to the delivery person / IEC Secretariat.
- Check the meeting date to see if he/she is available to attend the meeting.
- Identify the project/study related documents assigned for review.
- Notify the IEC Secretariat 3 days prior to the convened IEC meeting regarding missing documents, if any.
- The members should submit the Study Assessment Form/comments to the IEC Secretariat on or before the scheduled meeting. In case an IEC member is not in a position to attend the scheduled meeting, the responsibility of returning the packages and submitting the study assessment form/Comments would be that of the respective IEC member.

4a.8 Review the Protocol:

Review all elements as per section 4.3, 4.4, 4.5. The protocol will be reviewed by each member as per guidelines to review a study protocol described in AX1-V4/SOP04/V4.

4a.9 Use of study assessment forms and reviewer assessment form

It is the responsibility of the IEC members to use assessment form as a checklist while reviewing each research protocol. The duly filled, signed and dated assessment forms may be returned along with the research protocols to the Secretariat one day prior to the meeting. The assessment form is designed to standardize the review process. The study assessment form (AX1-V4/SOP04a/V4) helps to ensure that all elements of research study are reviewed and are accordingly documented during the discussion / meeting.

IEC members having expertise in the study should also score the studies seeking intramural funds as per Reviewer Assessment Form (AX2-V4/SOP04a/V4)

Note: The completed assessment form is the official record of the decision reached by the IEC for the specific protocol. The study assessment form is applicable only for first initial full board review and resubmission of the project.

IEC, TMC

4a.9.1 Collection of the assessment reports

The IEC Secretariat will collect the Assessment Forms AX1-V4/SOP04a/V4 and the comments from each reviewer and file them in the original set of the study file.

4a.10 At IEC meeting

The details of the review procedures and communication of the decision is described in detail in SOP05/V4

References

1.	World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000)
2.	International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996 Retrieved from-
3.	Cavazos N., Forster D., and Bowen A.J., Ethical Concerns in Placebo-controlled studies: An Analytical Approach, Drug Information Journal 36(2) 2002: pgs 249- 259, via WIRB documents
4.	Draft Guidelines for Compensation to Participants for Research Related Injury in India. http://icmr.nic.in/guidelines.htm
5.	ICMR guidelines 2006

Glossary

Document: Document may be in any form, e.g., paper, electronic mail (e-mail), faxes, audio or video tape, etc.

Expedited review/meeting: An expedited review is an accelerated review for minor changes to the approved protocol, research proposal with minimal risk and documents of minor nature. A review process is by IEC subcommittee and the decision is notified to the full board.

Extramural: The studies funded by external sources (external to TMC).

Full Board/ Regular Review: Review of initial, resubmitted, continuing review, amendments of protocols and or ICFs and any other documents which are tabled in a formally convened meeting of the full IEC committee for detailed discussion and decisions.

Initial Review: The first time review of the protocol done by one or two individual reviewers/lead discussants (IEC members) during the formally convened IEC meeting.

Intramural- The studies funded by the institution

Pre-clinical study: Animal and in vitro studies providing information on possible toxicities and mechanisms of action, and starting doses for human studies.

Phase I studies: Initial introduction of an investigational new drug (IND) into humans, studies designed to determine the metabolism and pharmacological actions of drugs in humans, and studies designed to assess the side effects associated with increasing doses .

Phase II study: A study of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes.

Phase III study: A study expands controlled and uncontrolled trials performed after preliminary evidence suggesting effectiveness of the drug has been obtained. They are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling

Phase IV study: A study that seeks to expand an approved medication's use into a new population, new indication, or new dose.

Reviewer Assessment Form: An official record that documents the scoring of the protocol seeking intramural funds.

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

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

Study Assessment Form: An official record that documents the protocol review process.

- Vulnerable subjects: Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests.

Annexure

AX1-V4/SOP04a/V4

Study Assessment Form to be used at the IEC meeting.
Study Assessment Form

Protocol Number :		Date (DD/MM/YY):	
Protocol Title :			
Principal Investigators:		MMC Registration No.	
Institute:		Contact No.	
Co – investigator(s):		Contact No.	
Delineation of responsibilities of investigators:			
Total No. of Participants:		No. of Study site/s:	
Funding Agency:		Contact No.	
Duration of the Study:		Status:	☐ New ☐ Revised ☐ Amended
Reviewer's name :		Contact No.	
Type of the Study :	☐ Intervention ☐ Epidemiology ☐ Observational ☐ Document based ☐ Individual based ☐ Genetic ☐ Social Survey ☐ Others, specify……		
Review Status:	☐ -Full board ☐ Expedited ☐ Emergency		
CTRI Registration	☐ Applicable ☐ Not Applicable		

Description of the Study in brief: Mark whatever applied to the study.

☐ Randomized	☐ Stratified Randomized	☐ Open-labeled
☐ Double blinded	☐ Placebo controlled	☐ Treatment controlled
☐ Cross-over	☐ Parallel	☐ Interim Analysis
☐ Multicenter study	☐ Screening	☐ Descriptive
☐ Use of Tissue samples	☐ Use of Blood samples	☐ Use of genetic materials

Study Objectives:

Please see my attached comments in a separate sheet
……
……
……
……
……

Mark and comment on whatever items applicable to the study

1	Objectives of the Study ☐ clear ☐ unclear	What should be improved?
2	Need for Human Participants ☐ Yes ☐ No	Comment:
3	Methodology: ☐ clear ☐ unclear	What should be improved?
4	Background Information and Data ☐ sufficient ☐ insufficient	Comment:
5	Risks and Benefits Assessment ☐ acceptable ☐ unacceptable	Comment:
6	Inclusion Criteria ☐ appropriate ☐ inappropriate	Comment:
7	Exclusion Criteria ☐ appropriate ☐ inappropriate	Comment:
8	Discontinuation and Withdrawal Criteria ☐ appropriate ☐ inappropriate	Comment:
9	Does the study involve modified or new claims, namely, indications, dosage forms (including sustained release dosage form) and route of administration of already approved drugs and combination of two or more drugs	Yes[ ] No [ ]
10	Does this study require permission from regulatory authorities?	Yes [ ] No [ ] If Yes- ☐ DCGI

		☐ ICMR ☐ other govt. Departments/Agencies
11	Involvement of Vulnerable Participants ☐ Yes ☐ No	Comment: ☐ children, ☐ pregnant or nursing women, ☐ economically or socially disadvantaged group ☐ mentally challenged/mentally differently abled group ☐ participants with reduced autonomy ☐ persons who are terminally ill have incurable disease, mental illness
12	Voluntary, Non-Coercive Recruitment of Participants ☐ Yes ☐ No	Comment:
13	Sufficient number of participants? ☐ Yes ☐ No	Comment:
14	Control Arms (placebo, if any) ☐ Yes ☐ No	Comment:
15	Are qualifications and experience of the Participating Investigators appropriate? ☐ Yes ☐ No Is the duty delegations as per invetsigator's expertise and study design ☐ Yes ☐ No	Comment: Comment:
16	Disclosure or Declaration of Potential Conflicts of Interest ☐ Yes ☐ No	Comment:
17	Facilities and infrastructure of Participating Sites ☐ Appropriate ☐ Inappropriate	Comment:

18	Community Consultation ☐ Yes ☐ No	Comment:
19	Involvement of Local Researchers and Institution in the Protocol Design, Analysis and Publication of Results ☐ Yes ☐ No	Comment:
20	Contribution to Development of Local Capacity for Research and Treatment ☐ Yes ☐ No	Comment:
21	Benefit to Local Communities ☐ Yes ☐ No	Comment:
22	Availability of similar Study / Results ☐ Yes ☐ No	Comment:
23	Are human biological material/data sent abroad? ☐ Yes ☐ No If yes, permission required	Comment: □ Health Ministry's Screening Committee(HMSC) □ Others, please specify
24	Are procedures for obtaining Informed Consent appropriate? ☐ Yes ☐ No	Comment:
25	Contents of the Informed Consent Document ☐ clear ☐ unclear	Comment:
26	Language of the Informed Consent Document ☐ clear ☐ unclear	Comment:
27	Whether Informed Consent document is as per the template ☐ Yes ☐ No	Comment:
28	Contact Persons for Participants mentioned? ☐ Yes ☐ No	Comment:

29	Privacy & Confidentiality ensured? ☐ Yes ☐ No	Comment:
30	Applied for waiver of consent	Yes [ ] No [ ]
31	Waiver of consent Granted Specify reasons	Yes [ ] No [ ]
32	Inducement for Participation ☐ Unlikely ☐ Likely	Comment:
33	Provision for Medical / Psychosocial Support ☐ appropriate ☐ inappropriate	Comment:
34	Provision for Treatment of Study-Related Injuries ☐ appropriate ☐ inappropriate	Comment:
35	Provision for Compensation ☐ appropriate ☐ inappropriate	Comment:
36	Provision for post-trial access ☐ appropriate ☐ inappropriate	Comment:
37	Provision for payments ☐ appropriate ☐ inappropriate	Comment:
38	Provisions for monitoring the data to ensure the safety of participants ☐ Yes ☐ No	Comment:

Assessment Report

Review Date (DD/MM/YYYY): Protocol number:

Protocol Title :		
Elements Reviewed	☐ Attached	☐ Not attached
Review of Revised Application ☐ Yes ☐ No	Date of Previous review:	
DECISION :	☐ Approved ☐ Approved with Modifications ☐ Resubmit ☐ Not approved	
Comment:		
Is there any conflict of interest (scientific, service or financial) between you and that of the **Investigators? ☐ Yes ☐ No**		
Signature :		Date**:**

AX2-V4/SOP04a/V4

Reviewer's Comments and Score
Tata Memorial Centre (TMH/ACTREC)
Assessment Form

TMC Project No. -

Principal Investigator-

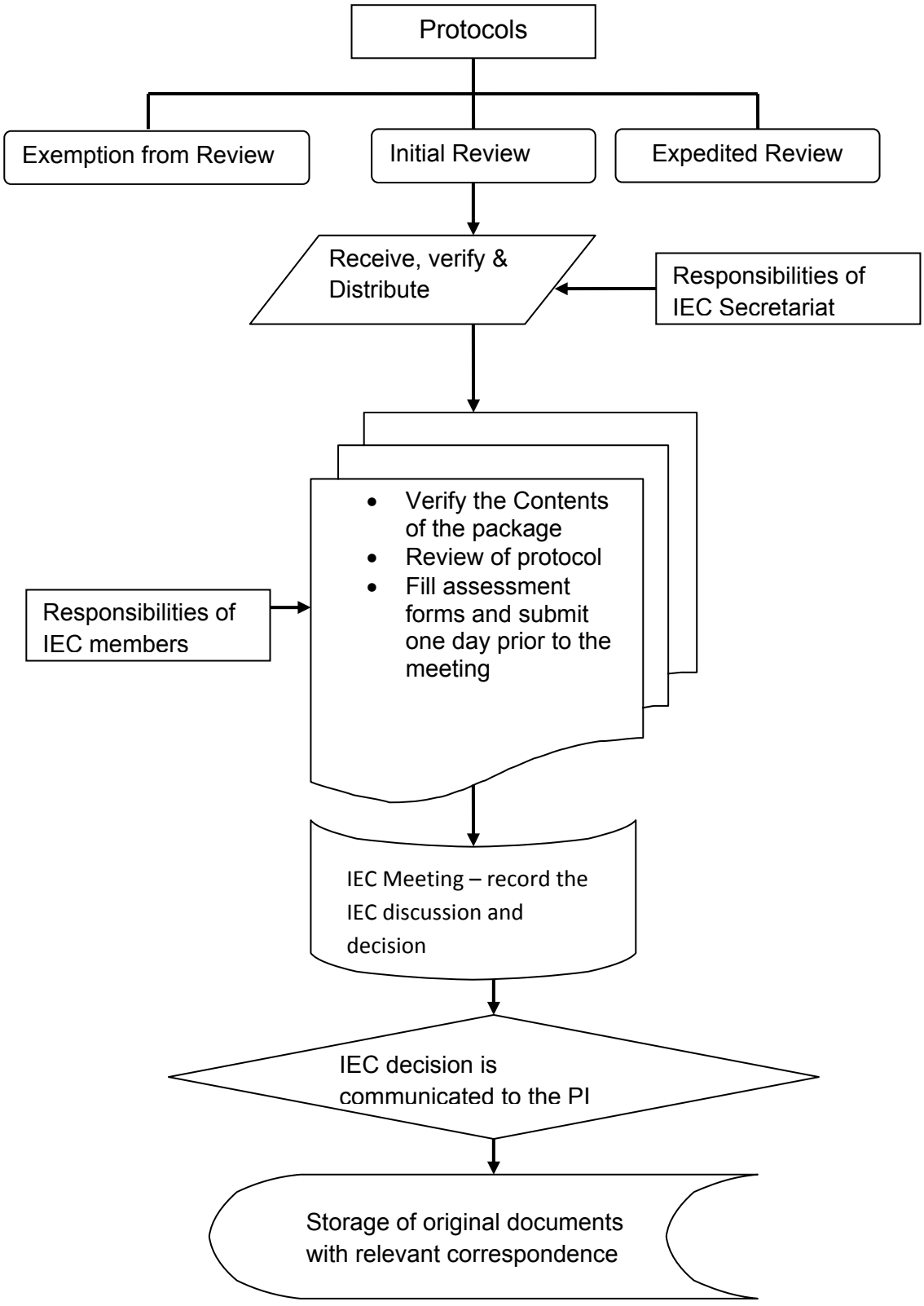
Review Criteria	***Max. Marks***	**Reviewer's Score**	**IEC Committee Score**
Innovation: Is the project original and innovative? e.g. Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this area?	**30**		
Relevance of the work in the context of contemporary Translation or clinical cancer research: * Does this study address an important research question or is it a predominantly service proposal? * If the aims of the application are achieved, how will scientific knowledge or clinical practice are advanced? * What will be effect of these studies be on the concepts, methods, technologies, treatments, services, or preventive interventions that drive this field?	**20**		
Appropriateness of study design, work plan & structure to achieve the stated objectives: Are the conceptual or clinical framework, design, methods & analyses adequately developed, well integrated, well reasoned & appropriate to the aims of the project?	**20**		
Potential of the work that would be conducted through research grant to lead into a larger and high impact study	**20**		
Investigator's capability, availability of Infrastructure & scientific environment to conduct the study within the time frame and carry it forward	**10**		
Total	**100**		

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

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

Reviewer's Signature & Name (below the line please): Date:

Flow Chart


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

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Expedited Review of Submitted Protocol/Documents

SOP Code: SOP 04b/V4 Date : 01/04/2016 Pages: 122 to 129

4b.1 Purpose

The purpose of this SOP is to provide criteria for those research studies which qualify for expedited review by IEC.

4b.2 Scope

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

4b.3 Responsibility

It is the responsibility of the Member Secretary to identify (as per section 4b.3) which research studies or documents are eligible for expedited review.

4b.4 Categorization of protocols

The Member Secretary, IEC will screen the study for its completeness and depending on the risk involved in the research study categorise it into three types, viz.

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

An investigator cannot categorize his/her study in to the above three types. This SOP describes expedited review in detail.

An investigator may apply for expedited review for the study protocol using. However decision to accept the request will be made by the Member Secretary, IEC.

4b.5 Expedited Review

Expedited review is a procedure through which certain kinds of research proposals may be reviewed and approved by a subcommittee (refer section 4b.6.2) without convening a meeting of the full Board.

The proposals presenting no more than minimal risk to research participants may be subjected to expedited review. Minimal risk would be defined as one which may be anticipated as harm or discomfort not greater than that encountered in routine daily life activities of the 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 (ICMR 2006). Refer to section 4a.4 to determine categories for minimal risk.

IEC may do expedited review only if the protocols involve -

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

   Minor changes in previously approved research during the period covered by the original approval may be eligible for expedited review where:

   I. The research is permanently closed to the enrolment of new subjects;

   II. All subjects have completed all research-related interventions

2. Revised proposal previously approved through full board review by the IEC or continuing review of approved proposals where there is no additional risk or activity is limited to data analysis.

   Continuing review of research previously approved by the convened IEC (e.g., not originally subject to expedited review) may be eligible for expedited review:

   A. Where
      a. the research is permanently closed to the enrolment of new subjects;
      b. all subjects have completed all research-related interventions; and
      c. 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.

3. Premature Termination/ Discontinuation/ Suspension/Withdrawal of study before site initiation
4. Research activities that involve only procedures listed in one or more of the following categories :
   a. Clinical studies of drugs and medical devices only when –
      i. Research is on already approved drugs except when studying drug interaction or conducting trial on vulnerable population

      or

      ii. Adverse Event (AE) or unexpected Adverse Drug Reaction (ADR) of minor nature is reported.
5. Research involving clinical materials (data, documents, records, or specimens) that have been collected for non-research (clinical) purposes.
6. When in emergency situations like serious outbreaks or disasters a full review of the research is not possible, prior written permission of IEC may be taken before use of the test intervention. Such research can only be approved for pilot study or preliminary work to study the safety and efficacy of the intervention and the same participants should not be included in the clinical trial that may be initiated later based on the findings of the pilot study.

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

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

b. Research on disaster management

A disaster is the sudden occurrence of a calamitous event at any time resulting in substantial material damage, affecting persons, society, community or state(s). It may be periodic, caused by both nature and humans and creates an imbalance between the capacity and resources of the society and the needs of the survivors or the people whose lives are threatened, over a given period of time. It may also be unethical sometimes not to do research in such circumstances. Disasters create vulnerable persons and groups in society, particularly so in disadvantaged communities, and therefore, the following points need to be considered when reviewing such research:

i. Research planned to be conducted after a disaster should be essential culturally sensitive and specific in nature with possible application in future disaster situations.
ii. Disaster-affected community participation before and during the research is essential and its representative or advocate must be identified.
iii. Extra care must be taken to protect the privacy and confidentiality of participants and communities.
iv. Protection must be ensured so that only minimal additional risk is imposed.
v. The research undertaken should provide direct or indirect benefits to the participants, the disaster-affected community or future disaster- affected population and a priori agreement should be reached on this, whenever possible, between the community and the researcher.
vi. All international collaborative research in the disaster-affected area should be done with a local partner on equal partnership basis.
vii. Transfer of biological material, if any, should be as per Government rules taking care of intellectual property rights issues.

7. Study related documents which would be considered for expedited review are as follows but may not restrict to:
   I. Minor deviations from originally approved protocol
   II. Inclusion or deletion of name/s of co-investigator/s
   III. Request for change in PI or hand over of trials or projects
   IV. Minor amendments in the protocol, CRF, eCRF
   V. Minor corrections in budget

VI. Other administrative revisions like change in the name, address of sponsor , change in contact details of PI and IEC

DHHS (CFR) criteria may be applicable only when research involving human subjects is conducted, supported or otherwise subject to regulation by any United States government federal department or agency funded by a U.S. federal agency.

The expedited review procedure is not applicable:

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

4b.6 Detailed instructions to the IEC secretariat:

4b.6.1 Receive the submitted documents

- Receive the application and documents submitted by investigators as described in SOP03/V4

4b.6.2 Expedited Review

Procedure: The PI submits a completed IEC submission form along with the study protocol, Waiver of Consent form, Case Record Form and any other documents [as applicable-Document Checklist (AX2-V4/SOP 03/V4)] to IEC. Principal Investigator may submit expedited review application form to IEC, if he/she feels the study meets the eligibility criteria for expedited review. Upon receipt of the application, IEC staff screens it for completeness and accuracy. Member Secretary, IEC makes a preliminary determination that the application/research proposal/documents meet the criteria for expedited review, including minimal risk, and identifies the research categories. If the application does not meet the criteria for expedited review, IEC informs the PI to resubmit the study for full or exempt review (as per SOP04a/04c).

After deciding that the study or documents qualify for an expedited review, Member Secretary informs the Chairperson. Member Secretary in consultation with the Chairperson forms a subcommittee comprising of the Member Secretary of the IEC, an external IEC member and one or two IEC members from TMC. The external member will chair the meeting. The project and all the necessary documents will be provided to the reviewer. Review may be made either by circulation of comments, email, telephone discussion or meeting. The Expedited Review process should ordinarily be completed in no more than 10 working days after it has been accepted and categorized for Expedited review by the Member Secretary of the IEC.

In reviewing the research, the reviewers may exercise all the authorities of the IEC except that the reviewers may not disapprove the research. If that is the case, it must go through full board review.

IEC members who are conducting expedited review must disclose to the IEC Member Secretary any conflicts of interest related to the study under review, and must not review those items. If IEC Member Secretary has any conflicts of interest related to the study under review, he must disclose to the IEC subcommittee Chair and must not review that project. Items identified to have a conflict of interest by the IEC Member Secretary are presented to an IEC subcommittee Chair or designee who does not have a conflict with the study.

4b.6.3 Communication between the IEC and the investigator

- The decision of the IEC subcommittee will be communicated to the Principal Investigator after the minutes of the subcommittee are finalized. The final decision of expedited review is only notified to the full board.
- If the project is approved or approved with modifications, this will be informed to the Principal Investigator in writing. If the project is approved with modifications, the modifications submitted by PI will be reviewed by the Member Secretary or reviewer for final approval.
- Expedited reviewers may not disapprove the research. If that is the case, it will be referred for full board review. This will be communicated to Principal Investigator.

References

1.	ICMR Ethical Guidelines for Biomedical research on Human Participants, ICMR (2006) - http://www.icmr.nic.in/ethical_guidelines.pdf
2.	International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996
3.	WHO Operational Guidelines for Ethical Review Committee that Review Biomedical Research (Geneva 2000) - www.who.int/tdr/publications/publications/
4.	Code of Federal Regulations 45cfr46

Glossary

Document: Document may be of any forms, e.g., paper, electronic mail (e-mail), faxes, audio or video tape, etc.

Expedited review/meeting: An expedited review is an accelerated review of research proposal with minimal risk, minor changes to the approved protocol and documents of minor nature. A review process is by IEC subcommittee and the decision is notified to the full board.

Annexure 1

AX1-V4/SOP04b/V4
Expedited Review Application Form

TMC Project No. *:*_____*(To be filled by IEC Secretariat)*

1. Principal Investigator's Name: _____
2. Department/DMG: _____
3. Title of Project: _____
4. Names of study team members:
   _____
   _____
5. Brief description of the project:
   _____
   _____
6. State reasons why expedited review from IEC is requested? (Tick applicable)
   ☐ Risks to subjects is more than minimal
   ☐ Risks to subjects are minimal
   ☐ Research involving materials (data, documents, records, or specimens) that have been collected, for non-research (clinical) purposes

   Are children included in the study? Yes ☐ No

   Does the research involve vulnerable population? Yes ☐ No

Any other reasons: _____

Principal Investigator's signature: _____ Date _____

Recommendations by the IEC Member Secretary:

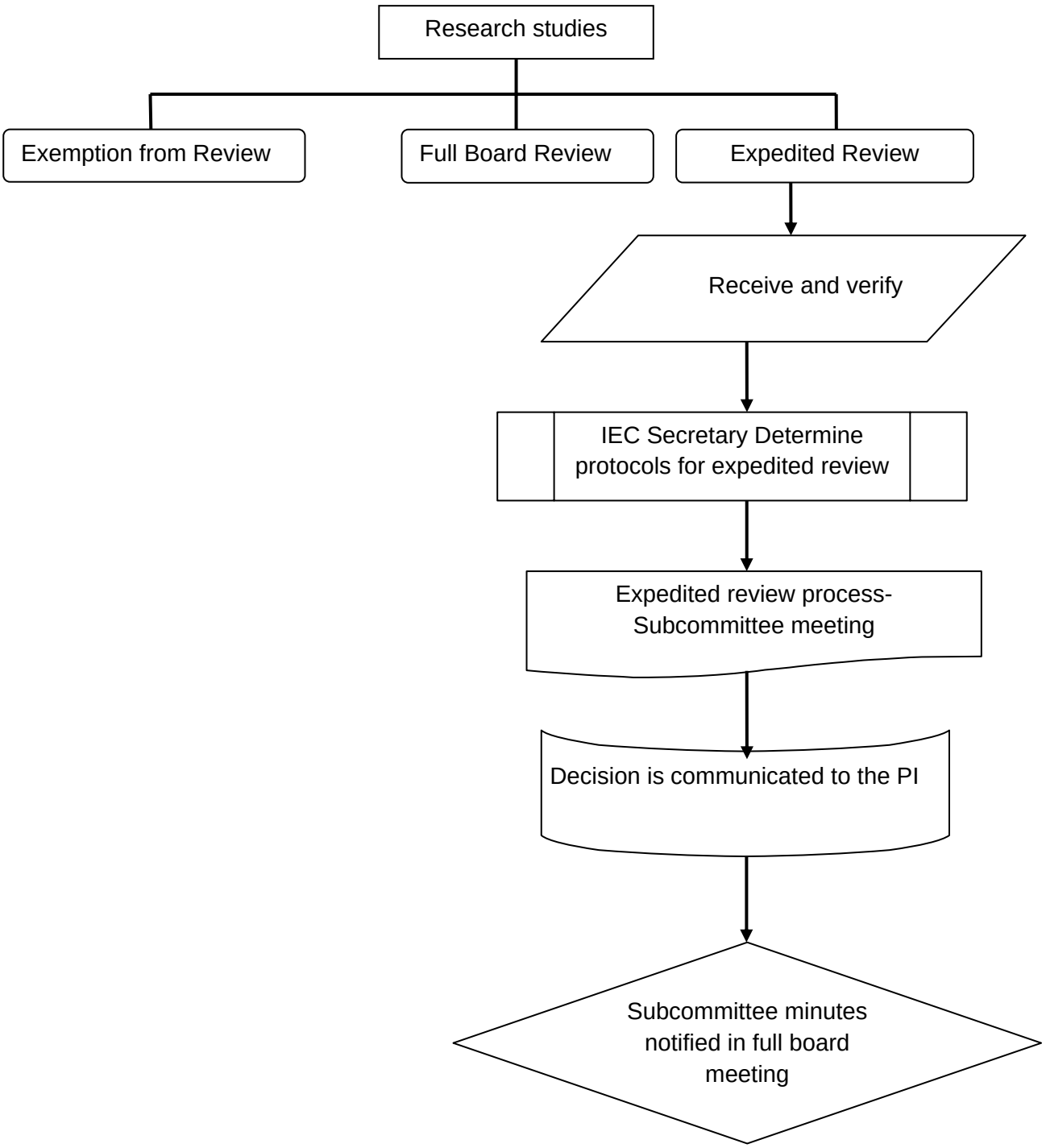
☐ Consider for expedited review
☐ Can not be consider for expedited review, Reasons _____
_____
_____

Signature of the Member Secretary:

Date- _____

Final Decision: ☐ Expedited Review ☐ For Full Board Meeting

Flow Chart


Research studies
Exemption from Review
Full Board Review
Expedited Review
Receive and verify
IEC Secretary Determine protocols for expedited review
Expedited review process- Subcommittee meeting
Decision is communicated to the PI
Subcommittee minutes notified in full board meeting

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Exemption from the Review for Research Projects

SOP Code: SOP 04c/V4 Date: 01/05/2014 Pages: 130 to 138

4c.1 Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe which research studies can be exempted from review and do not require the approval of the IEC. The Exemption Form AX1-V1/SOP04c/V4 is designed to standardize the process of exemption.

4c.2 Scope

This SOP applies to the studies submitted for exemption from review by the IEC. The specific points in the Exemption Form should guide the Member Secretary to determine whether the study qualifies for exemption from review. The decision should be taken by the Member Secretary in consultation with the Chairperson and should be informed to the members in the forthcoming IEC meeting.

4c.3 Responsibility

It is the responsibility of the Member Secretary to record the decision in the Exemption Form with reasons. The IEC Secretariat is responsible for recording and filing the Exemption Form. The Member Secretary/Chairperson must sign and date letter conveying the decision AX01-V1/SOP04c/V4.

4c.4 Categorization of protocols

The Member Secretary, IEC or secretariat shall screen the proposals for their completeness and depending on the risk involved in the research proposals categorize them into three types, viz., Exemption from review, Expedited review and Full review. An investigator cannot categorize his/her protocol in to the above three types. This SOP describes exemption from review in detail

4c.5 Exemption from review

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

Minimal risk would be defined as one which may be anticipated as harm or discomfort not greater than that encountered in routine daily life activities of the 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 (ICMR 2006).

The exemption from review may be seen in the following situations:

1. Research on educational practices such as instructional strategies or effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods

   Exceptions:

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

2. Research proposals which do not involve living human participants or data derived from them are exempt from IEC review. For example,
    a) Audits of educational practices
    b) Research on microbes cultured in the laboratory
    c) Research on immortalized cell lines
    d) Research on cadavers or death certificates provided such research reveals no identifying personal data
    e) Analysis of data freely available in the public domain
3. In circumstances where research appears to meet minimal risk criteria may need to be reviewed by the IEC. This might be because of requirements of:
    a. The publisher of the research
    b. An organization which is providing funding resources, existing data, access to participants etc.
4. No research can be considered as minimal risk if it involves but is not restricted to the following:
    I. Invasive physical procedures or potential for physical harm
    II. Procedures which might cause mental/emotional stress or distress, moral or cultural offence
    III. Personal or sensitive issues
    IV. Vulnerable groups
    V. Cross cultural research
    VI. Investigation of illegal behaviour(s)
    VII. Invasion of privacy
    VIII. Collection of information that might be disadvantageous to the participant
    IX. Use of information already collected that is not in the public arena which might be disadvantageous to the participant
    X. Use of information already collected which was collected under agreement of confidentiality
    XI. Participants who are unable to give informed consent
    XII. Conflict of interest e.g. the researcher is also the lecturer, teacher, treatment-provider, colleague or employer of the research participants, or there is any other power relationship between the researcher and the research participants.
    XIII. Deception
    XIV. Audio or visual recording without consent
    XV. Withholding benefits from “control” groups
    XVI. Inducements
    XVII. Risks to the researcher

IEC, TMC

4c.6 Detailed instructions to the IEC secretariat:

4c.6.1 Receive the submitted documents

- The Secretariat will receive the Exemption from Review Application Form AX1-V1/SOP04c/V4, Protocol and other documents submitted by the investigators.
- Acknowledge the submitted documents
- Hand over the received documents to the Member Secretary, IEC.

4c.6.2 Determine protocols eligible for exemption from review

The IEC-Member Secretary will determine whether a protocol qualifies for exemption from review based on criteria explained in (section 4c.3).

4c.6.3 Exemption Process

- If the protocol and related documents satisfy the criteria as listed in 4c.3, the IEC Member Secretary in consultation with the Chairperson will review the brief summary of the project and the Exemption Form.
- The Member Secretary will record the decision on the Exemption Form.
- The Secretariat will communicate the decision to the investigator.
- The Member Secretary will inform the IEC about the decision at the next full board meeting.
- In case the study does not qualify for exemption from review, the Member Secretary / Chairperson will refer the study for the full board meeting.
- Exempt research should fulfill organization's ethical standard, such as:

  - ❖ The research should hold no more than minimal risk to participants.
  - ❖ Selection of participants should be equitable.
  - ❖ If there is recording of identifiable information, there should be adequate provisions to maintain the confidentiality of the data.
  - ❖ If there are interactions with participants, the IEC should determine whether there should be a consent process that will disclose such information as:
    - i. That the activity involved in the research.
    - ii. A description of the procedures.
    - iii. That participation is voluntary.
    - iv. Name and contact information of the researcher.
    - v. There are adequate provisions to maintain the privacy and interests of participants.
- Exempt research does not require continuing review or submission of status report.

4c.6.4 Communication between the IEC and the investigator

- The decision regarding request for exemption from review, signed by the IEC Member Secretary/Chairperson, will be forwarded by the Secretariat to the Principal Investigator within 15 days after the decision regarding the exemption is taken.

IEC, TMC

- The Member Secretary will inform the IEC of the decision at the forthcoming regular meeting and minute it in the meeting notes.

References

1. ICMR's Ethical Guidelines for Biomedical research on Human Participants, ICMR (2006) - http://www.icmr.nic.in/ethicalguidelines.pdf (last accessed 20 April 2009)

2. WHO Operational Guidelines for Ethical Review Committee that Review Biomedical Research (Geneva 2000) - www.who.int/tdr/publications/publications/ (last accessed 14th September 2008)

3. Code Federal Regulations CFR
http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html

Glossary

Exemption from review: A research study is said to be exempt from review when it does not require the IEC approval for its conduct.

Annexure 1

AX1-V4/SOP04c/V4
Review Exemption Application Form

TMC Project No. :_____(To be filled by IEC Secretariat)

1. Principal Investigator's Name: _____
2. Department/DMG: _____
3. Title of Project: _____
4. Names of study team members:
   _____
5. Brief description of the project:

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

   Please check that your application / summary includes:
   - Procedures for voluntary, informed consent
   - Privacy & confidentiality
   - Risk to participants
   - Needs of dependent persons
   - Conflict of interest
   - Permission for access to participants from other institutions or bodies
   - Inducements

6. State reasons why exemption from IEC review is requested? (Tick applicable)
   - ☐ Audit of educational practices
   - ☐ Research on microbes cultured in the laboratory
   - ☐ Research on immortalized cell lines
   - ☐ Research on cadavers or death certificates which reveals no identifying personal data
   - ☐ Analysis of data freely available in the public domain
   - ☐ Any other (please specify) ----------

Principal Investigator's signature: _____ Date _____

IEC, TMC

Forwarded by the Head of the department:

Name: _____

Signature: _____

Date: _____

Recommendations by the IEC Member Secretary:

☐ Exemption

☐ **Can not be** exempted, Reasons _____

_____

_____

_____

☐ Discussion at full board

Signature of the Member Secretary: _____ **Date** _____

Final Decision:

☐ Exemption

☐ Can not be exempted,

Reasons _____

_____

☐ Discussion at full board

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

Final Decision at Full Board meeting held on _____

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

NOTE:

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

i. Invasive physical procedures or potential for physical harm
ii. Procedures which might cause mental/emotional stress or distress, moral or cultural offence
iii. Personal or sensitive issues
iv. Vulnerable groups

v. Cross cultural research
vi. Investigation of illegal behaviour(s)
vii. Invasion of privacy
viii. Collection of information that might be disadvantageous to the participant
ix. Use of information already collected that is not in the public arena which might be disadvantageous to the participant
x. Use of information already collected which was collected under agreement of confidentiality
xi. Participants who are unable to give informed consent
xii. Conflict of interest e.g. the researcher is also the lecturer, teacher, treatment-provider, colleague or employer of the research participants, or there is any other power relationship between the researcher and the research participants.
xiii. Deception
xiv. Audio or visual recording without consent
xv. Withholding benefits from “control” groups
xvi. Inducements
xvii. Risks to the researcher

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

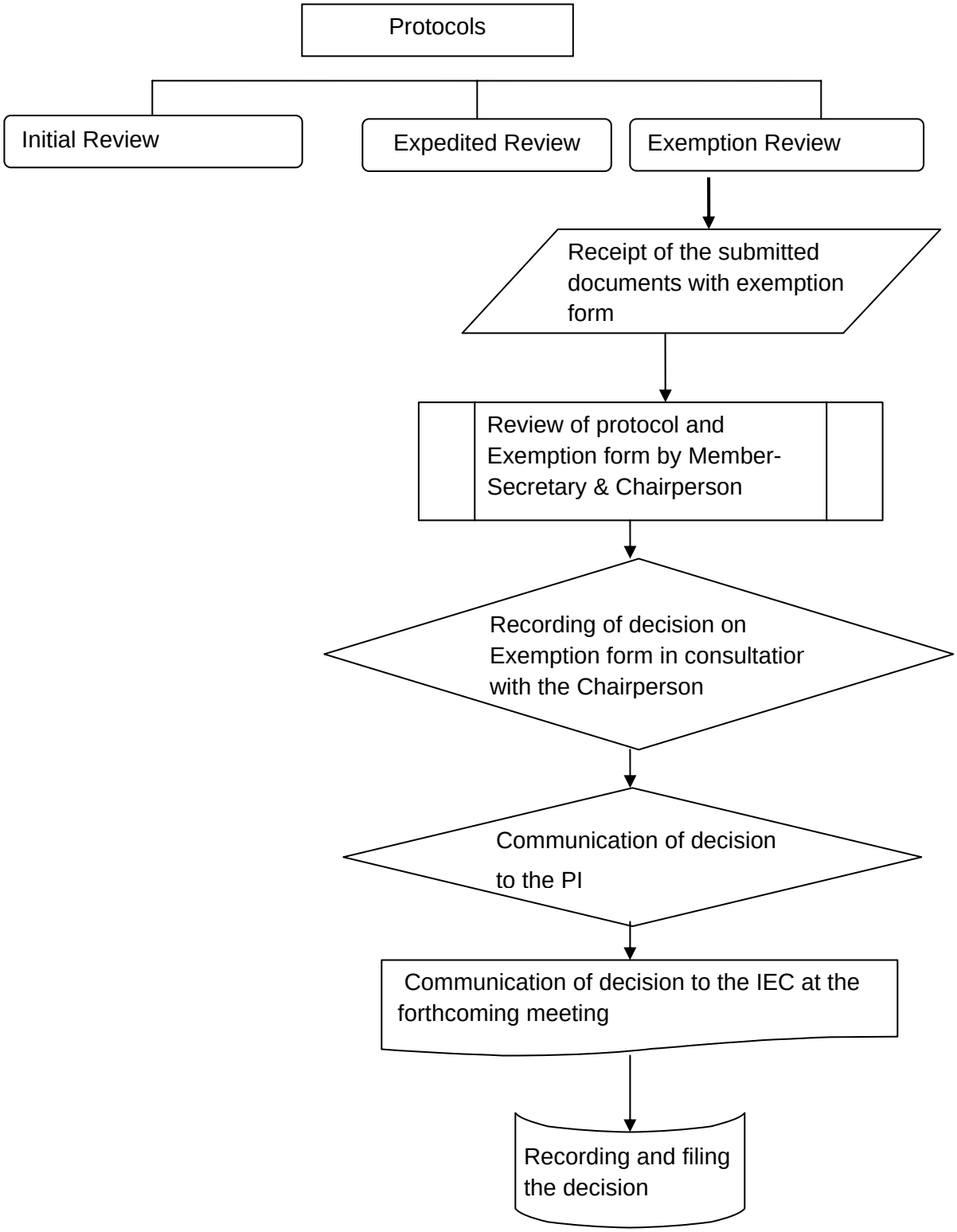
Please check that your application / summary has discussed:

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

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

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

Flow Chart


Protocols
Initial Review
Expedited Review
Exemption Review
Receipt of the submitted documents with exemption form
Review of protocol and Exemption form by Member-Secretary & Chairperson
Recording of decision on Exemption form in consultatior with the Chairperson
Communication of decision to the PI
Communication of decision to the IEC at the forthcoming meeting
Recording and filing the decision

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Agenda Preparation, Meeting Procedures and Recording of Minutes

SOP Code: SOP 05/V4 Date: 01/04/2016 Pages: 139 to 154

5.1 Purpose

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

The day, time, and venue of IEC meetings for committees are specified as follows:

Each IECs meet once in a month. The IEC-I will meet on last Wednesday of every month at 8.30 a.m. (unless otherwise notified). The IEC II will meet on second Friday of every month at 8.30 a.m. (unless otherwise notified). The IEC-III will meet on Third Friday of every month at 9.30a.m (unless otherwise notified)

Meeting room, 3rd Floor, IEC office, Main Hospital Building, TMH, Parel, Mumbai - 400012

Meeting room ACTREC, Paymaster Shodika, 1st Floor

Maximum interval between 2 regular meetings should not be more than 3 months.

5.2 Scope

This SOP applies to procedures to conduct the IEC meeting

5.3 Responsibility

It is the responsibility of the respective Member Secretary, IEC and IEC staff to prepare for the IEC meeting

5.4 Detailed instructions

5.4.1 Before full board IEC meeting

- Prepare the agenda of the IEC meeting
- Proposals submitted for initial review will be allocated to IEC-I/II via randomization. Investigators are advised to submit proposals well in advance to ensure that their projects would be reviewed in either of the two meetings scheduled in a given month.
- No limit is placed on the number of items on the agenda. The number of items is based on available expertise (members and consultants), urgency, order of submission to the IEC and IEC workload.
- Primary and secondary reviewers (lead discussant) will be assigned as necessary taking into account conflicts of interests of members. In addition, the IEC Administrator will check the agenda prior to the meeting to identify IEC members who may have a conflict of interest due to their participation as key personnel on a current or proposed research project. If a conflict of interest is identified, the study is assigned to another member who does not have a conflict of interest. An IEC member who has a conflict of interest with regard to a research project that will be reviewed at a convened IEC meeting must notify the IEC office of the conflict prior to the meeting. Once the IEC office receives notice of recuse, the IEC Member Secretary will seek an alternate IEC member to join the meeting for the review of that project if necessary to meet quorum.
- It is general practice (but not required policy) that IEC Chairs are not assigned primary reviewer (lead discussant) responsibilities except in circumstances when their expertise is the most appropriate.

5.4.2 Distribution of Study/Documents Packages to the IEC Members

- A hard copy of the Agenda, Study Assessment forms would be dispatched to all IEC members and soft copies of protocols under discussion will be sent on email preferably 7 days in advance of the scheduled meeting
- Verify (verbally, by e-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 case of any missing items, intimate the IEC office immediately so that the relevant documents could be made available to the members before the meeting
- It is the responsibility of the IEC member to identify any conflict of interest and notify the IEC office of the conflict prior to the meeting.

5.4.3 Preparation for the meeting

- Reserve the IEC meeting room on the scheduled meeting date and time. The meeting will be held in the meeting room of IEC, unless otherwise specified
- Ensure that the room, equipment (projectors, recorder, etc) and facilities are available in good working conditions
- All original files of studies on the agenda are kept in the meeting room for ready reference before the meeting
- E-copy of SOPs, Schedule Y, ICMR guidelines are kept available for ready reference
- Secretariat informs the scheduled meeting date and time to the Principal Investigators.
- The meeting will be re-scheduled or canceled if it becomes apparent that meeting requirements (quorum, sufficient expertise) will not be met.

5.4.4 Conduct of Meeting

- The members should gather in IEC meeting room on scheduled time. The Chairperson before beginning the discussion will:
  - Ensure that the quorum (SOP 03/V4 section no. 3.0) is fulfilled.
  - Request to declare conflict of interest either verbally or written on any study for discussion.
  - At the beginning of each convened IEC meeting, the IEC Chair or designee will ask the members if anyone has a financial or non-financial conflict of interest with regard to any of the research projects that will be reviewed at the meeting. The IEC Chair or designee will announce that members with a conflict of interest must excuse themselves from deliberation and voting on that research protocol.
  - If an 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. The excused member can answer questions from the IEC, but cannot be present for IEC deliberations and voting.

  - If the unanticipated conflict of interest affects quorum, that particular item will not be discussed and will be deferred to the next scheduled meeting.
  - Research involving vulnerable populations (vulnerable to coercion or undue influence) will be placed on the agenda only when at least one individual (IEC member or independent consultant) who is knowledgeable about or experienced in working with the population will participate in the meeting (or an independent consultant has been obtained). If expertise with a specific vulnerable population is needed but not available from the IEC members, a consultant will be obtained or the item will be scheduled for a later meeting when expertise is available.

- The projector is used for projection of agenda and recorder to record the meeting proceedings.
- The Member Secretary should discuss the minutes of the previous meeting of IEC as well as major issues/policies discussed in minutes of the other IEC and present the agenda for the current meeting
- The IEC may invite investigators to attend the full board meeting related to their studies, and clarify doubts, if any
- The meeting proceeds in the sequential order of the agenda; however the Chairperson may change the order, if the situation so demands
- The Member Secretary will request the lead discussant to discuss the research study. The lead discussant should submit the duly filled study assessment form only in case of initial review and resubmission preferably one day prior to the meeting.
- All the scientific members including the lead discussant should score the intramural projects and submit the scoring sheet at the end of the discussion or at the conclusion of IEC meeting.
- Amendments /Continuing review Application/SAEs/Documents will ordinarily be reviewed by previously assigned lead discussant
- In case the Secretary of the IEC is the Principal Investigator for project under discussion, the IEC member nominated as Acting Member Secretary will perform the function of the Secretary only for that study. The Secretary should declare his conflict of interest and leave the meeting room.
- In case the lead discussant cannot attend the meeting, Secretary, IEC or any other IEC member may brief the IEC about the research study and also discuss the written comments/duly filled study assessment form, if provided by the lead discussant
- During the initial or continuing review of the research, material provided to IEC members will be considered confidential and the board members will assure the confidentiality of the information provided to them
- The Member Secretary, IEC / IEC administrator minutes/records the proceedings of the IEC meeting

5.4.5 Decision Making Process

IEC completes the adequate review of the research studies submitted. The committees will review new studies, amendments, annual /continuing review of ongoing studies, SAE reports,

any other documents and assess final reports of all research activities through a scheduled agenda.

- A IEC member will withdraw from the meeting for the decision procedure concerning the study where conflict of interest exists
- If any IEC member has her/his own proposal for IEC review he/she will not participate in the IEC discussion or vote on that particular project
- Decision may only be taken when sufficient time has been allowed for review and discussion of study in the absence of non-members (e.g., the investigator, representatives of the sponsor, independent consultants) from the meeting, with the exception of IEC staff
- Decisions will only be made at meetings where a quorum (SOP02/V4) is present
- The documents required for a full review of the application should be complete and the relevant elements considered before a decision is made
- Only IEC members who attend the meeting will participate in the decision.
- Decisions will be arrived at through consensus/unanimous or majority opinion amongst the voting members of IEC. The decision-making is thus concerned with the process of deliberating and finalizing a decision. When a consensus is not possible, the IEC will vote.

  Voting Procedure;

  1. This may be in the form of voice vote, show of hands, or by secret ballot, as determined by the Chairperson, IEC.
  2. All members except the Chairperson are entitled to one vote. However, in case of a tie, the Chairperson will will vote to break the tie.

  The concurrence / voting of the members will be recorded in the minutes as - Agreed / Disagreed / Abstained / Recused.

  - Agreed: in favor
  - Disagreed- Against
  - Abstain: Present but did not agree/disagree
  - Recused: Listed under “Members Present” but not present for the discussion and decision on the study .
- Types of decision
  - **Approved**- The study is approved in its present form
  - **Approved subject to modifications**- This is a conditional approval. The revisions are required; these will be reviewed either by the Member Secretary, IEC or in some cases by the respective lead discussant on behalf of the full board. Such revised proposals will not be taken up for the full board review. If revisions are found satisfactory, approval will be granted. In cases of approved subject to modifications (conditional approval) clear suggestions and reasons for same for revision will be specified.
  - **Resubmit**- Extensive revisions are necessary. Principal Investigator has to comply with the changes suggested by IEC and respond to the queries. The revised project will then be reviewed in the next full board meeting.

- **Not approved**- The study is not approved in its current form. A negative decision on an application will be supported by clearly stated reasons. If the investigator wishes to appeal to the decision, he/she may do so by contacting the IEC Secretariat
- **Defer**- The decision cannot be arrived at present and therefore post pone to next meeting. Grounds for this: lack of quorum, lack of expertise etc

- **Noted:** Study documents that are notified to IEC
  An IEC may decide to reverse its positive decision on a study if it receives information that may adversely affect the risk/ benefit ratio/ safety of participants.
- Any advice by the IEC that is non-binding will be appended to the decision.
- The discontinuation of a trial will be recommended if the IEC finds that the goals of the trial have already been achieved midway, unequivocal results are obtained or if the IEC feels the continuation of the trial may potentially harm participants.
- If necessary, the investigator may be invited to present the protocol or offer clarifications in the meeting. Representative of the patient groups or community can be invited during deliberations to offer their viewpoint.
- 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.
- The proceedings of the IEC meetings will be documented and the meeting minutes will be signed by the Member Secretary.

5.4.6 After the IEC meeting

5.4.6.a Preparing the minutes and the decision letters

- The Member Secretary and IRB Administrators will compile the proceedings of IEC meeting in a concise and easy-to-read style and will check spelling, grammar and context of the written minutes
- The minutes of the meeting will be compiled by the IRB Administrators and finalized by the Member Secretary within 15 working days
- The minutes will record whether the decision was unanimous, or whether a vote was taken for the decision. The number of members voting for, against, and abstaining will be recorded. The recusal of the IEC member for conflict of interest is recorded in the IEC meeting minutes.
- The basis for requiring changes in or disapproving research; and a written summary of the discussion of controversial issues and their resolution must be recorded.

5.4.6.b Approval of the minutes and the decision

- The minutes of the IEC meeting will be signed by Member Secretary, IEC (or the Acting Member Secretary as in 5.4.4).
- The minutes of the IEC meeting will be ratified in the subsequent IEC meeting
- The IEC decisions will be communicated to the PIs

5.4.6.c Filing of the minutes of the meeting

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

5.4.7 Communicating Decision

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

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

- TMC Project No. and title of the research proposal reviewed
- The clear identification of the protocol of the proposed research or amendment, date and version number (if applicable)
- The names and specific identification number version numbers/dates of the documents reviewed, including the potential research participant information sheet/material and informed consent form
- The name and title of the Principal Investigator
- The name of the site(s)
- The date and place of the decision
- A clear statement of the decision reached
- Validity of approval will be for the complete duration of the study. This approval is subject to annual review.
- However failure to submit completed status report by the late due date may result in the expiration of approval.
- Location of study conduct
- Number of participants to be accrued
- To submit the continuing review application/annual status report
- To register the study in the Clinical Trials Registry (if applicable)
- Any suggestions by the IEC
- A conditional decision (i.e. approval with recommendations or modifications, suggestions for revision and the procedure, any other requirements by the IEC), such revised proposals will not be taken up for the full board review. The modifications will be re-reviewed and approved by Member Secretary, IEC or primary lead discussant / reviewers, or may be referred for full board review. However, in case of major changes, the revised documents will be discussed in full board meeting. If the IEC approves research with conditions, the date of approval is the date the conditions were determined to be met.
- In the case of a positive decision, the PI is notified of the following requirements through an approval letter (AX2-V4/SOP05/V4)
    - o A statement of the responsibilities of the PI; for example, confirmation of the acceptance of any requirements recommended by the IEC
    - o Submission of annual status reports/progress report(s) decided on case to case basis, usually yearly. Failure to submit completed status report by the late due date

(i.e. 10 months from time of approval or from the last review) may result in withdrawal of approval.

- The need to notify the IEC in the case of amendments to the recruitment material like the potential research participant information, or the informed consent form
- The need to report serious and unexpected adverse events related to the conduct of the study
- The need to report unforeseen circumstances, the termination of the study, or significant decisions by other IECs or DSMBs
- The information the IEC expects to receive in order to perform ongoing review
- The final summary or final report
- The schedule/plan of ongoing review by the DSMB of sponsored trials

- An IEC may decide to reverse its positive decision on a study if it receives information that may adversely affect the risk/ benefit ratio
- Any advice by the IEC that is non-binding will be appended to the decision
- In the case of a negative decision, the reasons should be clearly stated in the communication to the PI
- The PI will also be notified of the cap for accrual of number of participants
- All decision and approval letters will be signed by the Member Secretary, IEC or the nominated Secretary for that meeting. In case Member Secretary IEC is Principal Investigator, the decision letters will be signed by Acting Member Secretary / Chairperson / Co-Chairperson IEC.
- The decisions letters will be communicated to the Principal Investigator and wherever required to the organizational offices and officials and other concerned authorities.
- Member Secretary, IEC/Chairperson IEC, will sign and date the approval certificate in the original research protocol.
- The letter will mention whether the decision has been arrived at by consensus unanimous or majority opinion amongst the voting members of IEC, or by voting.
- If the decision has been arrived by voting, the letter will state the number of votes for and against approval of the project.

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

- If an investigator disagrees with the IEC decision to disapprove or terminate a study, the Investigator may submit a written appeal of the decision to disapprove of the IEC decision within 21 working days of being notified of the decision. The appeal should address the specific concerns of the IEC and the IEC basis for disapproval.
- The appeal will be reviewed by the full board. The Investigator may request to be in attendance at or be invited to the convened meeting to provide clarification or additional information to the IEC.
- The IEC may decide to accept or deny the appeal (Decision making process-Voting). The Principal Investigator will be notified in writing of the decision.

- If the appeal to the decision on disapproving a study is accepted, the Investigator is invited to submit a new study application to the IEC for review and approval, according to the conditions set forth by the IEC in accepting the appeal.
- If the appeal is denied, the IEC decision is final and the study may not be approved or resumed.

References

1. Schedule Y D&C Act 1940
2. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, (Geneva 2000)
3. ICMR guidelines 2006
4. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996

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 IEC members required to act on any proposal presented to the committee for action.

AX1 –V4/SOP05/V4

Agenda/Minutes format

I) Minutes-IEC & DSMSC

II) SAEs

III) Deviations

IV) Projects for Initial Review

V) Resubmission
Amendments
a)Protocol b) ICF c)IB d) CRF e) Any other

IV) Status Reports
V) Letters

AX2 –V4/SOP05/V4

Approval Letter Format

FORMAT FOR APPROVAL LETTER OF IEC
To,
Dr._____
Principal Investigator,
Tata Memorial Hospital.

Ref: Project No.

Dear Dr.

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

The following documents were reviewed and approved:

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

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

Name of member/Position on IEC/Affiliation/Gender/Expertise
_____ Chairman of the Institutional Ethics Committee
_____ Member secretary of the Institutional Ethics Committee
_____ Name of each member with designation

The study is approved in its present form till (date) _____. The Principal Investigator should submit continuing review application/annual status report failing which the IEC shall revoke the IEC approval. In order ensure that there is no lapse in the IEC approval period, it is mandatory to submit study status report 3 months prior to lapse of study validity.

The study should be initiated only after -

- **Registration of the study with Clinical Trials Registry India (CTRI) (if applicable).**
- **Submission of Finalized Clinical Trial Agreement**
- **DCGI approval to IEC (if applicable).**

Following points must be noted:

1. **IEC has approved recruitment/review of ____ participants on this study.**
2. **IEC has approved the conduct of the study at Tata Memorial Centre / Tata Memorial Hospital**
3. Principal Investigator and study team should be GCP trained
4. PI and other investigators should notify initiation of the study. Principal Investigator should intimate the IEC after accrual of first 10 participants in the study or after 6 months of initiation of study whichever is earlier.
5. PI and other investigators should co-operate fully with data and safety monitoring Sub-committee (DSMSC), who will monitor the study from time to time.
6. The decision was arrived at through consensus/unanimous or majority opinion amongst the voting members of IEC. Member(s) of the committee who is/are listed as investigator(s) on a research proposal opted out from all deliberations on the proposal and did not participate in decision making. Neither PI nor any of proposed study team members participated during the decision making of the IEC.
7. At the time of PI's retirement/intention to leave the institute, study responsibility should be transferred to colleague after obtaining clearance from HOD and/or convener of the PI's DMG and IEC. Status report, including accounts details should be submitted to HOD and extramural sponsors.
8. The IEC functions in accordance with its SOP and is compliant with the Schedule Y (Drugs & Cosmetic Act 1940), ICMR guidelines and Indian/ICH GCP
9. In the events of any protocol amendments, IEC must be informed and the amendments should be highlighted in clear terms as follows:
    a) The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)

b) Alteration in the budgetary status should be clearly indicated and the revised budget form should be submitted

c) If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Institutional Ethics Committee for approval.

d) If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.

e) If there are any amendments in the study design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IEC, only then can they be implemented.

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

10. Any Serious Adverse Events (SAEs) occurring on the study should be reported to IEC
11. Any deviation/violation/waiver in the protocol must be informed to the IEC.
12. Principal Investigator should conduct the study in accordance to the IEC approved protocol
13. Principal Investigator should comply with regulations and guidelines as applicable

Thanking You,

Yours Sincerely,

Member Secretary,

IEC.

AX3 –V4/SOP05/V4

Letter Format for project / Amendments

Conditional approval.

Dr…
Principal Investigator,
TMH/TMC.

Ref: Project No. Title

Dear Dr…

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

The following members of the IEC were present:

IEC comments were as follows-

a.

b.

c.

Status-

i. **Approved**
ii. **Approved subject to modifications/Resubmit. Kindly comply with the above suggestions of the IEC and submit the two copies of revised proposal or documents within six months for review. If you fail to submit within six months, this project will be closed by IEC and you will have to submit a new project.**

This decision was taken by consensus.

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

Thanking you,
Yours sincerely,

Member Secretary, IEC

IEC, TMC

AX4 –V4/SOP05/V4

Format for Documents

Date

Dr. ,
Principal Investigator,
TMC

Ref: Project No.____ Title "_____"

Dear Dr.

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

The following members of the IEC were present:

Status-

i. **Approved.**
ii. **Approved with modifications/Resubmit. Kindly comply with the above suggestions of the IEC and submit the two copies of revised proposal or documents within six months for review. If you fail to submit within six months, this project will be closed by IEC and you will have to submit a new project.**
iii. **Noted.**
iv. **Not Approved. If an investigator disagrees with the IEC decision, the Investigator may submit a written appeal of the decision to disapprove of the IEC decision within 21 working days of being notified of the decision. The appeal should address the specific concerns of the IEC and the IEC basis for disapproval.**

    The appeal will be reviewed by the full board. The Investigator may request to be in attendance at or be invited to the convened meeting to provide clarification or additional information to the IEC.

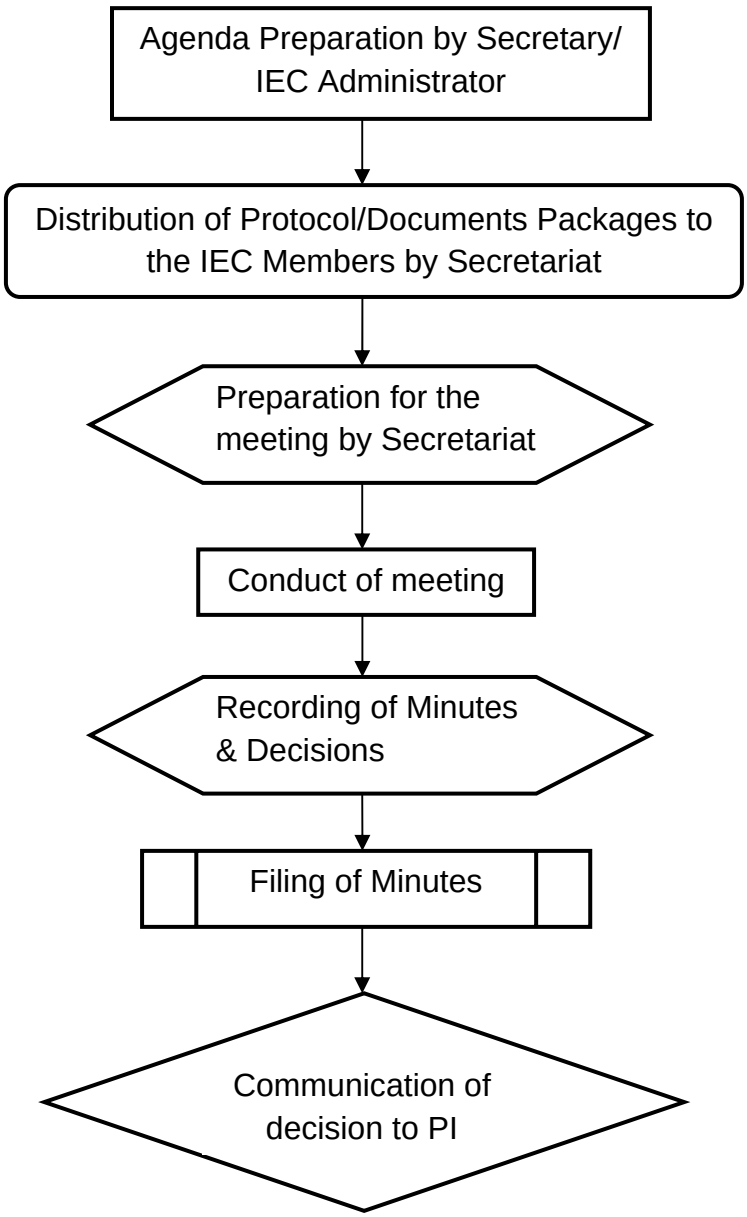
This decision was taken by consensus.

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

Thanking you,
Yours truly,

Member-Secretary,
IEC

Flow Chart


Agenda Preparation by Secretary/ IEC Administrator
Distribution of Protocol/Documents Packages to the IEC Members by Secretariat
Preparation for the meeting by Secretariat
Conduct of meeting
Recording of Minutes & Decisions
Filing of Minutes
Communication of decision to PI

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Review of Amended protocol / Protocol related documents

SOP Code: SOP 06/V4 Date: 01/04/2016 Pages: 155 to 161

6.1 Purpose

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

6.2 Scope

This SOP applies to amended study protocols/ documents and letters that are submitted for IEC approval. Amendments made to protocols or any other amendments related to the study may not be implemented until reviewed and approved by the IEC.

6.3 Responsibility

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

Receipt of the Amendment Package

- The amendment /documents along with the appropriate soft copy forwarded by the PI is received by the secretariat. The amendment /documents along with the covering letter should be accompanied by Amendment Reporting Form (AX2-SOP06/V4)
- The secretariat will confirm that the: changes or modifications in the amended version are underlined or color highlighted along with detailed summary of changes
- The Secretariat will check for completeness of the submission and inform the Principal Investigator telephonically to submit the required documents at the earliest, if any of the documents are missing/ incomplete.
- The secretariat of the IEC should follow the procedures as in SOP03/V4 (Procedures for Management of protocol submission)

The Member Secretary, IEC, classifies the amendments into minor or major and tables the major amendments on the agenda of the subsequent scheduled meeting (for Minor amendments refer to 6.4.3). The amendments and other documents which need full board review are processed as per the SOP 04a/V4

6.4 **Review amended protocols/documents/letters:** Review as per Section 4.3 SOP 04a/V4

6.4.1 Decision

- If the IEC approves the amendments, the decision is communicated to the PI.
- If the IEC does not approve the amendments, the secretary should immediately notify the investigator in writing of the decision and the reason for not approving the amendment.
- If the IEC recommends or suggests modifications to any of the documents, or the amendments, the secretariat sends a written communication to the investigator about

the specific changes asking him or her to make the necessary changes and resubmit the documents to IEC.

6.4.2 Storage of Documents:

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

6.4.3 Minor amendments and notifications:

Minor amendments (those that do not increase the risk or decrease the potential benefit to subjects) and minor changes in previously approved research during the period covered by the original approval: Where the research is permanently closed to the enrolment of new subjects; all subjects have completed all research-related interventions may be reviewed in the expedited review subcommittee meeting (Refer SOP No. 04b/V4.).

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

This may include but may not restrict to:

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

References

1. ICMR guidelines 2006
2. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research (Geneva 2000)
3. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996
4. Code of Federal Regulation (CFR), 21 §56.110, The United States of America, 1998

Glossary

Amendment: Any change in protocol and documents from that of previously IEC approved protocol/document.

IEC, TMC

AX1-V4/SOP06/V4

Amendment/Document Amendment Approval letter

Format for Approval for documents

Date

Dr. ,
Principal Investigator,
TMH

Ref: Project No. Title

Dear Dr.

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

Status: Approved / Approved with modifications / Resubmit / Not approved / Deferred

This decision was taken by consensus.

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

Thanking you,

Yours truly,

Member-Secretary,
IEC

AX2-V4/SOP06/V4

IEC Secretariat

Amendment Reporting Form

(Kindly tick in the boxes provided)

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

• Completed treatment : _____ • Patients on Follow-up: _____ • Patients lost to follow up: _____ • Any other: _____ • Any Impaired participants • . None_____ • Physically _____ • Cognitively _____ • Both _____	

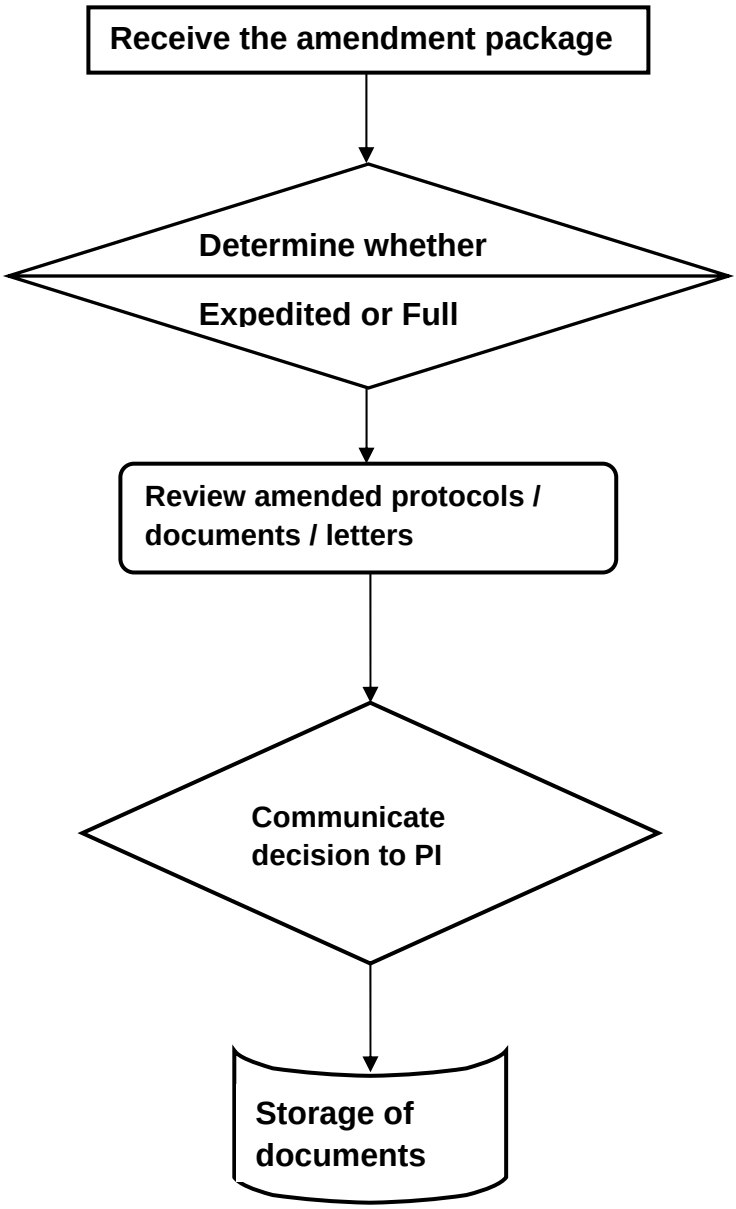
(**Important note:** Please submit summary list of changes should include document/Revised version no Section, page no, change(s) and risk/benefit or justification.

Table 1: Summary List of Changes

Name of document	Revised version/Date	Section	Page No	Change(s)	Risk/Benefit Assessment /Justification

Signature of the Principal Investigator & Date:

Flow Chart


Receive the amendment package
Determine whether
Expedited or Full
Review amended protocols / documents / letters
Communicate decision to PI
Storage of documents

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Continuing Review of Study Protocols

SOP Code: SOP 07/ V4 Date: 01/04/2016 Pages: 162 to 182

7.1 Purpose

The purpose of continuing 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.

7.2 Scope

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

7.3 Responsibility

It is the responsibility of the IEC secretariat to send reminders to PIs regarding the submission of Continuing Review Application/Annual Status Report.

All the approved studies will be reviewed at least annually. IEC is responsible for determining the date of continuing review if the project will be reviewed more frequently in the year including specific criteria used to make these determinations (e.g., an IEC may set a shorter approval period for high-risk protocols or protocols with a high risk: potential benefit ratio). This decision is taken during the IEC meeting wherein the project is finally approved.

IEC is primarily responsible for reviewing the study progress, the occurrence of unexpected events or problems, and the rate of accrual of participants. The protocol, informed consent documents and assent documents are examined to ensure that the information remains accurate. The IEC has delegated this responsibility of initial detailed review of Continuing Review Application to DSMSC.

The IEC has the same options for decision making on a continuing review application as for an initial review application. The decision is made as, approved to continue the study; approved with modifications; or not approved Refer SOP05/V4.

7.4 Detailed Instructions

7.4.1 Determine the date of continuing review

- The secretariat will look through the master file of projects approved by the IEC for the due date of continuing reviews.
- The Secretariat should receive the continuing review application well in advance i.e. 10 months after IEC final approval and atleast annually.

7.4.2 Notify the Principal Investigator or the study team

Reminders in writing/email are sent from IEC secretariat to the Principal Investigators for submission of /Continuing review applications for projects Principal Investigator should submit three hard copies of the report (1+2) and a soft copy.

7.4.3 Manage continuing review application upon receipt

- The Secretariat will receive the Continuing Review Application submitted by the Principal Investigator for each approved study.
- Upon receipt of the Continuing Review Application, the Secretariat of the IEC will perform the following (as per instructions in SOP03/V4)
- However IEC may verify from sources other than the investigators to ensure that no material changes had occurred since previous IEC review by conducting monitoring of the study. The projects for which this may be done includes complex projects involving unusual levels or types of risk to subjects; projects conducted by investigators who previously have failed to comply with the regulatory/IEC requirements, projects where concern about possible material changes occurring without IEC approval have been raised based upon information provided in previous continuing review reports or from other sources.

7.4.4 Verify the contents of the package

- The Secretariat will check for duly complete and signed application by Principal Investigator.
- An original copy with 2 photo copies and a soft copy will be submitted.

7.4.5 Review of Continuing Review Application

- If IEC determines that a project needs verification from sources other than the investigators that no material changes have occurred since previous IEC review, including specific criteria used to make these determinations (e.g., such criteria could include some or all of the following: (a) randomly selected projects; (b) complex projects involving unusual levels or types of risk to subjects; (c) projects conducted by investigators who previously have failed to comply with the regulatory/IEC requirements ; and (d) projects where concern about possible material changes occurring without IEC approval have been raised based upon information provided in continuing review reports or from other sources.)
- The DSMSC Secretary will review the Continuing review Application and will record his/her comments on the application and the same will be forwarded to the IEC Secretary
- In case any clarifications or queries are raised by the Secretary DSMSC the same will be intimated to PI and reply will be awaited. The IEC Secretary will decide whether to discuss the application along with the comments of the DSMSC and Principal Investigator’s response in the next full board meeting or expedited review meeting.

7.4.6 Prepare meeting agenda

The Secretariat 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 IEC

7.4.7 Review Process

The IEC Chairperson/ Member Secretary/ members will use the Continuing Review Application Form (AX1-V4/SOP07/V4) to guide the review and deliberation process. The IEC members could arrive at any one of the following decisions at the IEC meeting:

1. Approval to continue the study;; or not approved
2. Approved with modifications- - Studies for which modifications have been suggested by the IEC may not proceed until the conditions set by the IEC have been met. Studies should be amended and submitted to the IEC within one month for re-review
3. Not approved

The decision will also include any significant findings that have arisen during review process and this will be communicated to Principal Investigator. It is the responsibility of Principal Investigator to provide this information to the participants and once done submit the report to IEC.

- 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.
- The IEC Secretariat will maintain minutes of the meeting relevant to the continuing review as part of the official record of the review process.
- Continuing review of the study may not be conducted through an expedited review procedure, unless

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

7.4.8 Store original documents

The IEC secretariat will file the continuing review in master file of the research study.

7.4.9 Communicate the IEC decision to the Principal Investigator

The Secretariat will notify the Principal Investigator of the decision. If IEC 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 subject recruitment or enrollment is suspended, however incase of safety concerns the project is completely suspended. Principal Investigator will be communicated about the decision within 15 working days after the minutes are finalized.

7.4.10 Lapses in IEC Approval

Investigators must plan ahead to meet required continuing review dates. If an investigator fails to submit Continuing Review Application to the IEC or the IEC does not approve continuation of the research, the research must stop. All of the following research procedures must stop:

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

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

References

1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, (Geneva 2000)
2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996

AX1-V4/SOP 07/V4
Form A
Continuing Review Application
SECTION A

TMC Study No:

CTRI No (if applicable):

Date of Registration:

Protocol title:

Principal Investigator:

Phone No:

Email Id:

Institute:

Source of funding: Please tick
- ☐ Intramural
- ☐ Extramural – Please specify_____
- ☐ Pharma – Please specify_____
- ☐ Others- Please specify_____
- ☐ Not applicable

Account No (If Applicable):

Date of IEC approval:

Approval valid upto:

Period of report : _____/___/_____ to _____/__/_____

Start Date of study:

Date of accrual of first subject/sample:

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

Duration of study(overall) :

Study was initially reviewed by expedited review (Please tick) – ☐ Yes ☐ No

Is the study expected to extend beyond the projected duration: ☐ Yes ☐ No

If Yes- provide reasons for not being able to complete the work in stipulated time

Are you applying for extension for the same: ☐ Yes ☐ No

If yes- period of extension requested?

Section B: Mandatory for Interventional Research

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

1) No of study arms (If Applicable):

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

☐ Ongoing (Kindly select one option from below)

____Active Enrollment ongoing

____Accrual completed /Follow-up ongoing

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

_____

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

☐ Yes ☐ No ☐ NA

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

☐ Yes ☐ No ☐ NA

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

☐ Yes ☐ No ☐ NA

3) Provide the date of last status review report submitted to IEC for this project

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

4) Summary of Protocol participants: (If the study does not deal with patient accrual, please provide a summary of the progress on the study so far)

- Target accrual of trial (entire study) including healthy volunteers, patients and biomedical samples/blocks) _____
- Total patients/samples to be recruited at TMC (IEC ceiling)_____
- Screened: _____
- Screen failures: _____
- Total participants/samples accrued since protocol began _____
- New participants accrued since last review _____

- Date of accrual of last participant: _____
- Active on intervention- (exclude subjects who have completed intervention)
- No of participants who have completed intervention and are on follow-up:_____
- Patients lost to follow up: _____(includes subjects who have completed intervention)
- Consent Withdrawn: _____Reason and state at which phase of the study – before /during/after completion of intervention (Specify TMC case number/Sub Id)
- Withdrawn by PI: _____Reason and state at which phase of the study – before /during/after completion of intervention(Specify TMC case number/Sub Id)
- Deaths: _____ State at which phase of the study – before /during/after completion of intervention (Specify TMC case number/Sub Id)
- Any other: _____
- Any Impaired participants
  - None_____
  - Physically _____
  - Cognitively _____
  - Both _____

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

☐ Yes ☐ No ☐ NA

If 'Yes', attach in format below

TMC Case No/Sub Id	SAE Event	Report type	Arm	Date submitted to DSMSC

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

☐ Yes ☐ No ☐ NA

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

☐ Yes ☐ No ☐ NA

If 'Yes', attach in format below

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

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

☐ Yes ☐ No ☐ NA

If Yes please provide a summary-

8) Were there any Complaints about the research?

☐ Yes ☐ No

If Yes please provide a summary-

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

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

☐ Yes ☐ No

If 'YES', please provide in format below

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

10) Were any changes initiated in approved research without IEC approval to eliminate apparent immediate hazards to the participants:

☐ Yes ☐ No ☐ NA

If yes please provide in format below

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

11) Have any Informed Consent documents been amended since the last status report?

☐ Yes ☐ No ☐ NA

If 'YES', fill in format below

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

12) If the amendments were approved by IEC then please state whether all the patients were reconsented on the amended ICF on the next scheduled visit

☐ Yes ☐ No ☐ NA

Amendment No. Version Dated	Date of submission	Date of Approval

13) Is the recruitment on schedule?

☐ Yes ☐ No ☐ NA

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

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

☐ Yes ☐ No ☐ NA

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

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

☐ Yes ☐ No

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

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

☐ Yes ☐ No

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

17) 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 DSMSC, TMC)

18) When was study last monitored?

Date of monitoring _____

Monitored by _____

Number of subjects monitored _____

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

☐ Yes ☐ No ☐ NA

(If 'YES', submit as an attachment)

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

☐ Yes ☐ No ☐ NA

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

21) Is the report on interim data analysis available?

☐ Yes ☐ No

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

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

☐ Yes ☐ No

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

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

☐ Yes ☐ No

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

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

☐ Yes ☐ No

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

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

Total budget proposed for the project _____

Total budget sanctioned for the project _____

Total budget utilized for the project _____

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

☐ Yes ☐ No

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

26) Any other information:

SIGNATURES:

Principal Investigator:

Date

AX1-V4/SOP 07/V4
Form B

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

TMC Project No:
PROTOCOL TITLE:
Principal Investigator: **Phone no:** **Email Id:** **Institute**: ACTREC/TMH **Date of TMC IEC approval :_____ Approval valid upto: _____** **Start Date of study:** **Duration of study:** **Period of Report :_____/_____/_____ to _____/_____/_____** **Funding Source :** **Account no :**

1) Project Status

□ Ongoing

- o Active accrual on going
- o Accrual completed /Follow-up

□ Not started/Not initiated

If 'Not started' state reasons

_____

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

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

☐ Yes ☐ No

If '**YES**', Were these Protocol Amendments approved by TMC- IEC?

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

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

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

☐ Yes ☐ No ☐ NA

If '**Yes**', were these informed consent document amendments approved by TMC-ACTREC IEC?

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

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

5) Summary of Protocol participants:

- o Total patients/samples to be recruited at TMC (IEC ceiling)_____
- o Total participants accrued / samples collected since protocol began_____

- o New participants accrued /samples collected since last review _____
- o Screened: _____
- o Screen failures: _____
- o Date of accrual of last participant / Samples: _____
- o Number of active participants/Sample (analysis going on) _____
- o Number of samples analyzed: ___
- o Any other: _____

6) Is the recruitment on schedule?

☐ Yes ☐ No

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

7) Have there been any changes in the participant population, recruitment or selection criteria since the last status report was submitted to TMC- IEC?

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

□ No

□ NA

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

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

□ Yes (Kindly attach a sheet stating reasons)

□ No

□ NA

9) Have any participating investigators been added or deleted since the last status report was submitted to TMC- IEC?

□ Yes (Kindly attach a sheet with details)

□ No

□ NA

10) Have any new collaborating sites (institutions) been added or deleted since the last status report was submitted to TMC- IEC?

- Yes (Kindly attach a sheet with details)
- No
- NA

11) Were there any protocol deviations/violations in the study?

- Yes (Kindly attach a sheet with details)
- No
- NA

12) Is interim data analysis report available?

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

13). Has there been any presentation/publication related to the data generated in this study?

- □ Yes (Kindly attach a sheet enclosing the details)
- □ No

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

☐ Yes ☐ No

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

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

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

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

If Yes When was study last monitored?

Date of monitoring _____

Monitored by _____

Number of subjects monitored _____

16) Is the DMC report available?

- o YES (If '**YES**', submit as an attachment)
- o NO
- o NA

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

- o YES (If, '**YES**', please attach a copy of their comments)
- o NO
- o NA

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

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

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

c) Details of New Leads Obtained, if any:

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

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

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

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

Total budget proposed for the project: Rs. _____

Total budget sanctioned for the project: Rs. _____

Total amount utilized for the Project: Rs _____

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

Funding Source: _____

Amount : Rs. _____

SIGNATURES:

Principal Investigator:
Date:

AX2-V3/SOP 07/V3

Reminder letter to investigator

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

The above referenced project was approved by the IEC on XXXXXXX and is due for continuing annual review by the IEC.

Kindly submit the continuing review application on or before_____. In case the projects have been completed / terminated, kindly complete the appropriate forms and submit to DSMSC on or before (date).

Thanking you for your co-operation,

Yours truly,

Signature with date
Secretary, DSMSC

AX3-V3/SOP 07/V3

Continuing Review Letter

Date
Principal Investigator,
TMC

Ref: Project No./ Title

Dear Dr.

The continuing review application for the above referenced project was and discussed during the Institutional Ethics Committee (IEC) meeting held on date (place) (time)

The following members of the Institutional Ethics Committee were present:

IEC comments were as follows:

Status: IEC approved the continuation of the study, Approved with modifications/Not approved

This decision was taken by consensus.

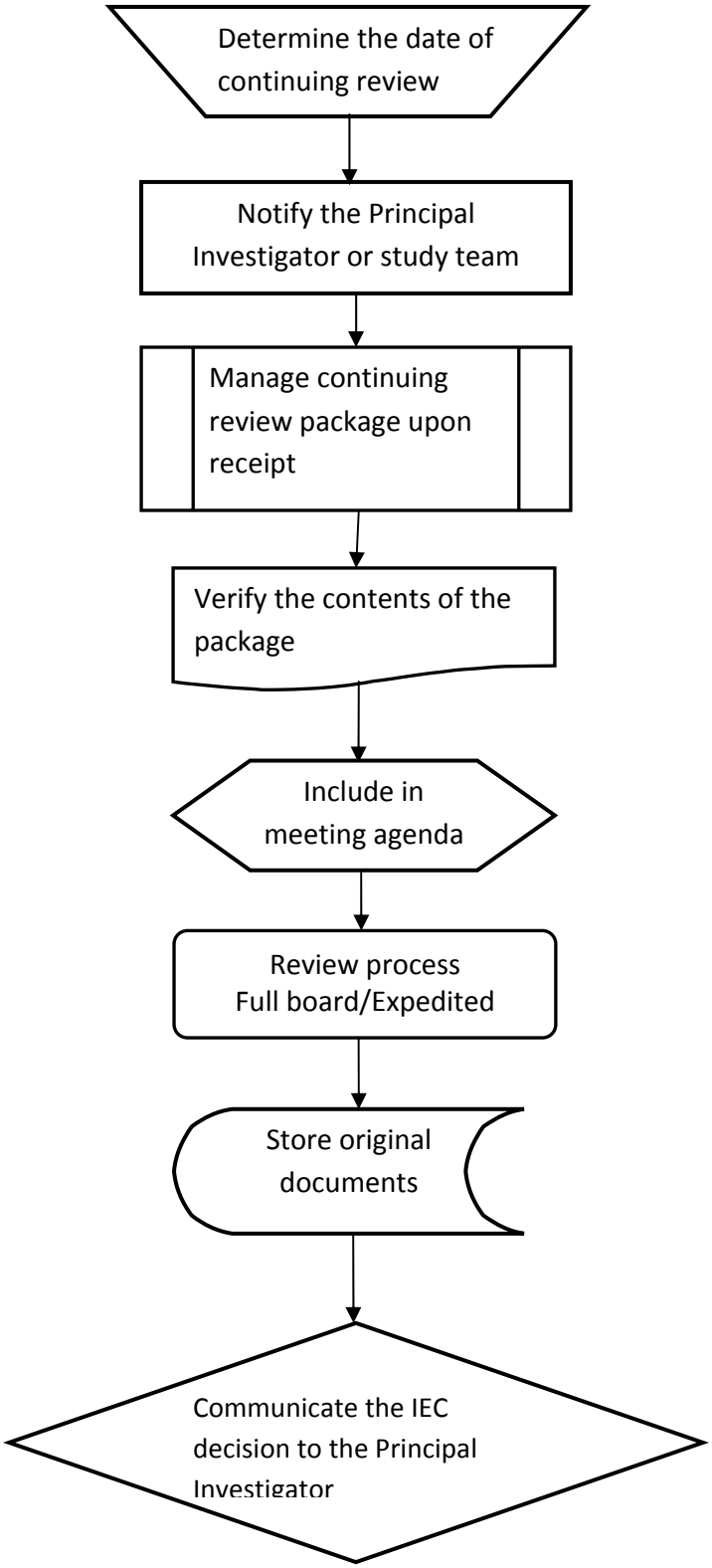
Neither Principal Investigator nor any of study team members participated during the decision making of the IEC.

Thanking you,

Yours faithfully,

Member-Secretary,
Institutional Ethics Committee

Flow Chart


Determine the date of continuing review
Notify the Principal Investigator or study team
Manage continuing review package upon receipt
Verify the contents of the package
Include in meeting agenda
Review process Full board/Expedited
Store original documents
Communicate the IEC decision to the Principal Investigator

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: **Review of Protocol Deviation / Violation / Waiver / Non-Compliance**

SOP Code: SOP 08/V4 Date: 01/04/2016 Pages: 183 to 194

8.1 Purpose

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

- Follow the procedures written in the approved protocol;
- Comply with national / international guidelines / institutional guidelines or rules or procedures mandated by the IEC for the conduct of human research
- Respond to the IEC requests regarding statutory, ethical, scientific or administrative matters.

8.2 Scope

This SOP applies to all IEC approved research studies involving human participants/data.

8.3 Responsibility

1. The IEC secretariat is responsible for receiving deviations /violations as per (AX1–V4/SOP08/V4) and waiver reports submitted by the Principal Investigator/others and placing it on the agenda of the meeting. The IEC secretariat is responsible for receiving noncompliance reports and taking the appropriate action. Reporting of deviation/ /violation in any other reporting format will not be accepted.
2. IEC members should review and take action on such reports.

8.4 Detailed instruction

a) Protocol violation/s

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

This usually

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

Examples:

- Participant being consented after the screening procedures are completed
- Participant being consented after the first dose of the drug has been given

b) Protocol deviation/s

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

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

Examples:

- Wrong version of the informed consent form being used.
- Sample collections at different time points than specified in the protocol.
- Participant following up on days not specified in the protocol.

c) Protocol Waiver

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

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

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

Examples of waivers are:

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

d) Non-compliance

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

i. Nonserious and Noncontinuing noncompliance involves isolated incidents, e.g. an unintentional mistake, an oversight, or a misunderstanding. The issue is not serious or continuing in nature.

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

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

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

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

8.4.1.a The IEC/DSMSC members performing monitoring of the project at trial site can detect a protocol deviation/non-compliance/violation

- If the project is not conducted as per protocol/ national/international regulations;
- While scrutinizing annual/ periodic reports/ SAE reports
- Based on any other communication received from the Investigator/ trial site/ sponsor/ study monitor/ CRO.

Additionally, information regarding noncompliance in studies that enroll human participants may come to the attention of the IEC through:

- Continuing reviews
- For cause monitoring
- Audit reports
- SAE reports
- DSMSC minutes
- Any other sources.

8.4.1.b The Secretariat can detect a protocol deviation/non-compliance/ violation from failure to:

- Comply with statutory requirements;
- Respond to requests from the IEC within a reasonable time limit;
- Respond to communication made by the IEC,

8.4.1.c The PI himself/herself should forward protocol deviation / violation / waiver reports to the IEC preferably within 10 working days of the PI's knowledge of the deviation/violation.

Investigators, research staff, or other individuals affiliated with TMC are required to report all suspected noncompliance to the IEC

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

8.4.1.e Any report/ communication brought to the notice of member secretary /Chairperson of IEC

8.4.1.f Communication received from the Director, TMC informing IEC about an alleged protocol violation/ non-compliance/ protocol deviation

8.4.2 Noting protocol deviation / violation / waiver / non-compliance by the Secretariat

- The IEC members who have performed monitoring of a particular trial and detect protocol deviations/non-compliance/violations will inform the Secretariat in writing.
- Whenever a protocol deviation / violation / non-compliance have been observed, the Secretariat will ensure that the issues as well as the details of non-compliance involving research investigators are included in the IEC meeting agenda.

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

8.4.3 Procedures for Handling Suspected Noncompliance

1. Upon receipt of an allegation, Member Secretary IEC in consultation with Chairperson, IEC will review the allegation and determine if it is valid. If the allegation is valid, then will undertake an inquiry. Chairperson, IEC may temporarily suspend the study, pending review in IEC.
2. Member Secretary IEC in consultation with Chairperson, IEC undertakes an inquiry of the allegations within 7 week days of the suspected noncompliance. The purpose of the inquiry is fact-finding, and may involve examination of study records and discussion with the research team, other personnel, research participants, witnesses, the complainant (if not anonymous), and others as appropriate.
3. Qualified IEC staff documents and compiles the information and Member Secretary IEC presents the findings to the IEC.
4. IEC determines whether the allegation is (1) non-serious and non-continuing or (2) serious or continuing noncompliance that warrants investigation by the IEC or (3) has no basis in fact.
5. IEC determines if immediate suspension of study procedures and/or study enrollment is required for the project in question, as well as for other projects under the same investigator. This initial decision is based on preliminary review of available information, communication with the principal investigator(s) involved in alleged noncompliance activities, and the seriousness of the allegations.
6. The principal investigator(s) involved in the allegations and associated research staff personnel, appropriate Department Head(s), and Institutional Head are notified in writing about any suspension.
7. National regulatory agencies are notified, if applicable.
8. In case of externally funded studies, notice is sent to the sponsor and to the concerned regulatory bodies.
9. If a study is suspended, further fact-finding and a timely review by a convened IEC determines the length of any suspension.

If the noncompliance activity is determined to be non-serious and non-continuing:

1. The issue is resolved by a subcommittee of IEC (comprising of member Secretary, IEC, DSMSC Secretary, one IEC member). Principal investigator(s), and concerned staff may be called for the discussion.
2. Member Secretary IEC documents the outcome of all communications in writing. This report includes any sanctions or corrective actions required on the part of the investigator and the timelines for resolution.
3. A copy of this report is sent to the principal investigator(s) involved in the noncompliance activities, associated research staff and others as deemed appropriate within 21working days.
4. A written response from the principal investigator acknowledging the report and describing corrective actions is required within 7 working days from the date of the corrective report.
5. The complainant will be provided information as deemed appropriate by the IEC Chair.
6. All communication is documented in a restricted IEC confidential file.
7. If during the inquiry of a non-serious or non-continuing noncompliance is determined that the noncompliance is serious or continuing, the matter will be referred to the full board IEC for their investigation.

If the noncompliance activity is determined to be a serious or continuing, the matter is forwarded to the IEC Secretariat for their investigation:

IEC Chair(s) and member Secretary IEC, readdresses the possible need for suspension of study procedures and/or study enrollment for the project in question, as well as for other projects under the same investigator, pending a timely review by a convened Institutional Review Board.

If research activity suspension is warranted:

- The principal investigator(s) involved in the noncompliance activities and associated research staff, Department Head(s) and Institutional Officials are notified in writing about any suspension.
- Concerned National regulatory agencies are notified, if applicable
- In case of national externally funded studies, notice is sent to the sponsor and to the concerned regulatory bodies.

The issue is presented to the next appropriate convened IEC. For urgent issues, member Secretary IEC may convene an emergency meeting of the IEC.

- The IEC will receive a copy of the most recently approved consent form, any necessary sections from the IEC approved protocol and all documented communications and discussions concerning the noncompliance from the inquiry phase. The complete IEC protocol will be available at the IEC meeting.
- The Principal Investigator will be invited to attend the meeting and provided an opportunity to respond to the allegation(s).
- The IEC may also meet with the complainant (if no anonymous) and others as needed.

- After the IEC has completed the investigation, the IEC will determine the appropriate course of actions, such as:
  - Modification of the research protocol;
  - Modification of the informed consent form or process;
  - Additional information provided to past participants;
  - Notification of current participants (required when such information may related to participants' willingness to continue to take part in the research);
  - Requirement that the current participants re-consent to participation;
  - Modification of the continuing review schedule;
  - Monitoring of research;
  - Monitoring of the consent process;
  - Suspension of the research;
  - Termination of the research;
  - Obtaining more information pending a final decision;
  - Referral to other organizational entities (e.g., legal counsel, risk management, institutional official, etc.);
  - Requirement of additional training or re-training;
  - Other appropriate actions

- A copy of IEC report is sent to the principal investigator(s) involved in the noncompliance activities, associated research staff and others as deemed appropriate within 21 working days.

8.4.4 Board discussion, Decision and Action

- If a protocol deviation / non-compliance / violation is detected by an IEC member during a monitoring visit, he/she will present the monitoring report which will be discussed at the full board meeting.
- If detected by the Secretariat/forwarded by Principal Investigator, the Secretary will present the protocol deviation / non-compliance / violation/waiver information.
- Each allegation is taken seriously and reviewed in a consistent, prompt, and professional manner. Additionally, care is taken to maintain confidentiality.
- The Chairperson/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 will be conducted

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

- Determine that no further action is required, or take other actions as appropriate.

- Inform the PI that the IEC has noted the violation/ noncompliance/ deviation, and instruct the PI to ensure that deviations/noncompliance/ violations do not occur in future and to follow IEC recommendations.
- Enlist measures that the PI would undertake to ensure that such deviations / noncompliance / violations do not occur in future.
- Observe the research or consent process,(depending on the nature and frequency of the deviation)
- Suggest modifications to the protocol
- Alter the interval for submission of the continuing review/annual project status
- Require additional training of the investigator and study team
- Reprimand the PI.
- Seeking additional information from the Principal Investigator.
- Audit of trial by the IEC.
- Suspend the study till additional information is made available and is scrutinized.
- Suspend the study till recommendations made by the IEC are implemented by the PI and found to be satisfactory by the IEC.
- Suspend the study for a fixed duration of time.
- Suspension or termination of the study
- Revoke approval of the current study.
- Inform DCGI/ other relevant regulatory authorities.
- Keep other research proposals from the PI/ Co-PI under abeyance.
- Review and/ or inspect other studies undertaken by PI/Co-PI.

8.4.5 Procedure for notifying the investigator and other concerned authorities

- The IEC secretariat records the IEC decision.
- The Member Secretary drafts a notification letter.
- The signed letter by Member Secretary is sent to the Principal Investigator and Department Head(s) and Institutional Officials (if required).
- The IEC secretariat sends a copy of the notification to the relevant national authorities and institutes if applicable, as in the case of a multi-centric trial.

8.4.6 Records and follow up to be kept by IEC secretariat

The IEC secretariat:

- Keeps a copy of the notification letter in the respective project file.
- Stores the file on the shelf with an appropriate label.
- Follows up the action after a reasonable time.

References

1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, (Geneva 2000) www.who.int/tdr/publications/publications / (last accessed 24 September 2008)
2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996- http://www.ich.org/LOB/media/MEDIA482.pdf (last accessed 24 September 2008)

Glossary

Protocol deviation: Changes or alterations in the conduct of the trial which do not have a major impact on the participant's rights, safety or well-being, or the completeness, accuracy and reliability of the study data.

Protocol violation: A protocol deviation that may affect the participant’s rights, safety, or well being or alter the risk benefit ratio, and/or affect the participants’ willingness to participate in the study, and/or impact the completeness, accuracy and reliability of the study data.

Non-compliance: Non-performance of the study in compliance with the approved protocol, national regulations, ICH GCP, and other applicable regulations and/or failure to respond to the IEC request for information/action.

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

AX 1-V4/SOP08/V4

Deviation (D)/Violation (V) Reporting Form

Please report single event in one reporting form
Specify if D/V

Note-

Protocol deviation: Changes or alterations in the conduct of the trial which do not have a major impact on the participant's rights, safety or well-being, or the completeness, accuracy and reliability of the study data.

Protocol violation: Changes or alterations in the conduct of the trial that may affect the participant's rights, safety, or well being or alter the risk benefit ratio, and/or affect the participants' willingness to participate in the study, and/or impact the completeness, accuracy and reliability of the study data.

Date of Occurrence: dd/mm/yyyy
Total number of deviations /violations/ reported till date on the study –

Total number of similar deviations /violations/ occurred for the same trial:
Participant No. :
Trial Id :
IEC Project No. :
Project Title:

Phase of Study i.e Active Intervention/Completed Intervention/Follow up

Study status:
No. of participants recruited:

D/V identified by-
- ☐ Principal Investigator / study team
- ☐ Sponsor / Monitor
- ☐ DSMSC/IEC

Classify the lapse (Tick the appropriate box) :
- ☐ Consenting
- ☐ Enrollment
- ☐ Laboratory assessment
- ☐ Investigational Product
- ☐ Safety Reporting

- ☐ Source documentation
- ☐ Staff
- ☐ Participant non-compliance
- ☐ Others (Please specify)

Complete Details of D/V:

Action taken by PI/Co-PI/Co-I:

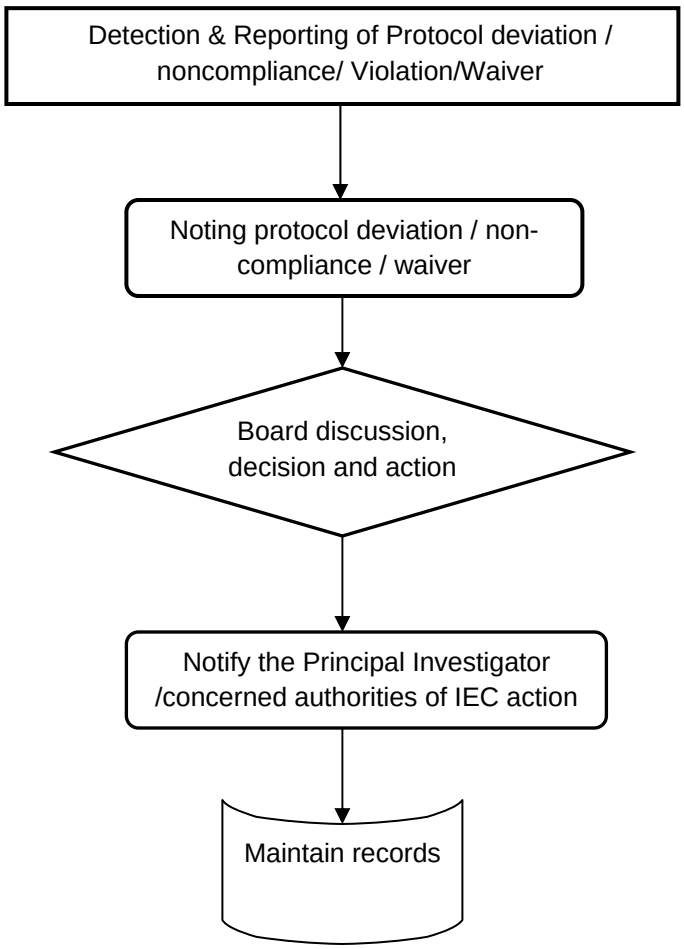
Impact on (if any):
Trial participant

Quality of data

Are any changes to the project/protocol required?
☐ Yes ☐ No

Name of PI:
Sign of PI:
Date:

Flow Chart


Detection & Reporting of Protocol deviation / noncompliance/ Violation/Waiver
Noting protocol deviation / non-compliance / waiver
Board discussion, decision and action
Notify the Principal Investigator /concerned authorities of IEC action
Maintain records

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Review of Serious Adverse Events (SAE) Reports

SOP Code: SOP 09/V4 Date: 01/04/2016 Pages: 195 to 213

9.1 Purpose

The purpose of this SOP is to describe the process on the submission, reporting, review of serious adverse events (SAEs) and unexpected events for any active study approved by the IEC.

Unanticipated risks are sometimes discovered during the course of studies. Information that may impact on the risk/benefit ratio should be promptly reported to and reviewed by the IEC to ensure adequate protection of the welfare of the study participants. The unanticipated risks may as well include any event that in the investigator's opinion, may adversely affect the rights, welfare or safety of subjects in the study.

9.2 Scope

This SOP applies to the DSMSC/IEC review of SAEs and unexpected events reports, both onsite and offsite, including follow up reports submitted by investigators. The detailed instructions regarding on site and off site SAE review are described in the following section 9.4.

Investigators, IEC members and DSMSC members must now follow the procedure as per current regulations. This amendment prescribes procedures for reporting of SAEs and the provision of compensation in case of injury or death during clinical trial.

9.3 Responsibility

The primary responsibility of the DSMSC/IEC is to review and address SAE and unexpected events involving risks to research participants. In addition, the committee is authorized to offer mediation under appropriate circumstances.

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

The IEC Secretariat is responsible for receiving the complete SAE / unexpected events reports and directing them to DSMSC for detailed review. Following the DSMSC meeting, the Secretary, DSMSC will then forward the minutes of the DSMSC meeting to the IEC. DSMSC minutes are discussed in the subsequent IEC meeting.

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

9.4 Detailed instructions

On site SAEs

9.4.1 Instructions for PI

- **All SAEs including Deaths** should be reported along with the justification for the Principal Investigator's causality assessment within 24 hours of their occurrence to
    1. IEC

2. Sponsor or its representative
3. CDSCO (in case of studies that require approval of the CDSCO)

- The report of the **serious adverse event of Death** along with the justification for the Principal Investigator's causality assessment shall be forwarded by the Investigator to
    1. The Sponsor
    2. Chairman of the IEC
    3. In case of studies that have required approval of the CDSCO, also report to the Chairman of the Expert Committee constituted by the CDSCO, with a copy of the report to the CDSCO and the Head of the Institution where the trial has been conducted within fourteen calendar days of the occurrence of the serious adverse event of death.

- The report of the **serious adverse event other than death** along with the justification for the Principal Investigator's causality assessment shall be forwarded to the
    1. Sponsor and
    2. Chairman of the IEC and
    3. In case of studies that require approval of the CDSCO, a report should be sent to the CDSCO and the Head of the Institution where the trial has been conducted within fourteen calendar days of the occurrence of the serious adverse event.

- In case the event is Death due to disease progression, 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 IEC as one signed hard copy (original) + soft copy

- Serious Adverse Event should be graded as per CTCAE Ver. 4.03

- Follow-up reports on the SAEs should be submitted within 14 calendar days of the initial report or when any additional information regarding the event is available, whichever is earlier.

- In case of research involving human subjects conducted, supported or otherwise subject to regulation by any United States government federal department or agency which takes appropriate administrative action (e.g. NIH, HHS), the PI must promptly communicate to the appropriate US Federal Department Agency head and the Office for Human Research Protection (OHRP) within 10 working days from the occurrence or knowledge of any of
    1. Any unanticipated problems involving risks to subjects or others
    2. Any serious or continuing noncompliance with the United States HHS policy
    3. Any serious or continuing noncompliance with the requirements or

determinations of the IEC;

4. Any suspension or termination of IEC approval

Contact details for the OHRP are:
Office for Human Research Protections
1101 Wootton Parkway, Suite 200
Rockville, MD 20852
Telephone: (240) 453-6900
Fax: (240) 453-6909
E-mail: OHRP@hhs.gov

9.4.2 SAE related activities before IEC meeting

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

9.4.3 Actions to be taken by Member Secretary, IEC

- The Member Secretary will review the SAE Report, write comments and forward it to the Secretary, DSMSC, immediately.
- If the SAE reported is “Death or outcome of any SAE reported is ‘death’, the Member Secretary, IEC, will review the SAE report (either hard copy or soft copy) and forward it to Secretary, DSMSC within 1 working day for immediate action either as hard copy or via email. If deemed necessary, Member Secretaries of IECs and Secretary, DSMSC will review the SAE death, either in person or by e-mail/ 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 DSMSC Secretary/IEC Member Secretary

- SAEs received from 1st – 31st of every month scheduled to be discussed in the subsequent DSMSC meeting are listed in next month's Agenda.

- Two lead discussants are assigned by Secretary DSMSC 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, DSMSC for finalization and signature
- The original signed hard copy of agenda is filed. The soft copies of meeting agenda and SAE reports are sent to DSMSC members via email for review.

9.4.4 After the DSMSC review of SAE

- After the DSMSC meeting, the Minutes are finalized by the Secretary, DSMSC.
- The IEC secretariat will send a formal letter signed by DSMSC Secretary to the investigator/s with instructions for specific actions as per the DSMSC decision.
- In case a PI fails to respond to the DSMSC letter, the matter will be discussed at the next full board IEC meeting and a decision will be taken for specific action by simple majority.
- The IEC 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 'DSMSC AGENDA and MINUTES file'
- Minutes are ratified in the next DSMSC meeting.
- The reply to DSMSC queries from PI are reviewed by Secretary DSMSC,
- These replies get discussed in the next scheduled DSMSC meeting and may be forwarded to IEC in case further opinion is required.
- The Member Secretary will table the SAEs and the DSMSC minutes in the next earliest respective full board meeting of IEC

9.4.4a Responsibilities of the IEC in case of studies that require approval of the CDSCO:

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

In case of serious adverse event other than death occurring to the clinical trial subject, the IEC shall forward its report on the serious adverse event after due analysis along with its opinion on the financial compensation, if any to be paid by the Sponsor or his representative, to the CDSCO, within thirty calendar

days of the occurrence of the serious adverse event.

9.4.4b Responsibilities of the IEC in case of Research involving human subjects conducted supported or otherwise subject to regulation by any United States government federal department or agency which takes appropriate administrative action (e.g. NIH, HHS).

Any serious or continuing noncompliance with the requirements or determinations of the IEC; or any suspension or termination of IEC approval must be communicated to the concerned US Federal Department Agency head as well as to the Office for Human Research Protection (OHRP), within 10 working days of the occurrence of the event.

Contact details for the OHRP are:
Office for Human Research Protections
1101 Wootton Parkway, Suite 200
Rockville, MD 20852
Telephone: (240) 453-6900
Fax: (240) 453-6909
E-mail: OHRP@hhs.gov

9.4.5 During the IEC meeting

The Secretary, DSMSC will inform all the IEC members about the SAEs and actions taken. The minutes of DSMSC meeting will be discussed.

- If appropriate, specific action or combination of actions will be taken, based on the consensus decision of the IEC discussion. Some of which are listed below:

  - Note the SAE report in the IEC records if information submitted is found to be adequate
  - Direct the PI to inform participants already enrolled in the study about the SAE and request them to undertake additional visits, additional procedures, additional investigations, etc. as per recommendation
  - Direct the PI to re-evaluate the event as to whether it is AE/SAE and report to IEC.
  - Direct the PI to inform participants already enrolled in the study about the SAE and obtain their consent regarding continuation in the research study, if necessary.
  - Request further follow up information
  - Request additional details
  - Recommend an amendment to the protocol, the ICD, Participant information sheet, investigator brochure and/ or any other document.
  - Recommend whether or not compensation should be paid to the patient /his nominee for trial related injury / death as per institutional policy.

- Suspend certain activities under the protocol (while going on with activities intended to protect the safety, well-being of participants who have already been enrolled);
- Suspend enrolment of new research participants;
- Suspend the study till amendments requested for by the IEC are accepted
- Suspend the study for a fixed duration of time;
- Suspend the study till additional information is obtained;
- Suspend the study till review is completed;
- Terminate the study;
- Any other action

9.4.6 Actions to be taken by Chairperson

The Chairperson, IEC on the basis of the information and comments received from the Member Secretary IEC and Secretary DSMSC, and applying his/ her judgment will direct the IEC Secretariat 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 IEC. The expert would be requested to provide an opinion in writing within 2-14 working days, depending upon the gravity and seriousness of the matter.
- 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 IEC Secretariat will take appropriate steps to ensure that IEC 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 IEC.
- 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 IEC
- Suspending enrolment of new research participants till further review by the IEC

9.5 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 IEC.

- 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 – AX2-V4 SOP09/V4) 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 – AX2-V4 SOP09/V4) will be reported to IEC Secretariat, and forwarded to Member Secretary, IEC and Secretary, DSMSC.
- If the IEC and DSMSC 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 IEC Secretariat, action on such reports will be taken by the Member Secretary, IEC and Secretary DSMSC, as per 9.3-9.4
- The IEC Secretariat will not accept the complete set of "Off site SAE reports" and/ or the log. However, the IEC will accept the log of the SAEs every 3 months and/or at the time of continuing review/ annual status report.

Off site SAEs (PSUR)

- The PSUR/Line listings submitted by PI on a monthly/quarterly/biannual basis are filed by DSMSC as a detailed review of the same is out of the scope of IEC/DSMSC.
- It is the PI's responsibility to review the listings in detail and report if a trend is observed and communicate the same to DSMSC.
- 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 IEC secretariat
- The SAEs are checked and stamped 'For DSMSC/Noted & File' and then forwarded to IEC for signature/review
- If any queries are raised by the IEC 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 IEC records if information submitted is found to be adequate
  - Direct the PI to inform participants already enrolled in the study about the SAE and request them to undertake additional visits, additional procedures, additional investigations, etc. as 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 IEC are accepted
- Suspend the study for a fixed duration of time;
- Suspend the study till additional information is obtained;
- Suspend the study till review is completed;
- Terminate the study;
- Any other action

9.6 DCGI Query on Serious Adverse Events

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

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

References

1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, (Geneva 2000).
2. International Conference on Harmonization, Guidance on Good Clinical Practice, (ICH GCP) 1996.
3. Nationwide Children's Hospital, Standard Operating Procedure: SAE Reporting and Reviewhttp://etrac.ccri.net/CRI/Doc/0/2137HUSRMVKKFBHAT542EHDME8/011%20Adverse%20Event.pdf.
4. Schedule Y (Drugs and Cosmetic Act 1940; amendment 2013.

Glossary

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

Adverse Drug Reaction- In the pre-clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not established all noxious or unintended responses to the product related to any dose should be considered adverse drug reactions. The phrase “responses to a medicinal product” means that a causal relationship between the product and the adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out. Regarding marketed products, a response to a product which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of diseases or for modification of physiological function.

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.

Onsite- Event occurring at TMC

Offsite- Event occurring at other centres / sites

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

AX1-V4/SOP09/V4

AX-V4/SOP9/V4 **SERIOUS ADVERSE EVENT REPORT** **Tata Memorial Centre**	**TMC PROJECT NO:**
	Regulated by DCGI: Yes / No **CTRI Reg. 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**

For DSMSC Office use:
(Strike out what is not applicable)
Item No: - -/N/A

Recd on:
Date of occurrence of event:

Investigator(s) shall report all SAE's including Death to the IEC, Sponsor and CDSCO within 24 hours of their occurrence of the knowledge of the PI. If a delay is expected kindly notify the same by email.

1.	Title of project:	
2.	Principal Investigator:	
3.	Report Date : Report Type : ☐ Initial ☐ Follow-up _____If Follow-up report, State Date of Initial report_____ ☐ Final _____If Final report, State Dates of Initial/Follow up report_____	
4.	Date of Occurrence of SAE :	
5.	Subject Case No : Subject Trial ID :	5a. Age : 5b. Gender : ☐ Male ☐ Female
6.	Study Arm to which subject is randomized : ☐ Test ☐ Standard Arm ☐ NA	
7.	Mention the total number of SAE (prior) occurred at this site : _____ Other site(s) : _____	
8.	Mention number of similar SAEs (prior) occurred for same study at this site :_____ Other site(s) : _____	
9.	A] State SAE Event term :	B] CTCAE Grade :

	(Kindly refer to CTCAE V4.03 where applicable) (where applicable)
10.	Does the Principal Investigator feel this SAE is related to participation in the trial ☐ Yes ☐ No Principal Investigator to provide justification for causality assessment
11.	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
12.	The cost of treatment/hospitalization was borne by, ☐ Patient ☐ Institute ☐ Sponsor/CRO

Drug information (refers to drug/ device/ procedure under investigation)

13.	IP/ Placebo (include generic name)/device/intervention:		
14.	Dose : Dosage Form :	15.	Route(s) of administration :
16.	Therapy Dates (From/To) :	17.	Therapy duration :
	Was study intervention discontinued due to event? ☐ Yes ☐ No		
18.	Did the reaction decline after stopping the drug / procedure (Dechallenge & Rechallenge information) ☐ Yes ☐ No ☐ NA		

Concomitant drugs and history (drugs that the patient maybe on)

19.	Concomitant drug(s) and date of administration :

20.	Patient relevant history (e.g. diagnosis, allergies): (Tick in the applicable box) (This is applicable only for regulated clinical trials) R = Risk Factor depending on the seriousness and severity of the disease, presence of co-morbidity and duration of disease of the subject at the time of enrolment in the clinical trial between a scale of 0.5 to 4 as under: a) 0.5 Terminally ill patient (expected survival not more than (NMT) 6 months) ☐ b) 1.0 Patient with high risk (expected survival between 6 to 24 months) ☐ c) 2.0 Patient with moderate risk ☐ d) 3.0 Patient with mild risk ☐ e) 4.0 Healthy Volunteers or subject of no risk ☐

SAE Details	
21.	Description of serious adverse event (indicate if this is follow-up report and if so, include follow-up information only)
22.	Describe the medical treatment provided (if any) to the research subject: This is an update on treatment given during hospitalization and /or used for management of the SAE.

Medication	Dose	Start date	End date

23.	Outcome was ☐ Resolved ☐ Ongoing ☐ Death
24.	Was the research subject continued on the research protocol? ☐ Yes ☐ No ☐ NA (Mark 'NA' in case of death)
25.	What phase of the research protocol is the patient in? ☐ On active treatment ☐ Short term follow-up ☐ Long term follow-up ☐ Surveillance/ Monitoring

26.	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: _____ Contact No. of PI: _____ Upon receipt of this report, the IEC/DSMSC will decide whether additional information is needed or whether further investigation of the incident is required. A follow-up report with further details should be submitted by PI within 10 days or earlier (of occurrence of the SAE) to the IEC
For IEC use only	

Final Assessment of DSMSC/ IEC (strike out what is not applicable)
Related/ Unrelated
Expected/ Unexpected
On active treatment/ Short term follow-up /Long term follow-up/ Surveillance/ Monitoring
Resolved/ Ongoing/ Death
SAE treatment supported by: Institute/ Sponsor
Compensation warranted: Yes/ No
If yes- please tick ☐ Adverse effect of investigational product(s) ☐ Violation of approved protocol, scientific misconduct or negligence ☐ Failure of investigational product to provide intended therapeutic effect where, the standard care, though available, was not provided to the subject as per the clinical trial protocol ☐ Use of placebo in placebo controlled trial where, the standard care, though available, was not provided to the subject as per the clinical trial protocol ☐ Adverse effect due to concomitant medication excluding standard of care, necessitated as part of approved protocol ☐ Injury to a child in utero due to participation of parent in clinical trial ☐ Any clinical trial procedures involved in the study I ____ agree _____ disagree with the assessment of the principal investigator. DSMSC Reviewer_____ date: _____ Explanation:

AX2-V4/SOP09/V4

Off site Safety Reports Classification Form

NOTE to 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 IEC along with the log.

If any one answer is **"No", it needs to be logged as prescribed format**. (AX3-V4/SOP 09/V4). This log should be submitted to the IEC 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 PI :

AX3-V4/SOP09/V4

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 IEC Secretariat every 3 months and/or along with Continuing Review report.
4. The log must be submitted to the IEC Secretariat 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 IEC Secretariat as and when received. If the IEC 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	:-
No. of Participants already enrolled	:-
No. of patients active on Treatment	:-
No. of patients on FU	:-
No. of Patients lost to follow up	:-
No. of Consent Withdrawn	:-
No. of patients withdrawn by Principal Investigator	:-
No. of patients completed treatment	:-

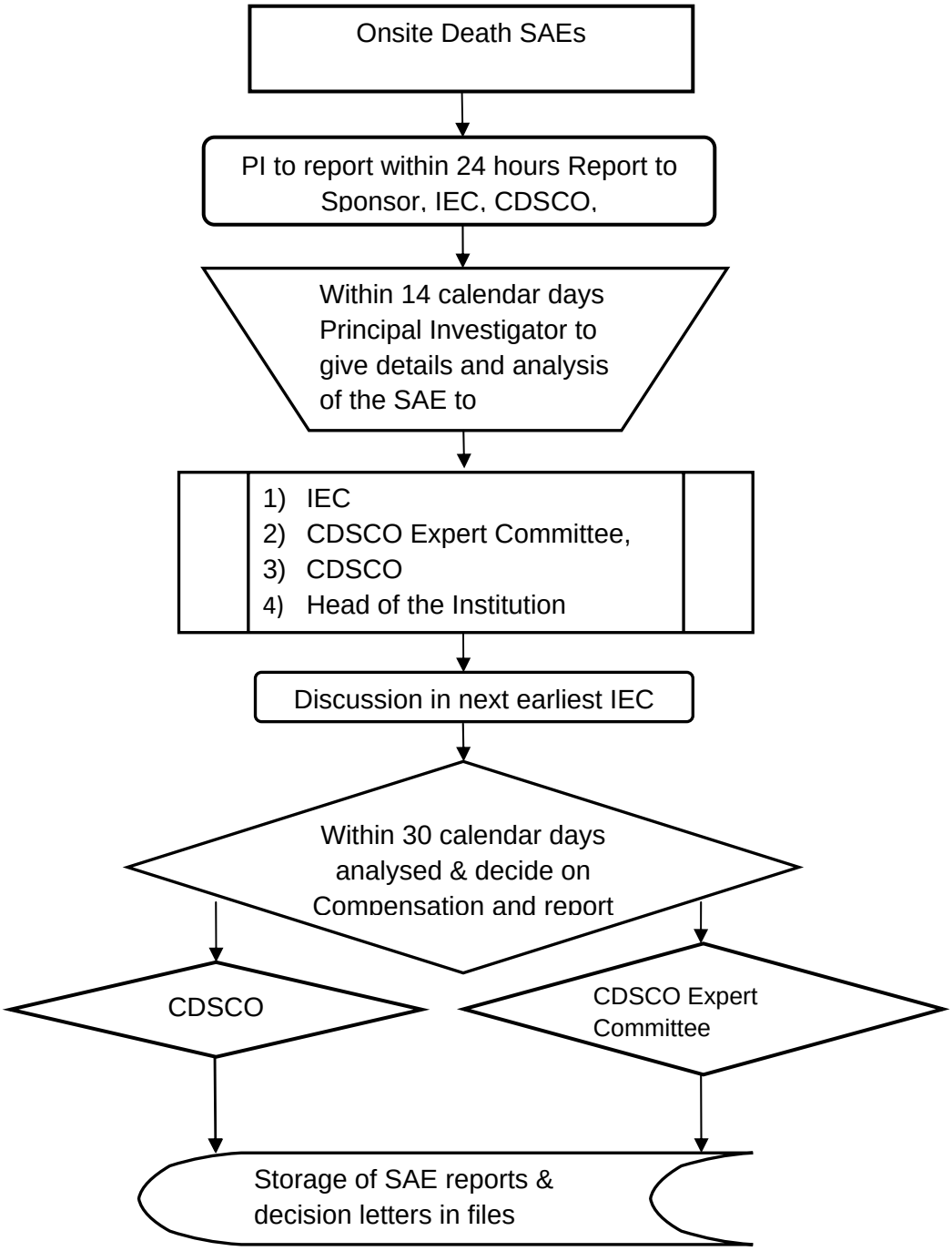
S. No.	Country	Date of Onset	Adverse event	Out Come	Remarks

PI Assessment:

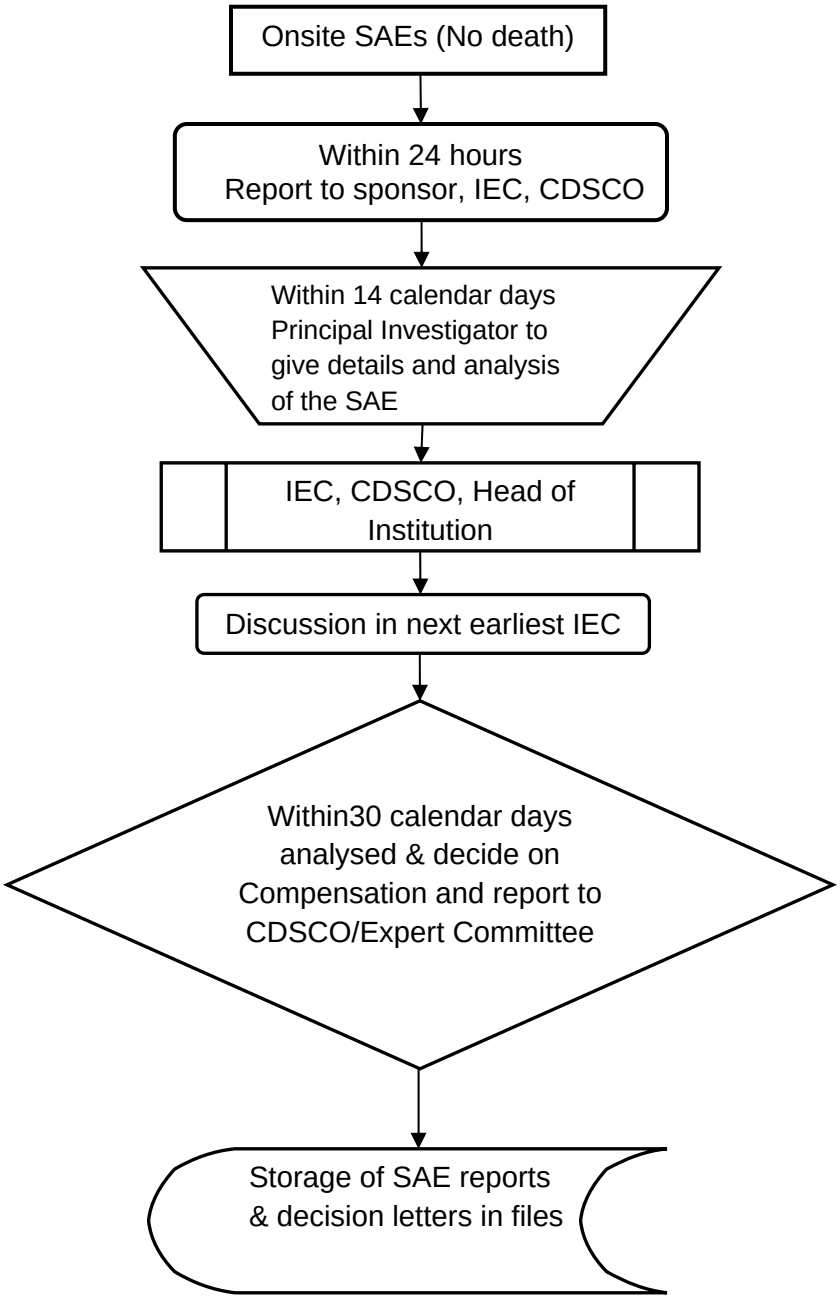
Do you observe a trend? ☐ Yes ☐ No

Name and Signature of Principal Investigator: Date:

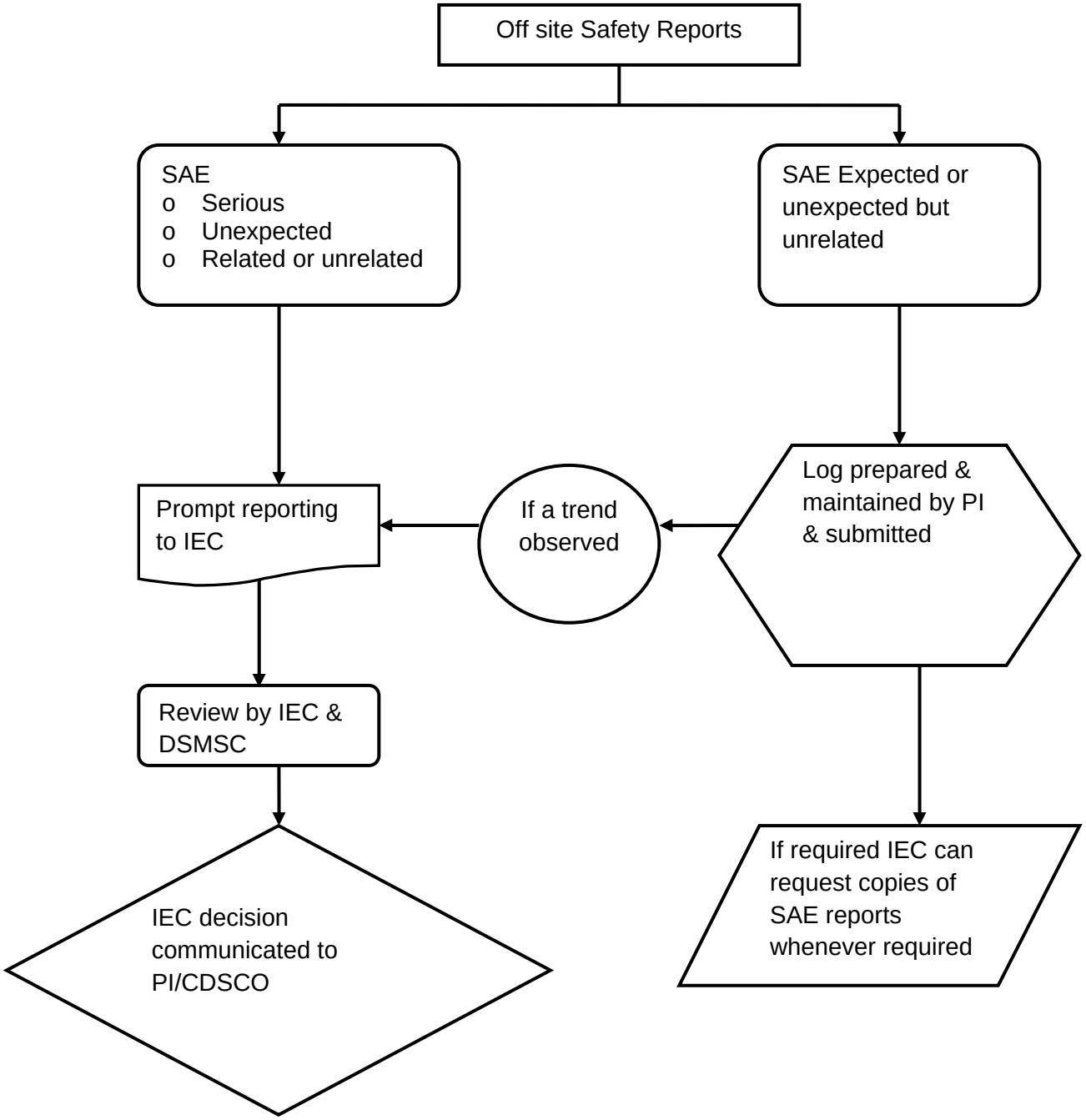
Flow Chart


Onsite Death SAEs
PI to report within 24 hours Report to Sponsor, IEC, CDSCO,
Within 14 calendar days Principal Investigator to give details and analysis of the SAE to
1) IEC
2) CDSCO Expert Committee,
3) CDSCO
4) Head of the Institution
Discussion in next earliest IEC
Within 30 calendar days analysed & decide on Compensation and report
CDSCO
CDSCO Expert Committee
Storage of SAE reports & decision letters in files

Flow Chart


Onsite SAEs (No death)
Within 24 hours
Report to sponsor, IEC, CDSCO
Within 14 calendar days
Principal Investigator to
give details and analysis
of the SAE
IEC, CDSCO, Head of
Institution
Discussion in next earliest IEC
Within30 calendar days
analysed & decide on
Compensation and report to
CDSCO/Expert Committee
Storage of SAE reports
& decision letters in files

Flow Chart


Off site Safety Reports
SAE
o Serious
o Unexpected
o Related or unrelated
SAE Expected or unexpected but unrelated
Prompt reporting to IEC
If a trend observed
Log prepared & maintained by PI & submitted
Review by IEC & DSMSC
IEC decision communicated to PI/CDSCO
If required IEC can request copies of SAE reports whenever required

Institutional Ethics Committee,

Tata Memorial Centre (IEC, TMC)

Title: Maintenance of Active Project Files, Archival / Disposal of closed files and Retrieval of documents

SOP Code: SOP 10/V4 Date: 01/04/2016 Pages: 214 to 219

10.1 Purpose

To provide instructions for preparation and maintenance of active study files and other related documents approved by the IEC, TMC, and storage/archival of closed files and retrieval of documents.

10.2 Scope

This SOP applies to all active protocol/study files, closed files and their related documents that are maintained in the IEC office and archival site.

10.3 Responsibility

It is the responsibility of IEC staff to ensure that all study files are prepared, maintained, and kept securely for complete period of the study and for five years after the closure of the project (under a proper system that ensures confidentiality and facilitates retrieval at any time).

10.4 Active study files maintenance & archival of closed files

A Study Master File is the file comprising all essential documents and correspondence related to the study/protocol. Study master files should be established at the time of initial submission in the IEC office.

- The study files are assigned unique identifiers (serial project 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. IEC Secretariat will have access to the files. The study files are maintained in an easily accessible and secure place for complete period of the study and at least 5 years after the study closure.
- All closed study files are separately archived.
- IEC staff will arrange for the closed project files to be archived once the completion/status reports are reviewed by the IEC. The completed/closed project files are clearly labeled and stored in the archival room. Only the IEC and the regulatory authorities would have access to these files.
- The records are stored by ITS on servers that are backed-up at regular intervals. Documentation of back-up for the IEC database and electronic files is kept by IT programmer.

10.5 Disposal of closed files and copies of protocols and documents submitted for IEC review.

The trial master file will be maintained in the IEC office for complete period of the study and for five 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 IEC review will be shredded by the authorized IEC personnel after the IEC meeting without any notification to the Principal Investigator. A log book of disposed documents will be maintained.

10.6 Accessibility / Retrieval

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

In case any investigator needs a copy of any document from the master file, he/she should make a written request. (AX1–V4/SOP10/V4). The IEC staff will furnish a copy of the required document within a week with the IEC Secretary's consent. The IEC will issue a copy of the following documents on formal written request.

For administrative purposes, the IEC Secretariat can retrieve archived file(s) without requiring the Chairperson's approval. For this purpose the IEC Secretary can authorize a staff member of the IEC secretariat to physically retrieve a file.

10.7 Final Disposal of Master files

The master files will be disposed off by the IEC secretariat after the archival period of 5 years. A formal written off register (AX2- V4/SOP 10/V4) will be maintained, providing details of the documents being written off / disposed off.

Glossary

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

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

Annexure

AX1 –V4/SOP10/V4

Document Request Form

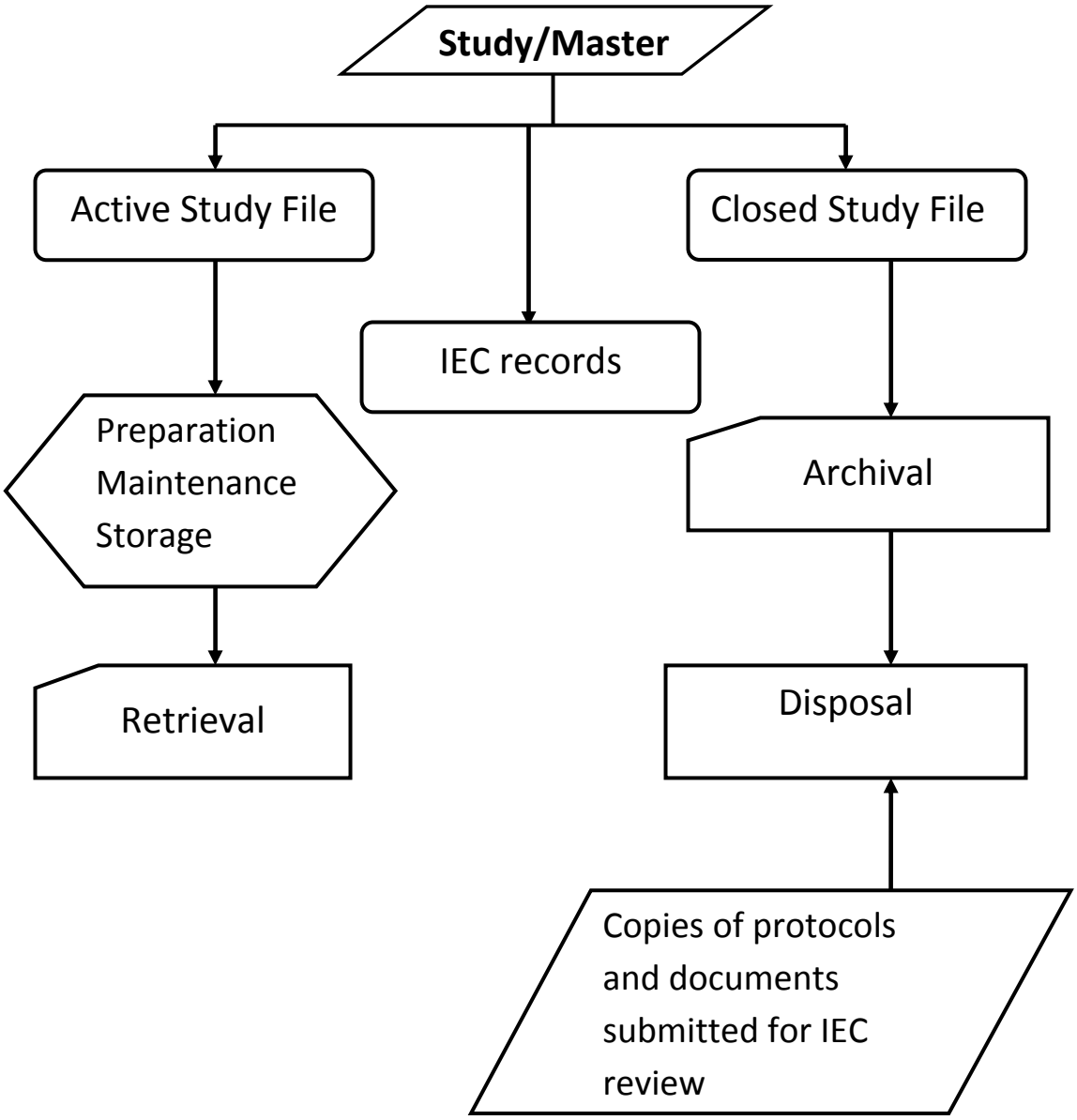
Project No :	Project Title:
Name of Principal Investigator/Requesting Person:	Date:
Documents requested (Specify document type and date of submission): Purpose of request:	
Principal Investigator / Requesting person’ s sign & date	
Permission of the Secretariat: Yes/No Signature of IEC Secretariat:	

AX2 –V4/SOP10/V4

Format of written off/disposal register

Project No	Title	PI	No. of Files	IEC Approval Date	Study Initiation Date	Study Closure Date	Name & Sign of Authorized Individual

Flow Chart


Study/Master
Active Study File
IEC records
Closed Study File
Preparation
Maintenance
Storage
Archival
Retrieval
Disposal
Copies of protocols and documents submitted for IEC review

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Documentation of the IEC activities

SOP Code: SOP 11/V4 Date: 01/04/2016 Pages: 220 to 223

11.1 Purpose

To describe the procedures for documenting the IEC activities.

11.2 Scope

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

11.3 Responsibility

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

11.4 Detailed Instructions

11.4.1 IEC records will include the following

1. IEC 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 IEC member
   e. Documentation of resignations/terminations

2. IEC membership roster/mandate- An IEC roster will be maintained for each committee. Changes in IEC membership shall be reported to the DCGI.

   The IEC roster will contain:
   i. Names of IEC member
   ii. Gender
   iii. Earned degrees
   iv. Scientific status
   v. Representative capacity
   vi. Affiliation status (e.g., unaffiliated or consultant)
   vii. Alternates to the IEC (if applicable)

3. IEC attendance roster
4. IEC meeting agenda and minutes
5. Standard Operating Procedures
6. Annual reports
7. Files - Workshops & Conferences organized by IEC (Continuing education for members and staff)
8. SOP Training Logs

9. Copies of all original research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved consent documents, applications for study re-approval, study progress reports and interim reports, modifications, serious adverse event report forms submitted by investigators, and other reports, IEC letters. These are maintained in the “master file.”

10. IEC records for initial and continuing review of research by the expedited procedure include:
    - The justification for using the expedited procedure.
    - Actions taken by the reviewer.
    - Any findings required by laws, regulations, codes, and guidance to be documented.

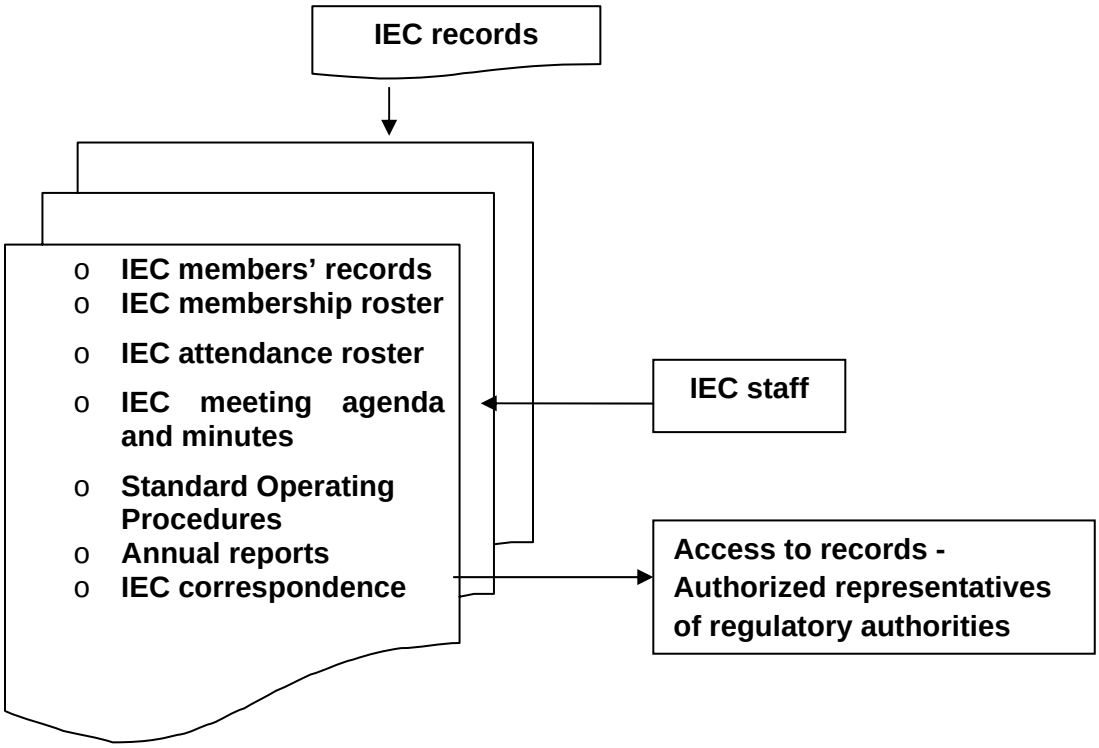
11. IEC records document the justification for exempt determinations. Maintains files on Exemption Requests and Emergency Use Notifications

12. Any other correspondence

11.4.2 Access to IEC records

IEC records will be made available for inspection to authorized representatives or regulatory authorities after receiving the request in writing.

Flow Chart


IEC records
o IEC members' records
o IEC membership roster
o IEC attendance roster
o IEC meeting agenda and minutes
o Standard Operating Procedures
o Annual reports
o IEC correspondence
IEC staff
Access to records - Authorized representatives of regulatory authorities

Institutional Ethics Committee,
Tata Memorial Centre (IEC, TMC)

Title: Review of Study Completion Reports

SOP Code: SOP 12/V4 Date: 01/04/2016 Pages: 224 to 229

12.1 Purpose

The purpose of this SOP is to provide instructions on the review of Study Completion Report for every study previously approved by the IEC.

12.2 Scope

This SOP applies to the review of the Study Completion Report which is an obligatory review of each investigator's activities presented to the IEC as a written report of study completed.

Although IEC provides a Study Completion Report Form (AX1-V4/SOP12/V4) to the investigator, additional information (letter format, form provided by the Sponsor, etc.) may be submitted to provide adequate and sufficient information. The report should include 250-300 words, with aims, methods, results, discussion and conclusion as in an abstract

12.3 Responsibility

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

12.4 Detailed instructions

12.4.1 Before each board meeting

- The secretariat will receive 1 hard copy + soft copy of Study Completion Reports from the PI.
- The Secretariat will follow instructions as in SOP 03/V4 (Management of Research study Submission) for receiving and checking the report packages.
- It is the responsibility of the IEC Secretariat to review the report for completeness before submission for the Board meeting.
- The Member Secretary should keep the study completion reports on the Agenda for IEC meeting. (Procedures for Agenda preparation, Meeting procedures and recording of Minutes- SOP 05/V4).

12.4.2 Before and during board meeting

- IEC member(s) should review a copy of the completion report.
- The members will discuss the report in the IEC meeting.
- If appropriate to the discussions, the chairperson may call for consensus to accept it or request further information or take any other action.

12.4.3 After the board meeting

- The secretariat will note the decision in the meeting minutes and the study will be considered as closed if the document is accepted.
- The IEC decision is communicated to the investigator. In case, further information / action is requested, the same should be followed by the PI and communicated to the IEC office within 30 days. This update will be tabled in the full board meeting of IEC.

- Once the report is accepted by IEC, the Secretariat will file the report in the study master file.
- The IEC secretariat will archive the entire study as per SOP 10/V4 section 10.4 and the report for a period of 5 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).
2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996.

Annexure

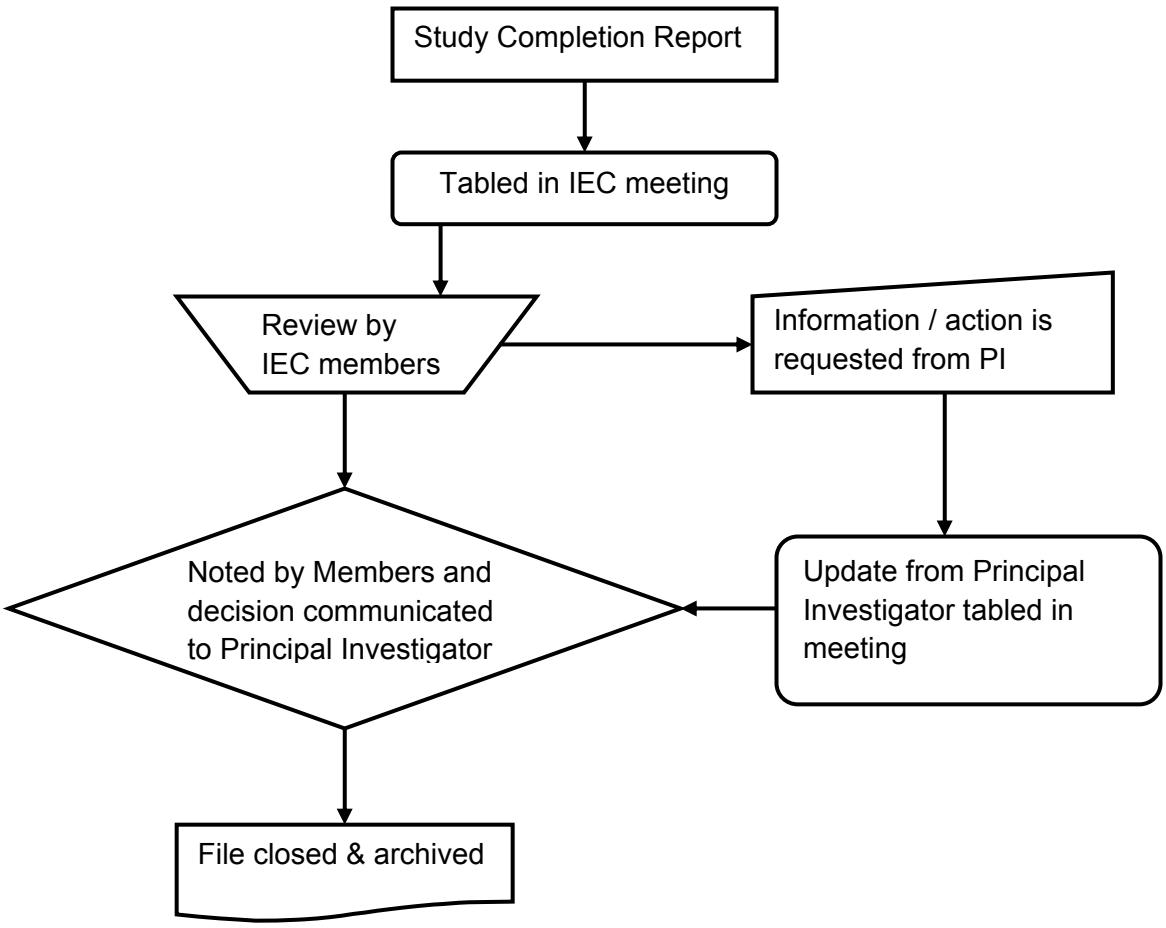
AX1-V4/SOP12/V4

Study Completion Report Form
TMC Project No. - Study Title: - Principal Investigator: -
Sponsor - Funding Source - Account No -
Duration of the study -
Study Start Date - If delayed start -state reasons - Completion Date -
Summary of Protocol participants: o Target accrual of study (entire study) including healthy volunteers, participants and biomedical samples/blocks)_____ _____ o Total participants/samples to be recruited at TMC (IEC ceiling)_____ o Screened: _____ o Screen failures: _____ o Enrolled: _____ o If total target could not be achieved – Kindly provide reasons o Consent Withdrawn: _____ TMC Case No& Reason for withdrawal o Withdrawn by PI: _____ TMC Case No& Reason for withdrawal o Active intervention: _____ o Completed intervention and on Follow-up: _____(includes participants who had received intervention) o Participants lost to follow up: _____ o Any other: _____ o Any Impaired participants • . None_____ • Physically _____ • Cognitively _____ • Both _____
No. of study arms/interventions :-

Objectives:-
Results (brief) (use extra blank sheets, if more space is required)- a) * 250-300 words, with aims, methods, results, discussion and conclusion as in an abstract b) Summary and Conclusions c) Details of new leads/information obtained, if any: *Note: In case of Pharma sponsored projects, if the final report is not available from sponsor, it may be submitted later to the IEC once it is ready.
Conclusion *
Presentation/publication related to the data generated in this trial • If yes: please enclose reprint of research publication • Did you inform to funding agency/ TRAC- Yes / No
Serious Adverse Events at our center (Total number and type) Note : applicable for Interventional study
Whether all Serious Adverse Events were intimated to the IEC (Yes/No)
Protocol deviations/violations (Type and Number) Whether all Protocol deviations/violations were intimated to the IEC (Yes/No)
Please specify if the raw data was submitted to TMC- Research Administrative Council (TRAC) (applicable only for investigator initiated studies). Budget sanctioned- Rs._____ Budget utilized-Rs._____ If underutilized provide reasons- (Kindly submit utilization certificate in case of institutional funded studies)
Signature of PI Date:

***mandatory fields**

Flow Chart


Study Completion Report
Tabled in IEC meeting
Review by IEC members
Information / action is requested from PI
Noted by Members and decision communicated to Principal Investigator
Update from Principal Investigator tabled in meeting
File closed & archived

Institutional Ethics Committee,

Tata Memorial Centre (IEC, TMC)

Title: Management of Premature Termination / Suspension / Discontinuation of the study / Withdrawal of study before site initiation

SOP Code: SOP 13/V4 Date: 01/04/2016 Pages: 230 to 237

13.1 Purpose

The purpose of this SOP is to describe how the IEC proceeds and manages the premature termination/suspension/discontinuation/withdrawal before site initiation of a research study. Research studies are usually terminated/suspended/discontinued as per the recommendation of the IEC, DSMSC, PI, sponsor or other authorized bodies wherein subject enrollment and subject follow-up are discontinued before the scheduled completion of the study.

13.2 Scope

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

13.3 Responsibility

It is the responsibility of the Chairperson, IEC to terminate any study that the IEC has previously approved when the safety or benefit of the study participants is doubtful or at risk, also to review the termination suggested by DSMSC, PI, Sponsor or other authorized bodies. The secretariat is responsible for management of the premature termination/ suspension/discontinuation documents.

13.4 Detailed instructions

13.4.1 Receive recommendation for study termination / suspension / discontinuation

- The secretariat will receive recommendation and comments from DSMSC, PI, Sponsor or other authorized bodies for premature termination/suspension / discontinuation of study.
- **Suspension/Termination/ Discontinuation by IEC**

  The IEC can terminate or suspend previously approved trial in following circumstances:
  - When research is not conducted in accordance with IEC policies.
  - When research is associated with unexpected serious harm to participant
  - Failure to submit CRA
  - For e.g. - Frequency of SAEs occurring at trial site may require the study to be prematurely terminated for the safety of the patients.
  - If protocol non-compliance/violation is detected
- **Suspension/Termination/ Discontinuation By Investigator/Sponsor:**

  An investigator may also put on hold a previously approved research when in the judgment of the investigator this is appropriate to protect the rights or welfare of participants or when new safety information appeared in the literature, or evolved from this or similar research

- Withdrawal of study before site initiation. An investigator may withdraw a study before site initiation due to reasons such as regulatory delays, logistic and budgetary infeasibility etc.
- Reports of Suspension/Termination/ Discontinuation/ by IEC will be tabled in the convened full board meeting.
- The secretariat will receive the study protocol termination/suspension/discontinuation prepared and submitted by the Principal Investigator and verify the contents of the report for inclusion of:
  - ❖ Premature Termination Report / suspension / discontinuation / Withdrawal of IEC approved study before site initiation (AX1- V4/SOP13/V4) signed and dated by the PI and/or other material (letter from Principal Investigator/sponsor etc)
  - ❖ The Secretariat will check the completeness of the information
  - ❖ The Secretariat will receive and acknowledge the reports.

13.4.2 Review and discuss the Premature Termination / suspension / discontinuation / report of Withdrawal of IEC approved study

- IEC will review the report of premature termination suspension/discontinuation/Study withdrawal by Principal Investigator before IEC approval at regular full board meeting or expedited review meeting.
- The Secretary in the meeting will inform of the premature termination suspension / discontinuation of the project and the IEC members will review the Premature Termination / Suspension / Discontinuation Report (AX1- V4/SOP13/V4) and Reports of Suspension / Termination / Discontinuation by IEC along with relevant SAE Report / DSMSC Reports.
- A suspension of IEC approval is a decision taken at the convened IEC meeting either to stop temporarily some or all previously approved research activities for a particular study, or to stop permanently some previously approved research activities. Suspended protocols remain open and require continuing review.
- A termination of IEC approval is a decision taken at the convened IEC meeting to stop permanently all activities in a previously approved research protocol. Terminated protocols are considered closed and no longer require continuing review.
- The IEC has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IEC policies, is not in compliance with the local regulations or that has been associated with unexpected serious harm to participants. Suspensions and terminations will be reported to concerned authorities and appropriate institutional officials when applicable
- Member Secretary IEC, documents in the IEC minutes the reasons for the suspension or termination / withdrawal of IEC approved study by Principal Investigator before site initiation and if applicable, any actions ordered to take place.

13.4.3 When IEC will suspend/terminate any study the following will be checked:

- Has PI notified about the suspension/termination of the trial to the currently enrolled participants.
- Whether procedures for withdrawal of enrolled participants take into account their rights and welfare (e.g., arranging for medical care off a research study).
- Have any adverse events or outcomes reported to the IEC

13.4.4 Notify the Principal Investigator

- The Secretariat 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 Secretariat will send the letter signed by Member Secretary/Chairperson to the PI within 15 working days after the meeting. Copies will be provided to the Head of the Institution / TRAC Chairperson, Head of Department of the Investigator and concerned regulatory authorities within 14 working days after the meeting.

  The letter includes:

  - ❖ The activities to be stopped;
  - ❖ Actions to be taken by the Investigator like PI to notify about the suspension / termination of the trial to the currently enrolled participants, whether arrangements for medical care of enrolled participants who are off a research study are made.
  - ❖ An explanation of the reasons for the decision;
  - ❖ A request to immediately notify the IEC with a list of names of participants who might be harmed by stopping research procedures and a rationale as to why they might be harmed.
- The investigator may appeal or respond to the convened IEC in writing.

13.4.5 Withdrawal of the suspension

- If a query is sent to PI, Principal Investigator should report to IEC on the actions taken as per IEC recommendations. This will be reviewed in the forthcoming full board meeting.
- The convened IEC then decides to lift the suspension, continue or modify the suspension, or terminate the study.

13.4.6 Store the Report

- The secretariat 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 5 years from the date of project termination / suspension / discontinuation.

References
1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, (Geneva 2000)
2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996

IEC, TMC

AX1- V4/SOP13/V4

Premature Termination / Suspension / Discontinuation Report

TMC Project No.:	
Protocol Title:	
PI:	
E-Mail:	
Study Site:	
Sponsor:	
IEC Approval Date:	Date of Last Progress Report Submitted to IEC

Please tick the appropriate

☐ Premature Termination
☐ Suspension
☐ Discontinuation

Reason for Termination/Suspension/Discontinuation:

Study Start Date:	Termination / Suspension / Discontinuation Date:

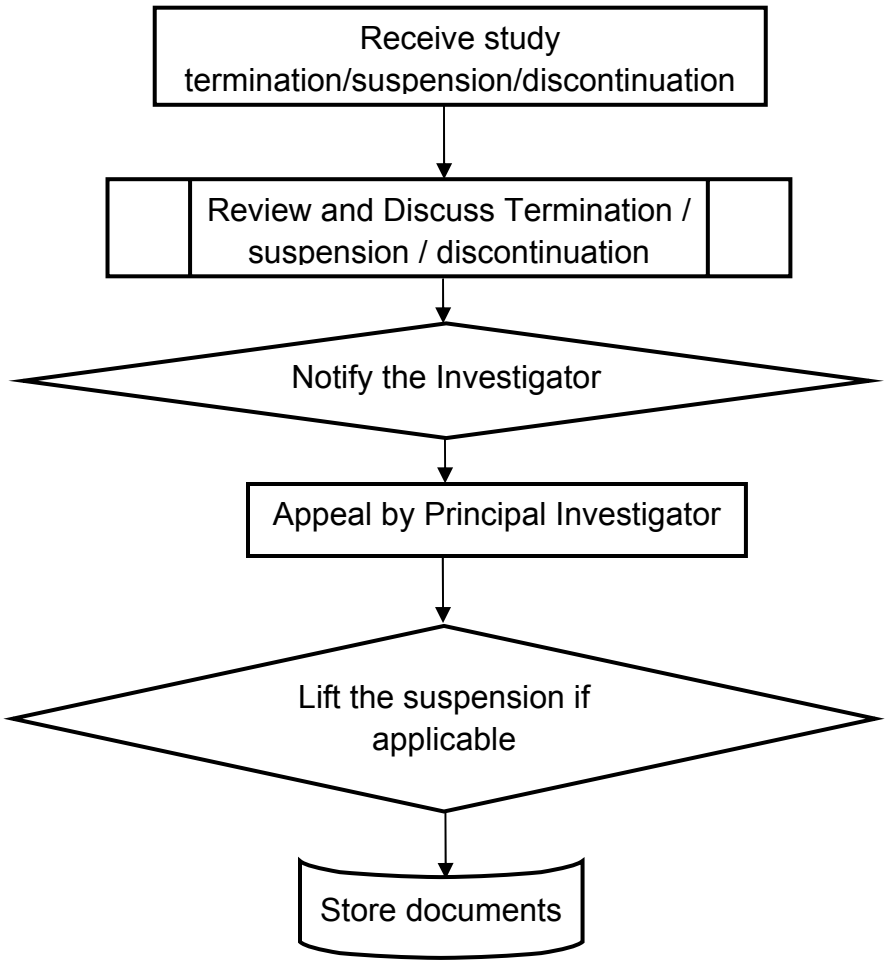
Study Participants

- Target accrual of trial (entire study) _____
- Total patients to be recruited at TMC (IEC ceiling)_____
- Screened: _____
- Screen failures: _____
- Enrolled: _____
- Consent Withdrawn: _____Reason: (Attach in format below)
- Withdrawn by PI: _____Reason: (Attach in format below)
- Active on treatment: _____
- Completed treatment : _____
- Patients on Follow-up: _____

o Patients lost to follow up: _____ o Any other: _____ o Any Impaired participants • None____ • Physically _____ • Cognitively _____ • Both _____
Type of SAEs (Total Nos.): Have any adverse events or outcomes reported to the IEC-
Have there been participant complaints or feedback about the study Yes □ No □ If yes Describe _____ Had there been any suggestions from the DSMSC Yes □ No □ If yes, have you implemented that suggestion Yes □ No □ Whether procedures for withdrawal of enrolled participants take into account their rights and welfare (e.g., making arrangements for medical care off a research study):
Summary of Results (if any) :

PI Signature:	Date:

Flow Chart


Receive study termination/suspension/discontinuation
Review and Discuss Termination / suspension / discontinuation
Notify the Investigator
Appeal by Principal Investigator
Lift the suspension if applicable
Store documents

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title : Review of Request for waiver of Written Informed Consent

SOP Code: SOP 14/V4 Date: 01/04/2016 Pages: 238 to 244

14.1 Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe the type of research projects for which the IEC 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 AX1-V4/SOP 14/V4 is designed to standardize the process of applying for consent waiver.

14.2 Scope

This SOP applies to the all protocols with a request of granting consent waiver submitted for review by the IEC. The decision should be taken by the IEC members at the expedited subcommittee meeting or during full board meeting.

14.3 Responsibility

It is the responsibility of the Member Secretary to table the request along with the project for expedited or full board review.

14.4 Detailed instructions

- When a request for waiver of consent is submitted by the Principal Investigator along with the study documents to the IEC secretariat, in the given format AX1-V4/SOP 14/V4 stating the reasons for the consent waiver; the following steps are taken:
  - ✓ The IEC Secretariat will check if the concerned documents are filled completely and the required list of documents is enclosed.
  - ✓ The IEC members will review the request taking into consideration the types of studies for which waiver of consent may be granted.
  - ✓ The IEC will ensure that there are adequate mechanisms described in the protocol for protection of the identity of the research participants and maintaining confidentiality of the study data. This is necessary as the participant cannot be assured directly about confidentiality of health data through a formal informed consent process, when consent waiver is granted.
  - ✓ The decision 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 IEC will provide reasons for the same.

14.5 Type of research projects which may qualify for consent waiver :

A request to waive written informed consent must be accompanied by a detailed explanation. The investigator 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 met 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) e.g. a retrospective review of patient case records to determine the incidence of disease/ recurrence of disease. [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].
2. When it is impractical to conduct research since confidentiality of personally identifiable information has to be maintained throughout research as maybe required by the sensitivity of the research objective. (ICMR 2006 guidelines).

   e.g. conducting interviews with citizens about their religious beliefs/ people with HIV and AIDS/conducting phone interviews with homosexuals.

   The only record linking the participant and the research would be the consent document and when there is a possible legal, social or economic risk to the participant entailed in signing the consent form as they might be identified as such by signing the consent form, the requirement for obtaining consent can be waived of by the IEC.
3. In case of telephonic interviews, waiver of written informed consent may be requested but this does not mean that verbal consent cannot be utilized.

   The following points need to be considered.

   a. The following documents need to be submitted for the IEC review
      - A script for verbal consent - a verbal consent script provides all of the elements of consent in a more informal style. In addition, each subject should be provided with an information sheet that describes the study and gives contact names and numbers.
      - The interview schedule (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, investigators will be asked to keep a log of those who were approached about the study, and offered verbal consent. A simple chart can indicate the subjects as participant 1, participant 2, and participant 3. A column can indicate that verbal consent was given and a date. Since a 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.
4. Research on publicly available information, documents, records, work performances, reviews, quality assurance studies, archival materials or third party interviews, service programs for benefit of public having a bearing on public health programs, and consumer acceptance studies.
5. Research on anonymised biological samples from deceased individuals, left over samples after clinical investigation, cell lines or cell free derivatives like viral isolates, DNA or RNA from recognized institutions or qualified investigators, samples or data

from repositories or registries and data, documents, records, or specimens that have been collected for non-research (clinical) purposes.

6. 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 IEC can allow waiver of consent for recruiting participant in a research study. However, informed consent should be administered whenever participant regains consciousness / capacity to consent or to relative / legal guardian when available later.

   The points 7-11 DHHS (CFR) criteria may be applicable only when research involving human subjects is conducted, supported or otherwise subject to regulation by any United States Government federal department or agency funded by a U.S. federal agency.

7. An IEC 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 IEC 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

8. An IEC 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 IEC finds and documents that:

   i. The research involves no more than minimal risk to the subjects;
   ii. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
   iii. The research could not practicably be carried out without the waiver or alteration; and
   iv. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

9. The informed consent requirements in this policy are not intended to preempt any applicable local laws and concerned regulations which require additional information to be disclosed in order for informed consent to be legally effective.
10. Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable local laws and concerned regulations The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) 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 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.

11. An IEC may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:
    1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
    2) 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.
    3) In cases in which the documentation requirement is waived, the IEC may require the investigator to provide subjects with a written statement regarding the research.
    4) The IEC is allowed to waive parental permission by determining that the criteria for waivers or alterations are met.
    5) The IEC is allowed to waive the requirement for written documentation of the consent process by determining that the criteria for waivers are met.

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. Website http://www.hhs.gov/ohrp/humansubjects/guidance/45 CFR 46.htm, paragraph 46.116

AX1-V4/SOP14/V4

Application form for requesting waiver of consent

1. Principal Investigator's name: _____
2. Department: _____
3. Title of project: _____

   _____

   _____
4. Names of other Co-investigators:

   _____

   _____

   _____

   _____
5. Request for waiver of informed consent:

   - Please tick the reason(s) for requesting waiver (in box provided)

     1. Research involves 'not more than minimal risk' ☐
     2. There is no direct contact between the researcher and participant ☐
     3. Emergency situations as described in ICMR Guidelines (ICMR 2006 Guidelines- http://www.icmr.nic.in/ethical_guidelines.pdf) ☐
     4. Any other (please specify)

        _____

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

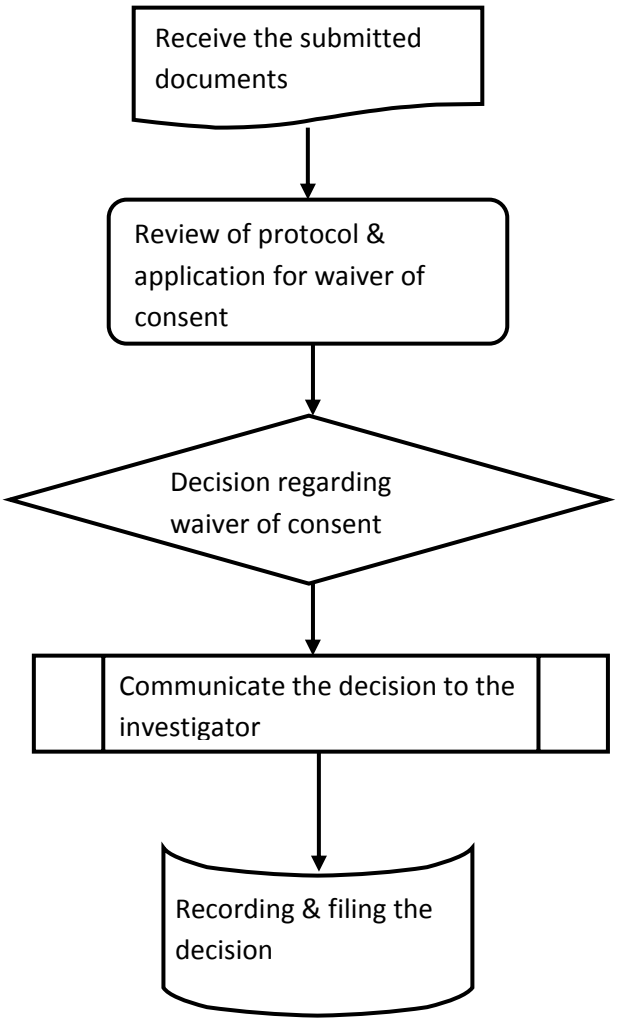
     _____

   - State the measures described in the protocol for protecting confidentiality of data and privacy of research participant

     _____

Principal Investigator's signature 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
Recording & filing the decision

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Study Monitoring

SOP Code: SOP 15/V4 Date : 01/04/2016 Pages: 245 to 254

15.1 Purpose

The purpose of this Standard Operating Procedure (SOP) is to provide the procedures for monitoring the study.

15.2 Scope

This SOP applies to any visit and/or monitoring of IEC approved study protocols. Clinical trials sponsored by external funding sources and industry are continually audited for compliance and monitored for progress by the external monitors. Institutional clinical studies without outside sponsorship are the focus of the monitoring system of this committee. However if any of the aforementioned studies require a “for cause” monitoring, as thought necessary by the IEC, these SOPs will also apply to the same.

15.3 Responsibility

Data and Safety Monitoring Subcommittee of IEC is charged with the mission of developing and enacting quality assurance procedures to monitor the overall progress of institutional clinical trials and for ensuring adherence to clinical trial and procedural requirements.

This includes review of the overall progress of each study to insure the safety of participants, validity of data, that the projected accrual goals are met on a timely basis, that excess accrual is avoided, that eligibility and evaluability rates do not fall below minimum acceptable standards, that risks are not excessive, that adverse events are appropriately monitored and reported to the appropriate agencies. Inherent in this process is the goal of enhancing the quality of the research by providing the investigator with constructive criticism.

The DSMSC Secretary assigns the DSMSC members /monitors from the Data and Safety Monitoring Subcommittee to monitor the trials. The monitoring is conducted by at least 2 members of the DSMSC who have enough expertise and understanding of the clinical aspects of the disease/ patient population being studied, with an adequate understanding of relevant biostatistics and clinical trial conduct and methodology.

The Principal Investigator should constitute its own DSMB in case of studies with sample size $\geq$ 200 participants or on the advice of the IEC for certain trials. The Data and Safety Monitoring Board (DSMB) is an independent group of experts that advises Principal Investigator, serve in an individual capacity and provide their expertise and recommendations. The primary responsibilities of the DSMB are to 1) periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, and, when appropriate, efficacy, and 2) make recommendations to Principal Investigator concerning the continuation, modification, or termination of the trial. The DSMB considers study-specific data as well as relevant background knowledge about the disease, test agent, or patient population under study. DSMB Membership - Expert(s) in the clinical aspects of the disease/patient population being studied; One or more biostatisticians; and, Investigators with expertise in current clinical trials conduct and methodology. No member of the DSMB should have direct involvement in the conduct of the study. Furthermore, no member should have financial, proprietary, professional, or other interests that may affect impartial, independent decision-making by the DSMB.

15.4 Detailed instructions

15.4.1 Selection of study

- Investigator initiated studies will be identified for routinely monitored (at least annually) by the degree of intervention, sample size, complexity of the study and risk involved.
- Principal Investigator should intimate the IEC after accrual of first 10 participants in the study or after 6 months of initiation of study whichever is earlier.
- Pharma sponsored studies are not routinely monitored but for cause monitoring may be conducted.
- For cause monitoring will be performed for the study for reasons identified by any member of IEC, approved by Chairperson. For cause monitoring could be initiated, in any of the following conditions:

  - For high number of protocol violations
  - Too many studies carried out by a Principal Investigator
  - High number of SAE reports
  - High recruitment rate
  - Non-compliance or suspicious conduct
  - Any complaints related to the research
  - Any other cause as decided by IEC

15.4.2 Before the visit

- For cause/routine monitoring of the project, the IEC Chairperson/ Secretary will inform DSMSC to perform the task of monitoring during discussion of the study, on receipt of annual status reports or review of SAEs.
- 2 members of the DSMSC who have enough expertise and understanding of the clinical aspects of the disease/ patient population being studied, with an adequate understanding of relevant biostatistics and clinical trial conduct and methodology will be allocated the task of monitoring a particular trial
- The Secretariat will intimate the PI regarding the scheduled monitoring visit. DSMSC 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 Principal Investigator 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 IEC approved project files for verification and Study Monitoring Visit Report Form (AX1-V4/SOP15/V4).

15.4.3 During the visit

The monitor will –

- Review the informed consent document to make sure that the PI is using the current, approved version
- Review randomly the participant's source files for proper informed consent documentation.(usually about 10%, or maybe higher)
- Observe the informed consent process, if possible,
- Check investigational product accountability is adequately controlled and documented throughout the product flow (arrival, dispensing, use, return from the participant and return/destruction after the study). Storage times, conditions and expiry dates must also be acceptable and sufficient supplies available wherever applicable.
- Observe laboratory and other facilities necessary for the study, if possible.
- Review the study/ source files to ensure appropriate documentation
- Verifying that the investigator follows the approved protocol and all approved amendment(s), if any.
- Ensuring that the investigator and the investigator's trial staff are adequately informed about the trial
- Verifying that the investigator and the investigator's trial staff are performing the specified study functions, in accordance with the approved protocol and any other written agreement between the sponsor and the investigator/institution, and have not delegated these functions to unauthorized individuals.
- Verifying that the investigator is enrolling only eligible participants.
- Verifying that source documents and other study records are accurate, complete, kept up-to-date and maintained.
- Checking the accuracy and completeness of the CRF entries, source documents and other study related records against each other.
- Determining whether all Serious Adverse Events (SAEs) are appropriately reported within the time periods required by GCP/ Regulatory agencies, the protocol, the IEC/IEC, the sponsor, and the applicable regulatory requirement(s). Case record forms would be checked to review the safety data i.e. Adverse Events (AEs) and Serious Adverse Events (SAEs) for the volume or severity of adverse events.
- Collect views of the study participants, if possible.
- Fill the Study Monitoring Visit Report Form AX1-V4/SOP15/V4 and write the comments.

15.4.4 After the visit

- The monitor will complete the report (use the form AX1-V4/SOP15/V4) **within 14 days** describing the findings of the monitoring visit and submit the same to the DSMSC office. After the form is received at DSMSC office, it is checked for completeness.
- Form is reviewed by DSMSC secretary, and the form is forwarded to IEC Secretary for action

- The IEC Secretary/DSMSC member representative/lead discussant for the project can present the monitoring visit findings in the full board meeting.
- The Secretariat will place the report in the correct files.
- Full board recommendations to change the study/ premature termination/ continuation of the project will be informed to the Principal Investigator in writing within **14 days of the meeting**.
- Grounds for recommending suspension or termination of a clinical trial to theIEC include, but are not limited to:
  1. Zero accrual for 1-2 years or long-term, low accrual.
  2. Stopping rule violations.
  3. Major violations in the conduct of the study (including serious IEC violations) that result in an unacceptable audit rating.
  4. The decision to recommend suspension or termination of a clinical trial is carefully considered and takes into account whether corrective actions had been requested at previous reviews and were not implemented.

  If the decision is made to recommend suspension or termination of a clinical trial, the recommendation will be sent to IEC. IEC has the ultimate authority to effect termination or suspension of a clinical trial.

Glossary

Monitor - DSMSC/IEC member who reviews the overall progress of institutional clinical trials and for ensuring adherence to clinical trial and procedural requirements.

Monitoring visit - The act of overseeing the progress of a study, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, & the applicable regulatory requirements.

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.

Annexure

AX1-V4/SOP15/V4
Study Monitoring Visit Report

1) TMC Project No:

2) Title:

3) Principal Investigator:

4) Institute:

5) Type of study: ☐ Investigator initiated ☐ Pharma ☐ Thesis

   Source of funding: ☐ Intramural ☐ Extramural ☐ Pharma

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:
- ☐ Ongoing
- ☐ Accrual Completed
- ☐ Follow-up
- ☐ Completed
- ☐ Suspended
- ☐ Terminated
- ☐ Closed
- ☐ Closed Prematurely

In case of the response to the above question is option 5, 6, or 8 kindly provide reason: _____

13) Recruitment Status:
- Total participants to be recruited - _____
- Screened: _____
- Screen failures: _____
- Enrolled: _____
- Withdrawn: _____ Reason: _____
- Discontinued: _____ Reason: _____
- Completed: _____
- Active: _____

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

15) Protocol
a) Have there been any amendments to the Protocol? ☐ Yes ☐ No
If Yes then state changes leading to amendment:
_____
b) Is the Protocol version approved by IEC? ☐ Yes ☐ No
c) 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
b) Have there been any amendments to the ICF? ☐ Yes ☐ No
If Yes then state changes leading to amendment:
_____
_____
_____
_____
c) Is the Informed consent form version approved by IEC? ☐ 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
Have all the deviations/violations notified to IEC? ☐ 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 DSMSC within 7 working days and deaths within 24hrs of the knowledge of PI?

☐ Yes ☐ No ☐ NA

Comments (If Any)

_____

21) Are the Investigational drugs accountability and prescription procedures performed and documented?

☐ Yes ☐ No ☐ NA

If 'Yes' kindly state the issues:

_____

_____

22) Any are there any changes to the study personnel? ☐ Yes ☐ No ☐ NA

If 'Yes' kindly state the same:

_____

_____

Is the change notified to IEC? ☐ Yes ☐ No ☐ NA

23) No of participants monitored during this visit: _____

24) Duration of the visit: _____

25) Any outstanding tasks/action items from the visit?

_____

_____

_____

_____

Monitoring visit conducted by:

Name of DSMSC member_____

Signature and Date _____

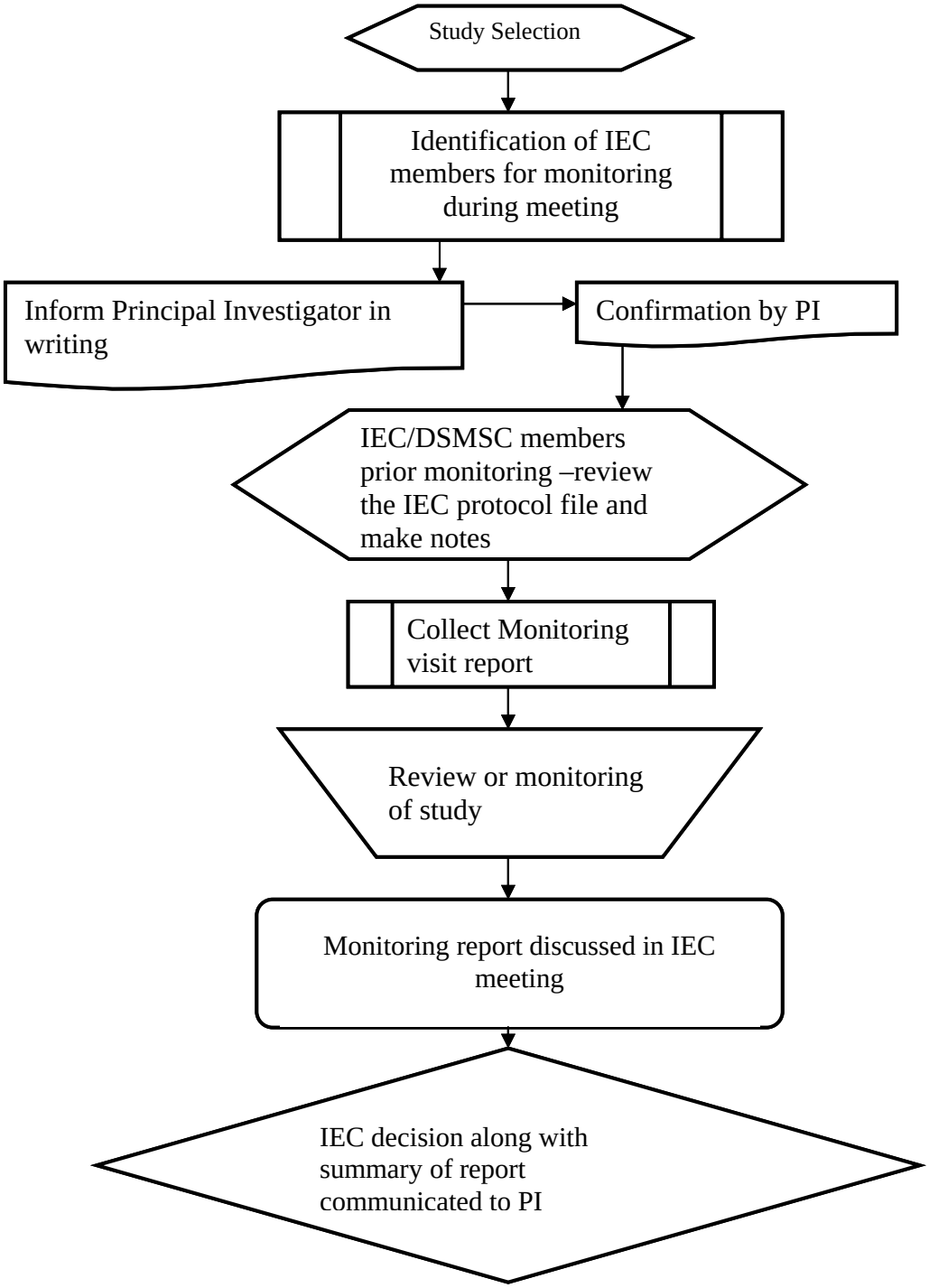
Name of DSMSC member_____

Signature and Date _____

Name of study team member present: _____

Signature and Date: _____

Flow Chart


Study Selection
Identification of IEC members for monitoring during meeting
Inform Principal Investigator in writing
Confirmation by PI
IEC/DSMSC members prior monitoring –review the IEC protocol file and make notes
Collect Monitoring visit report
Review or monitoring of study
Monitoring report discussed in IEC meeting
IEC decision along with summary of report communicated to PI

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: **Dealing with participants / patients requests and complaints**

SOP Code: SOP 16/V4 Date : 01/04/2016 Pages: 255 to 259

16.1 Purpose

The IEC considers protection of the rights and welfare of the human subjects participating in a clinical research approved by the IEC as its primary 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 IEC, Member secretary, and the IEC address and phone number 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 research study.

16.2 Scope

This SOP applies to all requests concerning the rights and well-being of the research participants participating in studies approved by the IEC.

16.3 Responsibility

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

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

16.4 Detailed instructions

When the IEC member/ 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 AX1-V4/SOP 16/V4)
- The Member Secretary will inform the Chairperson about the query/complaint received.
- The Chairperson / 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 Chairperson will initiate a process to identify and address any injustice that may have occurred.
- The Chairperson will direct the Member Secretary to 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 IEC members for enquiry in order to resolve the matter.
- The Chairperson/ Member Secretary/ designated 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 IEC 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 AX1- V4/SOP 16/V4 and the form will be signed and dated.
- The IEC members will be informed about the action taken and the outcome in the forthcoming IEC meeting.

16.5 Filing the request document

- 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 Ethics Committee do?" IEC: Ethics and Human Research 26, no.1(January-February 2004):9-13

IEC, TMC

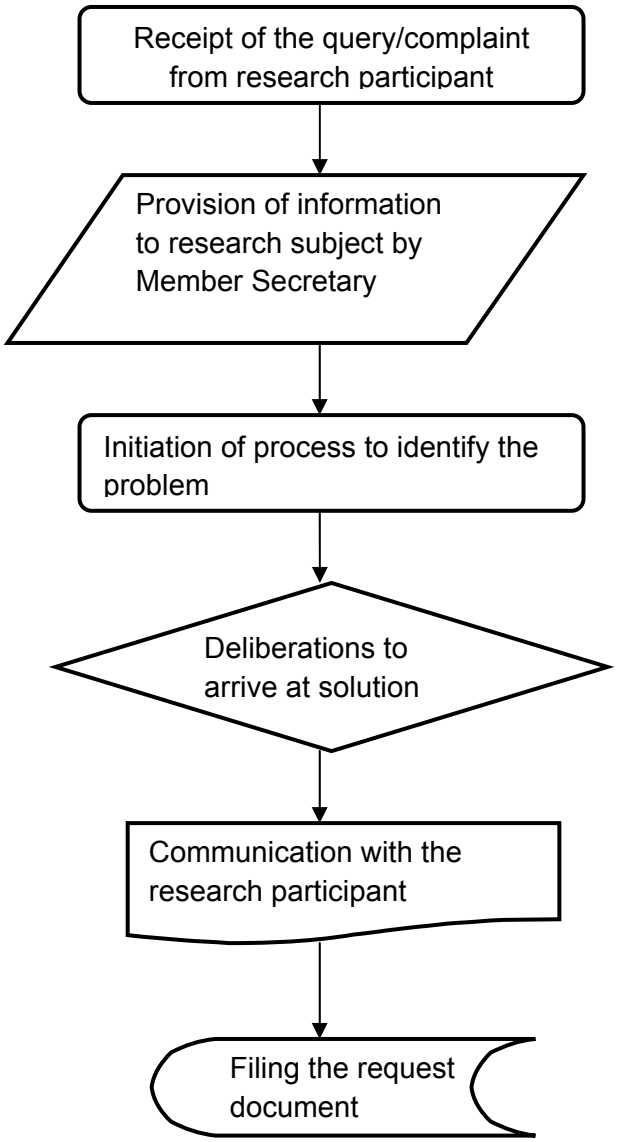
AX1- V4/SOP 16/V4

Request/ complaint Record Form Date Received:	
Received by :	
Request from :	⏲ Telephone call No…… ⏲ Fax No…… ⏲ Letter / Date…… ⏲ E-mail / Date…….. ⏲ Walk-in / Date / Time…… ⏲ Other, specify ……...
Participant's Name:	
Contact Address: Phone:	
Title of the Study :	
Starting date of participation :	
Request:	
Action taken:	
Outcome:	

Name of the Chairperson/ Member Secretary - _____

Signature of the Chairperson/ Member Secretary _____ Date -_____

Flow Chart


Receipt of the query/complaint from research participant
Provision of information to research subject by Member Secretary
Initiation of process to identify the problem
Deliberations to arrive at solution
Communication with the research participant
Filing the request document

Institutional Ethics Committee, Tata Memorial Centre (IEC, TMC)

Title: Reviewing Research Studies Involving Vulnerable Populations

SOP Code: SOP 17/V4 Date: 01/04/2016 Pages: 260 to 278

17.1 Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe procedures to review research protocol involving vulnerable populations. The SOPs provide clear, unambiguous instructions so that the related activities of the Board are conducted in accordance with Indian laws and relevant, National and International Guidelines. It describes the requirements concerning review of research that involves groups that could be potentially vulnerable to coercion in regard to autonomy, and present conditions that may affect risk/benefit determinations or bearing unequal burden in research.

17.2 Scope

- This SOP applies to all policies and procedures of review and assessment applied to all research dealing with vulnerable population that require additional consideration or protection, submitted and approved by the IEC.
- Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests.

  Vulnerable groups: Effort may be made to ensure that individuals or communities invited for research be selected in such a way that the burdens and benefits of the research are equally distributed.
  a. Research on genetics should not lead to racial inequalities;
  b. Persons who are economically or socially disadvantaged should not be used to benefit those who are better off than them;
  c. Rights and welfare of mentally challenged and mentally differently able persons who are incapable of giving informed consent or those with behavioral disorders must be protected. Appropriate proxy consent from the legal guardian should be taken after the person is well informed about the study, need for participation, risks and benefits involved and the privacy and confidentiality procedures. The entire consent process should be properly documented;
  d. Adequate justification is required for the involvement of participants such as prisoners, students, subordinates, employees, service personnel etc. who have reduced autonomy as research participants, since the consent provided may be under duress or various other compelling reasons.
- Individuals whose willingness to volunteer in a research study may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate may also be considered vulnerable.

  - Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention.

"Vulnerable" or "special" classes of participants include as listed below

This list may not be exhaustive as there may be circumstances in which other groups are considered vulnerable, women for example, in an orthodox patriarchical society, or terminally ill cancer patients.

- Pregnant women, human fetuses and neonates,
- Prisoners,
- Children,
- Cognitively impaired persons
- Students and employees, sub-ordinates
- Minorities (as defined by national constitution and / or socio-economically backward, refugees and such others.)
- Economically and/or educationally disadvantaged
- AIDS/HIV+ subjects.
- Terminally ill Participants
- Geriatic population

Vulnerable populations:

The following is required when children are enrolled in research:

- Children will not be involved in research that can be carried out equally well with adults.
- The purpose of the research is to obtain knowledge relevant to health needs of children. For clinical evaluation of a new drug the study in children should always be carried out after the phase III clinical trials in adults.
- For studies prior to phase III the drug has a therapeutic value in a primary disease of the children.
- The settings of the research provide the child and parent adequate medical and psychological support.
- Interventions intended to provide direct diagnostic, therapeutic, or preventive benefit for the individual child participants must be justified in relation to potential risks involved in the study and potential benefits to society.
- The risk presented by interventions not intended to benefit the individual child participant is low when compared to the importance of the knowledge that is to be gained.
- Interventions that are intended to provide therapeutic benefit are likely to be at least as advantageous to the individual child participant as any available alternative interventions.
- A parent or legal guardian of each child has given proxy consent.
- The assent of the child should be obtained to the extent of the child's capabilities such as in the case of mature minors or adolescents, unless there is no medically acceptable alternative to the therapy provided or tested, and consent has been obtained from at least one parent or guardian.
- If research involves adults unable to consent, the ethics committee must consider additional safeguards to protect their rights and welfare: When conducting non-therapeutic research, consent must be obtained directly from the participant, unless:

- The objectives of the clinical trial cannot be met by means of a trial in participants who can give consent personally.
- The foreseeable risks to the participants are low.
- The negative impact on the participant's wellbeing is minimized and low.
- The clinical trial is not prohibited by law.
- The opinion of the ethics committee is expressly sought on the inclusion of such participants, and the written opinion covers this aspect.

➢ Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Participants in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

When adults are unable to consent, the IEC determines:

➢ A non-therapeutic clinical trial (i.e. a trial in which there is no anticipated direct clinical benefit to the participant) should be conducted in participants who personally give consent and who sign and date the written consent document.

➢ Non-therapeutic clinical trials may be conducted in participants with consent of a legally acceptable representative provided the following conditions are fulfilled:

- The objectives of the clinical trial cannot be met by means of a trial in participants who can give consent personally.
- The foreseeable risks to the participants are low.
- The negative impact on the participant's wellbeing is minimized and low.
- The clinical trial is not prohibited by law.
- The opinion of the IEC is expressly sought on the inclusion of such participants, and the written opinion covers this aspect.
- Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Participants in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

The following is required when Pregnant or nursing women are enrolled in research:

Pregnant or nursing women : Pregnant or nursing women should in no circumstances be the participant of any research unless the research carries no more than minimal risk to the foetus or nursing infant and the object of the research is to obtain new knowledge about the foetus, pregnancy and lactation. As a general rule, pregnant or nursing women should not be participants of any clinical trial except such trials as are designed to protect or advance the health of pregnant or nursing women or foetuses or nursing infants, and for which women who are not pregnant or nursing would not be suitable participants.

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

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

b. Research related to termination of pregnancy: Pregnant women who desire to undergo Medical Termination of Pregnancy (MTP) could be made participants for such research as per The Medical Termination of Pregnancy Act, GOI, 1971.
c. Research related to pre-natal diagnostic techniques: In pregnant women such research should be limited to detect the foetal abnormalities or genetic disorders as per the Prenatal Diagnostic Techniques (Regulation and Prevention of Misuse) Act, GOI, 1994 and not for sex determination of the foetus.

17.3 Categorization of protocols

Vulnerable population will be subjected to full board Initial review (SOP 4aV4). Research involving vulnerable populations is not eligible for expedited review or exemption from review.

17.4 Review Process

- The IEC evaluates whether additional safeguards have been included in the study to protect the rights and welfare of vulnerable participants.
- The IEC requires at least one or more individuals who are knowledgeable about or have experience in working with these participants are part of the review process.
- New study submissions, amendment and continuing review applications involving vulnerable populations (except prisoners, which should be reviewed by the full board) may be reviewed by the convened board or by expedited review, as decided during initial review and as per SOP 04a/04b.

The research protocol involving vulnerable population will be reviewed according to current requirement and guidelines. The decisions are arrived at using the approved checklist for reviewers (Refer Annexure 1-5).

If the research includes a vulnerable population that is not covered in the above list or there are no national or international guidelines for ensuring protections, IEC will evaluate the research proposal to ensure that precautions are taken to protect the participants.

The protocol should be reviewed keeping in mind the following points:

- Measures to protect autonomy,
- Risk/benefit determinations with respect to the vulnerability
- Whether vulnerable participants are bearing unequal burden in research.

Member of the IEC who would be reviewing such protocols should be well versed with the potential harm or risk of such population participating in the study. The checklist for different vulnerable population provided in Annexure (A-F) should be used. Special justification is required for inviting vulnerable individuals to serve as research participants and, if they are selected, the means of protecting their rights and welfare must be strictly adhered to.

The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations. The central issue for the IEC to consider is whether the potential subject's ability to exercise free choice is limited in some way.

Reviewing research protocol involving vulnerable population: When researchers are likely to approach participants who lack the ability to consent, the IEC evaluates whether:

- ✓ The proposed plan for the assessment of the capacity to consent is adequate.
- ✓ Assent/surrogate consent of the participants is a requirement wherever possible, and, if so, whether the plan for assent/ surrogate consent is adequate.
- ✓ There is adequate room for ensuring the involvement of the LAR and/or impartial witness in the consenting process.
- ✓ When a research participant regains consciousness from unconscious state or is mentally competent to understand the study. If such an event is expected then procedures to address it should be spelt out in the informed consent form.

17.5 Responsibility

The IEC Secretariat is responsible for receiving, verifying, and managing the hard copies of the received research protocols pertaining to vulnerable groups based on new and evolving applicable regulations and guidelines as per the checklist.

The Secretariat should create a study specific file, distribute the packages and study assessment forms to the IEC members for review with the updated checklist (1-5), and communicate the review results to the investigators.

- It is the responsibility of the IEC Secretariat to maintain up-to-date tools (e.g. checklist) for review of research pertaining to vulnerable groups based on new and evolving applicable national and international regulations and guidelines.
- Maintain file for update-checklist (1-5) which conforms to recent / current applicable regulations and guidelines.

The Member Secretary will assign two or more members of the IEC who have a thorough understanding of the ethical review process and experience in the field of research to review such type of protocols. The reviewers should be familiar and trained in the concept of vulnerability and protections for participants with diminished autonomy.

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

IEC members are responsible for verifying, and reviewing the research protocols pertaining to vulnerable populations using study assessment form and checklist (Refer SOP17, Annexure 1-5).

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

IEC Members will review the protocol and the informed consent document or assent form (Refer SOP 4a.5.4).

The suggestions that are agreed upon by the IEC members present at the meeting will be discussed.

17.6 IEC Meeting

- The details of review procedures and communication of decision is described in detail in SOP05/V4
- Document review of risk assessment in IEC minutes for the protocols involving vulnerable population.
- IEC Member Secretary will minute the discussions

Reference

[1] Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants (Geneva 2011) - www.who.int/...guideline.../operational-guidelines-ethics-biomedical-... (last accessed 4 February 2013)

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

[3] ICMR's Ethical Guidelines for Biomedical research on Human Participants, ICMR (2006) - http://www.icmr.nic.in/ethical_guidelines.pdf

[4] Schedule Y (Drugs and Cosmetic Act 1940; amendment Jan 2013

[5] Good Clinical Practices for Clinical Research in India http://cdsco.nic.in/html/GCP.htm

[6] World Medical Association Declaration of Helsinki, http:// www.wma.net/en/30publications/10policies/b3

[7] ICMR-DBT Guidelines for Stem Cell Research 2012 (Draft), icmr.nic.in/stem_cell_guidelines.pdf (last accessed 4 February 2013)

[8] Code of Federal Regulations, http://www.hhs.gov / ohrp / humansubjects / guidance / 45cfr46.html

Annexure

Annexure 1	AX01/SOP 17/V4	Checklist - Requirements for Research Involving Children
Annexure 2	AX02/SOP 17/V4	Checklist - Requirements for Research Involving Pregnant or nursing women, Fetuses& nursing infant
Annexure 3	AX03/SOP 17/V4	Checklist - Research Involving Cognitively Impaired Adults
Annexure 4	AX04/SOP 17/V4	Checklist - Research Involving Students, Employees or Residents
Annexure 5	AX05/SOP 17/V4	Checklist - Considerations for Genetic Research

Annexure 1

AX1- V4/SOP 17/V4

Checklist –Requirements for Research Involving Children

Investigator IEC :

Study Title:

RISK DETERMINATION	BENEFIT ASSEMENT	IEC ACTION
□ Minimal (i)	With or without direct benefit	Approvable
□ Greater than minimal risk	Potential to child	Approvable
□ Greater than minimal risk	No direct benefit to individual but offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	Approvable case – by - case (ii) with special safeguards

(i) Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

(ii) Risk may not be more than a minor increase over minimal risk, consent of both parents required under normal circumstances.

(iii) Approval to proceed with this category of research must be made by the IEC with input from selected experts

	Yes	No	NA
Does the research pose greater than minimal risk to children?	☐	☐	☐
If yes: Are convincing scientific and ethical justification given?	☐	☐	☐
If yes: Are adequate safeguard in place to minimize these risks?	☐	☐	☐
Does the study involve normal volunteers?	☐	☐	☐

	Yes	No	NA
If yes: Is the inclusion of normal volunteers justified?	☐	☐	☐
Have appropriate studies been conducted on animals and adults justified?	☐	☐	☐
If No: Is the lack of appropriate studies conducted on animals and adults justified?	☐	☐	☐
Will older children be enrolled before younger ones?	☐	☐	☐
Is permission of both parents necessary?	☐	☐	☐
If Yes: Are conditions under which one of the parents may be considered: not reasonably available" described?	☐	☐	☐
If Yes: Are the conditions acceptable?	☐	☐	☐
Will efforts be made ensure that parents' permission to involve their children in research studies is free from coercion, exploitation, and /or unrealistic promises?	☐	☐	☐
Are provisions made to obtain the assent of children over 7 and, where appropriate, honoring their dissent?	☐	☐	☐
Are provisions made to protect participants' privacy and the confidentially of information regarding procedures?	☐	☐	☐
Are there special problems that call for the presence of a monitor or IEC member during consent procedures?	☐	☐	☐
Are special needs of adolescents such as counseling and confidentiality accounted for in the research design?	☐	☐	☐
Are there any special problems such as confidentiality and reporting that might arise in sensitive research about child abuse or sexual practices of teenagers?	☐	☐	☐
Does the research involve a which has implications for other family member ?(for example, genetic risk , HIV infection , Hepatitis C)	☐	☐	☐
If Yes: Are adequate mechanisms in place to deal with other members of the family?	☐	☐	☐
Should parents be required to be present during the conduct of the research? (Are proposed participants to be very young ? Are the procedures involved painful? Must subject stay overnight in the hospital when they otherwise would not have to?)	☐	☐	☐

Comments: _____

_____

Primary Reviewer Date

Annexure 2

AX2- V4/SOP 17/V4

Checklist - Requirements for Research Involving Pregnant or nursing women, Fetuses & nursing infant

Investigator: ***IEC #:***

Study Title:

Research Involving Pregnant or nursing women, Fetuses & nursing infant

RISK DETERMINATION	BENEFIT ASSEMENT	IEC ACTION
□ Minimal (i)	With or without direct benefit	Approvable
□ Greater than minimal risk	Potential benefit	Approvable
□ Greater than minimal risk	No direct benefit to individual but offer general knowledge about disorder and may benefit to the society or future generations are likely to benefit.	Approvable case –by-case (ii) with special safeguards

	Yes	No	NA
Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant or nursing women, nursing infant; and fetuses;	□	□	□
The risk to the fetus or nursing infant is not greater than minimal, or any risk to the fetus which is greater than minimal is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus or nursing infant;	□	□	□
Any risk is the least possible for achieving the objectives of the research;	□	□	□
The woman's consent or the consent of her legally authorized representative is obtained in accord with the informed consent provisions , unless altered or waived in accord with SOPs	□	□	□
The woman or her legally authorized representative, as appropriate, is fully informed regarding the reasonably foreseeable impact of the research on the fetus or resultant child;	□	□	□
If the research involves minors who are pregnant, assent and permission will be obtained in accordance with the Schedule Y and ICMR guidelines	□	□	□

	Yes	No	NA
No inducements, monetary or otherwise, will be offered to terminate a pregnancy;	☐	☐	☐
Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and	☐	☐	☐
Individuals engaged in the research will have no part in determining the viability of a fetus.	☐	☐	☐
Does this research promises therapeutic or preventive benefits (e.g. Example of such trials are, to test the efficacy and safety of a drug for reducing perinatal transmission of HIV infection from mother to child, trials for detecting foetal abnormalities and for conditions associated with or aggravated by pregnancy)	☐	☐	☐
Does the study involves discontinuation of nursing for the sake of participation in research Is the cessation of breast-feeding to the nursing child justified? Is breast feeding harmful to the infant? Does the research has provisions for compensation in terms of supplying supplementary food such as milk formula?	☐	☐	☐
Can this research be conducted in women who are not pregnant or nursing	☐	☐	☐
Does this research protect or advance the health of pregnant or nursing women or foetuses or nursing infants,	☐	☐	☐
Is this research related to termination of pregnancy and is as per the Medical Termination of Pregnancy Act, GOI, 1971. Does this research violate any provisions of the Medical Termination of Pregnancy Act, GOI, 1971	☐	☐	☐
Is this research related to pre-natal diagnostic techniques in pregnant women Is this research limited to detect the foetal abnormalities or genetic disorders as per the Prenatal Diagnostic Techniques (Regulation and Prevention of Misuse) Act, GOI, 1994 and not for sex determination of the foetus Does this research violate any provisions of the Prenatal Diagnostic Techniques (Regulation and Prevention of Misuse) Act, GOI, 1994	☐	☐	☐

THIS RESEARCH INVOLVES FETUSES AFTER DELIVERY

		Yes	No	NA
1.	Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to fetuses;	☐	☐	☐
2.	The individual(s) providing consent is fully informed regarding the reasonably foreseeable impact of the **research** on the fetus or resultant child;	☐	☐	☐
3.	No inducements, monetary or otherwise, will be offered to terminate a pregnancy;	☐	☐	☐
4.	Individuals engaged in the **research** will have no part in any decisions as to the timing, method, or procedures used to terminate pregnancy;	☐	☐	☐
5.	Individuals engaged in the **research** will have no part in determining the viability of a fetus.	☐	☐	☐

AND

A.	**Fetuses of uncertain viability**	**Yes**	**No**	**NA**
1.	Does the research hold out the prospect of enhancing the probability of survival of the particular fetus to the point of viability, and any risk is the least possible for achieving the objectives of the research;	☐	☐	☐
	OR			
	The purpose of the **research** is the development of important biomedical knowledge which cannot be obtained by other means and there will be no risk to the fetus resulting from the **research**;	☐	☐	☐
2.	The legally effective informed consent of either parent of the fetus or , if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained.	☐	☐	☐

And/or

B.	Nonviable fetuses	Yes	No	NA
1.	Vital functions of the fetus will not be artificially maintained;	☐	☐	☐
2.	There will be no risk to the fetus resulting from the research;	☐	☐	☐
3.	The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and	☐	☐	☐
4.	The legally effective informed consent of both parents of the fetus will be obtained in accord with the ICMR guidelines except that the waiver and alteration provisions do not apply. However if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable fetus will suffice to meet the requirements of this paragraph. The consent of a legally authorized representative of either or both of the parents of a nonviable fetus will not suffice to meet the requirements of this paragraph.	☐	☐	☐

Comments:

_____ _____

Primary Reviewer **Date**

Annexure 3

AX3- V4/SOP 17/V4

Checklist- Research Involving Cognitively Impaired Adults

- The purpose of this checklist is to provide support for IEC members or the Designated Reviewer when reviewing research involving cognitively impaired adults as participants.

  1. For review using the this checklist is to be completed by the Designated Reviewer to document determinations required by the regulations and protocol specific findings justifying those determinations and retained.
  2. For review using the convened IEC is to document determinations required by the regulations and protocol specific findings justifying these determinations.

1. **Research Involving Cognitively Impaired Adults in which there is Anticipated Direct Benefit to the subject** (All items must be "Yes")		
☐ Yes	☐ No	One of the following is true (Check the box that is true) • The risk to the participants is presented by an intervention or procedure that holds out prospect of direct benefit for the individual subject. • More than minimal risk to participants is presented by monitoring procedure that is likely to contribute to the participants well – being.
☐ Yes	☐ No	The risk is justified by the anticipated benefit to the participants.
☐ Yes	☐ No	The relation of anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.
☐ Yes	☐ No	The proposed plan for the assessment of the capacity to consent is adequate.
☐ Yes	☐ No	Assent is required of: (One of the following must be "**Yes**") One of the following is true (**Check box that is true**) ☐ All Participants ☐ All Participants capable of being consulted. ☐ None of the participants
☐ Yes	☐ No	The consent document includes a signature line for a legally authorized representative.

2. **Research Involving Cognitively Impaired Adults in which there is No Anticipated Direct Benefit to the subject** (All items must be "Yes")		
☐ Yes	☐ No	The proposed plan for the assessment of the capacity to consent is adequate.
☐ Yes	☐ No	The objectives of the trial cannot be met by means of study of participants who can give consent personally.
☐ Yes	☐ No	The foreseeable risks to the participants are low.
☐ Yes	☐ No	The negative impact on the subject's well-being is minimized and low.
☐ Yes	☐ No	The trial is not prohibited by law.
☐ Yes	☐ No	Participants have a disease or condition for which the procedures in the research are intended.
☐ Yes	☐ No	Participants will be particularly closely monitored.
☐ Yes	☐ No	Participants will be withdrawn if they appear to be unduly distressed.
☐ Yes	☐ No	The proposed plan for the assessment of the capacity to consent is adequate.
☐ Yes	☐ No	Assent is required of (One of the following must be "**Yes**") One of the following is true (**Check box that is true**) ☐ All Participants ☐ All Participants capable of being consulted. ☐ None of the participants
☐ Yes	☐ No	The consent document includes a signature line for a legally authorized representative.

Annexure 4

AX4- V4/SOP 17/V4

Checklist-Research Involving Students, Employees or Residents

Participants who are students, employees or residents require special considerations.

The proposed plan for the assessment of the capacity to consent is adequate.	☐ Yes	☐ No
Have the participants been assured that their status (education, employment, and/or promotion) will not be affected by any decision to participate or not?	☐ Yes	☐ No
Have the risks to participants been minimized?	☐ Yes	☐ No
Have participants been assured that participation is voluntary (no signs of coercion)?	☐ Yes	☐ No
Have participants been assured that confidentiality will be protected or maintained?	☐ Yes	☐ No

Annexure 5

AX5- V4/SOP 17/V4

Checklist - Considerations for Genetic Research

Investigator:
IEC#
Study Title:

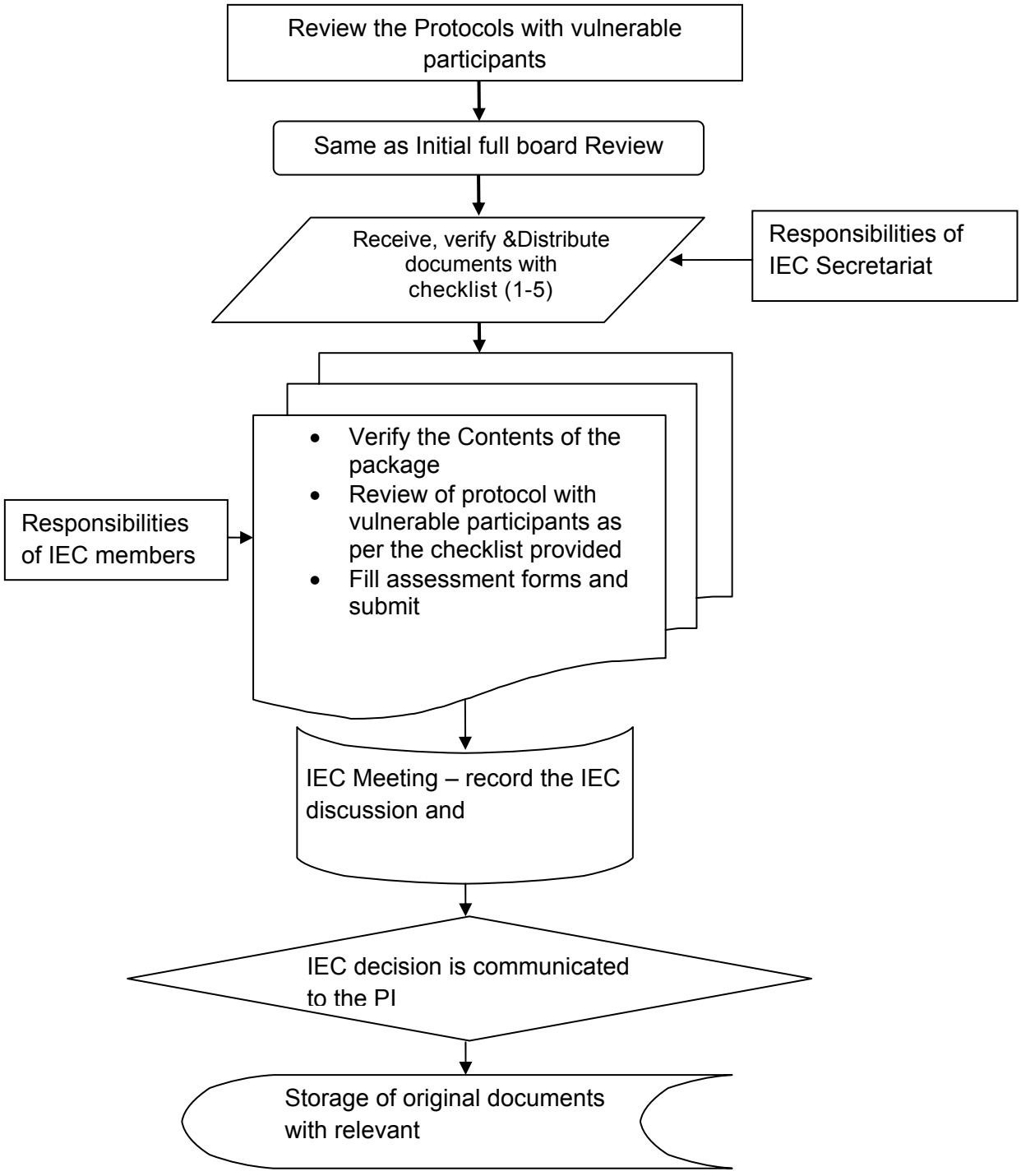
1. Will the samples be made anonymous to maintain confidentiality? If yes, stop here	☐ Yes	☐ No
2. Has the investigator established clear guidelines for disclosure of information, including interim or inconclusive research result?	☐ Yes	☐ No
3. Has the appropriateness of the various strategies for recruiting participants and their family members been considered?	☐ Yes	☐ No
4. Does the proposed study population comprise family members?	☐ Yes	☐ No
5. Will family members be implicated in the studies without consent?	☐ Yes	☐ No
6. Will the samples be destroyed in the future?	☐ Yes	☐ No
7. Is genetic counseling being offered?	☐ Yes	☐ No

Comments:

_____ _____

Primary Reviewer Date

Flow Chart


Review the Protocols with vulnerable participants
Same as Initial full board Review
Receive, verify &Distribute documents with checklist (1-5)
Responsibilities of IEC Secretariat
Responsibilities of IEC members
Verify the Contents of the package
Review of protocol with vulnerable participants as per the checklist provided
Fill assessment forms and submit
IEC Meeting – record the IEC discussion and
IEC decision is communicated to the PI
Storage of original documents with relevant

SOP History		
Version	**Type (draft/final)**	**Date**
V1	**Final**	**01/09/2009**
V1	**Final**	**01/01/2013**
V2	**Final**	**15/10/2013**
V3	**Final**	**01/05/2014**
V4	**Final**	**01/04/2016**