Institutional Ethics Committee

Standard Operating Procedures

VERSION 1.0 DATED 03/12/2019

Preface

The Institutional Ethics Committee (IEC) established in 2019 is responsible for the scientific, ethical and regulatory oversight of research conducted at Tomo Riba Institute of Health and Medical Sciences (TRIHMS) and serves to protect the rights and welfare of human subjects.

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

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

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

The ultimate mandate of these SOPs will be to further the cause of conduct and adherence to the highest standards of human research.

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Institutional Ethics Committee,
Tomo Riba Institute of Health & Medical Sciences
(IEC, TRIHMS)

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

SOP Code: SOP 01/V1 Date: 03/12/19 Pages: 1 to 13

1.1 Purpose
This SOP defines the process for writing, reviewing, distributing, and amending SOPs within the IEC, TRIHMS. The SOP also defines procedure for documentation, archival, retrieval, destruction of SOP to ensure that the latest SOPs are followed.

The SOPs will provide clear, unambiguous instructions to conduct activities of the IEC in accordance with the ICMR guidelines 2017, Schedule 'Y" (Drugs and Cosmetic Act 1940: Amendment 20th Jan 2005 Amendment 2017), WHO Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants 2011, and International Conference on Harmonization, Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance April 1996, Code Federal Regulations Title 21

1.2 Scope
This SOP covers the procedures of writing, reviewing, distributing, and amending SOPs within the IEC, TRIHMS and to define control of SOP documents at the IEC

1.3 Responsibility
It is the responsibility of the 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. It is the responsibility of the IEC Member Secretary and staff for maintaining control on all the SOPs.

The IEC Secretary is responsible for ensuring that the current approved version of the SOP is available on the Institute website. The SOP will bear the effective date. The IEC Secretary will notify all concerned user via email of document updates (recent version). For the user, electronic access will be limited to a read-only format, thereby protecting against unauthorized changes made to the document. When SOPs are revised, the IEC Secretary will inform the IT department to remove obsolete copies from the website and upload the current approved version of the SOP.

SOPs will be reviewed by the members of IECs. The Chairperson and Secretary of IECs will approve the SOPs. The SOPs will then be signed by the Director, TRIHMS 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 IEC Secretary 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 the 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, sign and date SOPs
- Return all out-of date SOPs to IEC office

Secretary 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, Secretary 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-V1/SOP01/V1). This Formulation of new SOP/ Revision of an SOP Form (AX5-V1/SOP01/V1) 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 all the three IEC committees, one or two committee members and administrative staffs as members of SOP team. This designated team will proceed with the task of the 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-V1/SOP01/V1)

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/V1 is SOP number 01 with V=version no.01

Each Annexure (AX) has unique code with format AXn–Vp/SOP xx/Vy. **e.g.** AX1–V1/SOP01/V1 indicates AX is Annexure, 1 is Annexure no. , V1 is version 01, belonging to the SOP 01/V1

Each SOP will be prepared according to the template for Standard Operating Procedures (AX2 – V1/SOP01/V1). 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 Secretary & Chairperson and Director, TRIHMS.

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 the 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, TRIHMS 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 –V1/SOP 01/V1)
- One complete original set of current SOPs will be archived in the SOP master file, by the IEC
  Secretary and maintained in the IEC Office.
- A copy of the SOP master file will be maintained in the individual offices of IEC and DSMU.

1.4.10 Review and request for revision of an existing SOP

- Any member of the IEC, Secretary 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-V1/SOP 01/V1)
- 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 Secretary assists the Member Secretary of the SOP at least once in every 3 years and records the dates of review in the SOP master file.

1.4.11 Document Control

Detailed instructions

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

Master copy- shall be an approved original copy of documents and Master copy shall be kept in the IEC office with access control.

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

Uncontrolled copies - shall be copy of master copy and Uncontrolled copies shall be kept in the IEC with access control. Uncontrolled copy is a reference copy of the master copy for the users such as researchers/research staff, sponsor, regulators and any other stake holders in research.
Uncontrolled copies shall be distributed only on request. The issuance log of uncontrolled copies will be maintained.

1.4.12 Manage and archive old SOPs

- Old SOPs should be retained and clearly marked “Obsolete” and archived in a file by the Secretary. The process of evolution of previous SOPs of the IEC will be documented in a defined format (AX3 –V1/SOP01/V1).

- The master copies of the superseded documents shall be labelled as ‘Obsolete'. The obsolete copies shall be retained by the IEC as per the archival SOP. A list of obsolete documents shall be prepared.

- Retrieved controlled copies of the superseded documents shall be destroyed as per SOP 10.

- Retrieval of uncontrolled copies shall not be done

AX1-V1/SOP 01/V1

List of SOPs of Institutional Ethics Committee

Sl No.	SOP TITLE	SOP CODE	Page Nos.
1	Preparing Standard Operating Procedures (SOPs): Writing, Reviewing, Distributing, Amending, Control of SOPs for the Institutional Ethics CODE Committee (IEC), TRIHMS	01/V1	
2(a)	Constitution of Institutional Ethics Committee, TRIHMS	02a/V1	
2(b)	Constitution of Data Safety and Monitoring Unit (DSMU), TRIHMS	02b/V1	
3	Management of Research Study Submissions	03/V1	
4	4a Full board Review of Submitted Protocol	04a/V1	
	4b Expedited Review of Submitted Protocol/Documents	04b/V1	
	4c Exemption from the Review for Research Projects	04c/V1	
5	Agenda Preparation, Meeting Procedures and Recording of Minutes	05/V1	
6	Review of Amended protocol/ Protocol related documents	06/V1	
7	Continuing review of study Protocols	07/V1	
8	Review of Protocol Deviation/ Violation / Non-Compliance/ Waiver	08/V1	
9	Review of Serious Adverse Events (SAE) Reports	09/V1	
10	Maintenance of Active Project Files, Archival/Disposal of closed files and Retrieval of documents	10/V1	
11	Documentation of the IEC activities	11/V1	
12	Review of study completion reports	12/V1	
13	Management of Premature Termination / Suspension / Discontinuation of the study/ Withdrawal of study before site initiation	13/V1	
14	Review of Request for Waiver of Written Informed Consent	14/V1	
15	Site Monitoring	15/V1	
16	Dealing with participants/patients requests and complaints	16/V1	
17	Reviewing Research Protocols Involving Vulnerable Populations	17/V1	
18	Review of Academic Clinical Trial	18/V1	
19	Training for IEC members	19/V1	
20	Assessment and Audit of IEC	20/V1	

AX2- V1/SOP01/V1
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-V1/SOP01/V1
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-V1/SOP01/V1

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-V1/SOP01/V1

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/YY)
Discussed in IEC Meeting hold on:-	
SOP revision required: Yes( ) No( )	
New SOP to be formulated: Yes ( ) No( )	
If no, why not ?	
Date of SOP revised:	
Date of SOP approved:	
Date SOP become effective:	

AX6-V1/SOP01/V1

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			

AX6-V1/SOP01/V1

List of obsolete documents

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

Institutional Ethics Committee,
Tomo Riba Institute of Health & Medical Sciences
(IEC, TRIHMS)

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

SOP Code: SOP 02a/V1 Date:03/12/2019 Pages: 14 to 40

Tomo Riba Institute of Health and Medical Sciences (TRIHMS) is the first medical college of the Govt. of Arunachal Pradesh. TRIHMS is the part of history of Arunachal Pradesh, being the first of its kind, state of art of 250 bedded hospital along with Medical College, equipped with most modern equipment, for the investigation and management of the poor patient of Arunachal Pradesh who are spread in so many kilometres of the state. In view of promoting & conducting quality medical research in the institution, the Director, TRIHMS in the year 2019, constituted the first Ethics Committees after due approval from Principal Secretary, Health and Family Welfare Dept., Government of Arunachal Pradesh. All research proposals will be scientifically evaluated and approved by institutional Ethics Committee (IEC) TRIHMS.

All the research proposals which would be primarily carried out in TRIHMS, Naharlagun will be reviewed by the IEC, TRIHMS located at TRIHMS, Naharlagun.

Name and Address of the IEC TRIHMS:

Institutional Ethics Committee, TRIHMS

College Main Building,

Naharlagun, Arunachal Pradesh - 791110

Phone: 0360-2350331

Fax : 0360-2350791

Email- trihmsap@gmail.com and iectrihms@gmail.com

The IEC of TRIHMS has a common mandate and functions according to IEC, TRIHMS SOPs. In case the number of IECs increases in future, they shall function in accordance with the existing SOPs.

The Institutional Ethics Committees (IECs) of TRIHMS are constituted by the Director TRIHMS, after the due approval from Principal Secretary, Health and Family Welfare Dept., Government of Arunachal Pradesh. The Principal Secretary, Health and Family Welfare Dept., Government of Arunachal Pradesh who serves as appellate has the power to dissolve the IEC or reappoint the IEC.

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 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 the 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 TRIHMS.
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 endeavour to be a national standard of reference.
6. To issue and periodically, update and revise SOPs and guidelines for effective functioning of IECs as and when necessary.
7. Continuing the education in clinical research bioethics by holding 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 TRIHMS

- The IEC endeavours 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 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 establishes its own Standard Operating Procedures based on the ICMR guidelines , Schedule Y (Drugs and Cosmetics Act 1940 WHO Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants and ICH-GCP.
- The IEC is guided in its reflection, advice and decision by the Ethical principles expressed in the Declaration of Helsinki and CFR 45 (US FDA)
- It makes further reference to the International Ethical Guidelines for e.g. The Nuremburg Code (1945), the Belmont Report 1979, the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Geneva 2002), and the European Convention on Human Rights and Biomedicine.
- IEC seeks to fulfil the requirements for international assurances and is established and functions in accordance with the national law and regulations.

2.6 Composition

- IEC is composed of a minimum of 7, and maximum of 15 members. The members are selected so as to have an adequate representation of different specialities in TRIHMS. It includes scientific and non-scientific members, clinicians and non - clinicians, a clinical pharmacologist, members of the community/ NGO, a lawyer-expert in ethics, a social worker / layperson / patient representative to represent different points of view.
- The Committees will comprise of Chairperson, Co-Chairperson, Member Secretary, and other active members who represent an appropriate balance of professional, ethical, legal, cultural, educational, and community interests.
- The Committee should have adequate representation of age, gender, community, etc. to safeguard the interests and welfare of all sections of the community / society. Members are expected to be aware of local, social and cultural norms, as this is the most important social control mechanism.
- The members should have various backgrounds to promote complete and adequate review of research activities commonly conducted by TRIHMS.

Composition of IEC

The composition should be as follows:-

1. Chairperson (not – affiliated to TRIHMS)

2. Deputy Chairperson (not – affiliated to TRIHMS)

3. Member secretary (TRIHMS Staff member)

4. 1-2 Clinicians (not affiliated to TRIHMS)

5. Minimum three Doctors (TRIHMS staff members)

6. Clinical Pharmacologist (TRIHMS Staff member)

7. One legal expert or medico-legal expert

8. One representative of social scientist / philosopher / ethicist / theologian/ welfare association

9. One representative of non-governmental voluntary agency/ members of the community

10. One lay person from the community (non-affiliated)

2.6.1 Membership

The Director, TRIHMS, appoints the Chairperson, and the Member Secretary of the IEC with due approval of Principal Secretary, Health and Family Welfare Dept., Government of Arunachal Pradesh. All IEC members will be appointed by Director TRIHMS in consultation with the Chairperson and Member Secretary of the IEC and will be approved by Principal Secretary, Health and Family Welfare Dept., Government of Arunachal Pradesh. 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/ doctors 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, Dean, Administrative officers etc. who are responsible for business development will not serve as members.
- New members will be identified according to the composition requirement specified in Section 2.6 of this SOP provided that 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, TRIHMS will be appointed for duration of 5 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 and acceptance of respective member for the same.
- In case of the resignation/discontinuation of the Member Secretary, Chairperson or member, a replacement will be appointed by the Director, TRIHMS with consultation with IEC Chairperson and Secretary 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 5 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 before the completion of tenure. Member secretary designate should be inducted into the IEC as an observer before he/she takes on the mantle in the new IEC. Other member- designates 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–V1/SOP02a/V1) and terms of reference 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 by the Director, TRIHMS with consultation with IEC Chairperson and Secretary. IEC members who decide to resign must provide the Director, TRIHMS along with Secretary and Chairperson, IEC, the written notification/email of their proposed resignation date at least 30 calendar days prior to the next scheduled meeting. In case of resignation, Director, TRIHMS 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. Then respective appointments will be made by Director, TRIHMS in consultation with the Member Secretary and Chairperson, IEC.

2.6.2. d Termination / Disqualification procedure

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

- Conduct unbecoming of 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 without prior intimation and subsequent review of the membership by the IEC; if deemed necessary, the IEC may decide to terminate the membership. Chairperson, IEC may make a recommendation to the Director, TRIHMS, for necessary action.
- Relocation to another city or any such matter.

In all such circumstances, Director, TRIHMS 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. The appointment letter issued to all members should specify the Terms of Reference (TOR) i.e. Role and responsibility of the member in the committee etc.
- Members must submit a one page current CV, MCI Registration No. (if applicable) and training certificates in Ethics and valid 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, TRIHMS SOPs.
- Members are required to sign the Confidentiality / Conflict of Interest Agreement (AX1-V1/SOP 02/V1) 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 is 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 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-V1/SOP02a/V1) 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 TRIHMS Institute, 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 of TRIHMS'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 respect among the IEC members. The Chairperson shall ensure active participation of all members (particularly non-affiliated, non-medical/ non- technical members) in all discussions and deliberations. The Chairperson shall ratify minutes of the previous meetings, handle complaints

against researchers and EC members, conflict of interest issues and requests for use of EC data etc.

Deputy-Chairperson

The IEC Deputy-Chairperson should be a highly respected individual from outside TRIHMS, 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 TRIHMS, committed to the task of coordinating and managing the activities of the committee. He/she will be responsible for scheduling the meetings, describing the agenda and ensuring that the function of the committee is conducted as per the norms and policies described in this SOPs.

- Specific roles of Member Secretary (As per ICMR Guidelines 2017)
- Member Secretary will be responsible for ensure training of EC Secretary and EC members.
- Ensure SOPs are updated as and when required.
- Ensure adherence of EC functioning to the SOPs.
- Prepare for and respond to audits and inspections.
- Ensure completeness of documentation at the time of receipt and timely inclusion in agenda for EC review.
- Assess the need for expedited review/ exemption from review or full review.

In the absence of the Member-Secretary of IEC, the Member Secretary of other IECs or DSMU Secretaries may function as acting Member 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 IEC Secretariat

The Secretariat is composed of the Member Secretaries of the IECs, and the administrative support staff. The supporting staff consists of staff members of TRIHMS appointed by the Director, TRIHMS. The Director, TRIHMS has deputed the responsibility of issuing terms of reference for the IEC staff to the Member Secretary, IEC.

The IEC Administrative Staff: Working Rules

1. The administrative support to the IEC will comprise of private secretary, administrative assistants, IT support and attendant/s or /helper/s ,the support staff will assist 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 meetings and

will be recorded in minutes. These will be forwarded to the Director, TRIHMS for approval / decision.

2. The administrative staff will be appointed by conducting formal interviews as per TRIHMS administrative policy.

Duties of the IEC Administrative Officer

- Review of new research applications for consistency, completeness, and compliance with the regulations and institutional guidelines prior to convene IEC review.
- Providing necessary administrative support for IEC related activities to the Member Secretary, IEC.
- Organizing IEC meetings regularly.
- Preparing the agenda and drafting minutes of the meetings.
- Organizing an effective and efficient tracking procedure for each proposal received.
- Updation of the software system and the IEC online portal.
- Preparing, maintaining and distributing study files.
- Supervision of the maintenance, archival, and shredding of the study files.
- Corresponding with the IEC members, external experts and investigators on all IEC related matters.
- Arranging training for study personnel and IEC members.
- Receipt of IEC processing fees for pharma-funded projects and the issue of official receipts for the same.
- Supervision of the pre and post arrangements of IEC meetings.
- Answering queries of the investigators.
- Supervision of filing of study related documents.
- Quality check of all study related documents submitted to IEC as well as correspondence from IEC.
- Preparation for accreditation, audits.
- Organizing training for investigators, key study personnel, IEC members, and IEC staff.
- Participating in the development and subsequent implementation of SOPs.
- Participating in, or presenting, research related education sessions
- Initiating research studies in ethics/audits

Duties of the Administrative Assistant

- Drafting letters, receipt, voucher preparations etc
- Template preparations as instructed by the IRB administrators.
- Liaising with other departments.
- Meeting attendance preparation/ preparation of dispatch folders.
- Hospitality management during IEC meetings.

3. Duties of the attendant/s /helper/s:

a. Assisting the Secretary 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. Shredding of the closed files as per SOP 10

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

2.8 Roles and Responsibilities of the IEC members

- The members' primary responsibilities will be to determine 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 and other documents pertaining to the study.
- Submit assessment forms to the IEC Secretary.
- Review progress reports and monitor ongoing studies.
- Review Serious Adverse Events (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.
- Monitoring by IEC members, if required
- 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 Secretary, periodically

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

Clinician and Doctors:

- Scientific review of protocols including review of the intervention, benefit-risk analysis, research design, methodology, sample size, site of study and statistics
- Ongoing review of the protocol (SAE, protocol deviation or violation, progress and completion report)
- Review medical care, facility and appropriateness of the principal investigator, provision for medical car, management and compensation.
- Thorough review of protocol, investigators brochure (if applicable) and all other protocol details and submitted documents.

Basic Medical Scientist:

- Scientific and ethical review with special emphasis on the intervention, benefit-risk analysis, research design, methodology and statistics, continuing review process, SAE, protocol deviation, progress and completion report
- For clinical trials, pharmacologist to review the drug safety and pharmacodynamics.

Legal experts:

- Ethical review of the proposal, ICD along with translations, MoU, Clinical Trial Agreement (CTA), regulatory approval, insurance document, other site approvals, researcher's undertaking, protocol specific other permissions, such as, stem cell committee for stem cell research, HMSC for international collaboration, compliance with guidelines etc.
- Interpret and inform EC members about new regulations if any

Social Scientists /philosopher /ethicist /theologian / member of welfare association and representative of NGO agency/ members of the community

- Ethical review of the proposal, ICD along with the translations.
- Assess impact on community involvement, socio–cultural context, religious or philosophical context, if any
- Serve as a patient/participant/ societal / community representative and bring in ethical and societal concerns.

Layperson:

- Ethical review of the proposal, ICD along with translation(s).
- Evaluate benefits and risks from the participant's perspective and opine whether benefits justify the risks.
- Serve as a patient/participant/ community representative and bring in ethical and societal concerns.
- Assess on societal aspects if any

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

In the absence of the Chairperson, the Deputy-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/ Doctors

    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;

2.10 Decision making procedures

- 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, or written opinion from respective member as determined by the Chairperson, IEC.
- All members of the IEC including the Chairperson and the Member Secretary present in the room have the right to vote/express their decision and should exercise this decision. If there is equality of votes, the chair will have a casting vote.
- 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 managed, and it has the final authority to determine whether a conflict of interest has been managed 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, 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.

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, TRIHMS and accreditation agencies. 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-TRIHMS IEC members and independent consultants are given honorarium as

per IEC TRIHMS recommendations.

AX1-V1/SOP02a/V1

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 TRIHMS'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 TRIHMS Date

Tomo Riba Institute of Health & Medical Sciences

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-V1/SOP02a/V1

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-V1/SOP02a/V1

Confidentiality Agreement Form for Observer Attendees/Auditor

I, _____, understand that I am allowed to observe IEC activities and attend the IEC meeting/ scheduled during their tenure/period as an Observer/Auditor.

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

In the course of the observership /audit 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

AX7-V1/SOP02a/V1

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

This is in recognition of the fact, that I, Dr/Mr/Ms./Mrs …… herein referred to as the "Undersigned", have been appointed as IRB Administrator/ Administrative Assistant/ Administrative staff of the Institutional Ethics Committee and would be required to handle the administrative activities of the IRB as per the SOP mandate in a humane, scientific and ethical manner according to the applied national, local regulations, institutional policies and guidelines.

Whereas, the appointment of the Undersigned as IRB Administrator/ Administrative Assistant/ Administrative staff 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 the Undersigned is to conduct the day-to-day activities of the IRB in the capacity of IRB Administrator/ Administrative Assistant/ Administrative staff as defined by the IEC SOP.

The Undersigned, as part of the Administrative support staff 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 the Administrative support staff 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 the performance of this agreement is consistent with TRIHMS's policies and any contractual obligations it may have to third parties.

_____ _____

Undersigned Signature Date

Conflict of Interest

The Undersigned recognizes that the potential for conflict of interest shall always exist but has faith in the IEC and the Chairperson to manage the conflict issues so that the ultimate outcome is the protection of human participants.

In accordance with the policy of the IEC, the Undersigned shall not participate in IEC meeting proceedings in which there exists a conflict of interest, except to provide information as requested by the IEC.

The Undersigned shall immediately disclose to the Chairperson of the IEC, any actual or potential conflict of interest that may exist in relation to any particular proposal submitted by the Undersigned for review by the Committee, and abstain from participation in discussions or recommendations in respect of such proposals.

The Undersigned shall immediately disclose to the Chairperson of the IEC all personal conflicts of interest and conflicts of interest of spouses/domestic partners and dependent children.

Agreement on Confidentiality and Conflict of Interest

- I, the Undersigned, in the course of my activities as staff of the IEC Secretary, may be provided with confidential information and documentation (which will be referred to as the "Confidential Information").
- I, the Undersigned, 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 and not to use the Confidential Information for any purpose outside the IEC's mandate, and in particular, in a manner which would result in 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 IRB Administrative staff.
- I, the Undersigned, agree to immediately inform the Committee any conflict of interest that I may have and recuse myself from the IEC meeting proceedings and leave the room while the discussion is ongoing."
- I, the Undersigned, agree to inform the Committee of all personal conflicts of interest and conflicts of interest of my spouses/domestic partners and dependent children.

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

Name of the dependent children (if applicable) - _____

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

_____ _____

Undersigned Signature Date

_____ _____

Director of the TRIHMS Date

Tomo Riba Institute of Health & Medical Sciences

Financial Disclosure Form

8. 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. _____

9. 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. _____

10. 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. _____

11. 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. _____

12. 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. _____

13. 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. _____

14. 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

Institutional Ethics Committee,
Tomo Riba Institute of Health & Medical Sciences
(IEC, TRIHMS)

Title: Constitution of Data Safety and Monitoring Unit (DSMU), TRIHMS

SOP Code: SOP 2b/V1 Date: 03/12/2019 Pages: 41 to 49

The Data Safety Monitoring Unit (DSMU) is a unit of the IEC comprising of clinicians of varied expertise from the hospital, supported by IEC staff with a primary responsibility to review serious adverse events, safety reports and annual status reports of the projects approved by the IEC. This unit reports to the IEC.

The Data Safety Monitoring Unit is a unit of the IEC essentially responsible for monitoring IEC approved projects, to ensure patient safety and assess data during the course of the study in a manner that contributes to the scientific and ethical integrity of the study.

DSMU- I based in TRIHMS will function as a unit of the IEC for TRIHMS (IEC-I & II).

2.2 Purpose

The DSMU has been established to enhance the quality of the ongoing research which has been approved by IEC by safety review, periodic monitoring and annual review.

2.2 Mandate

As first Medical college of Arunachal Pradesh, the TRIHMS needs to ensure that research data generated by the investigators are of high quality, reliable and verifiable. To accomplish this objective, the DSMU is charged with the mission of developing and implementing quality assurance procedures to monitor the overall progress of institutional clinical trials and ensuring adherence to procedural requirements.

This includes -

- Review of overall progress of IEC approved clinical trials/studies to ensure the safety of participants.
- Checking the enrollment to ensure that the projected accrual goals are met on a timely basis and do not fall below minimum acceptable standards.
- Serious adverse events and off-site serious adverse events are appropriately monitored and reported to the IEC.
- Ensure that eligibility criteria are followed as per IEC approved study protocol and risk-benefit ratio to the patient remains acceptable.
- Enhance the quality of the research by providing the investigator with constructive criticism.
- Provide regular reports to the Institutional Ethics Committee

2.3 Scope

This Standard Operating Procedure (SOP) describes the Terms of References (TOR), which provide the framework for constitution, responsibilities, and activities of the Data Safety and Monitoring Unit.

2.4 Responsibility

The DSMU has following responsibilities-

- Assess and evaluate Serious Adverse Event reports (SAEs) on all trials being conducted at TRIHMS.
- Monitor the overall progress of institutional clinical trials/studies and ensure adherence to protocol specific procedural requirements.
- Ensure that the safety of participants, validity of data and projected accrual goals are maintained.
- Provide regular reports (monitoring) to the Institutional Ethics Committee.
- Creation, development, revision and implementation of guidelines for the DSMU.
- Continuing education and training programs to ensure that DSMU members are qualified to perform their specific duties.

2.5 Scientific and Ethical Basis

Refer section 2.5 of SOP02a/V1_Constitution of IEC

2.6 Composition

- The DSMU will be multidisciplinary including medicine, surgery, oncology, pharmacology, community medicine and basic scientists.
- The Members of DSMU will be trained in causality assessment as per the regulations to routinely implement them in assessing the relatedness of adverse events.
- All DSMU members will be employees of TRIHMS
- The Secretary and Joint Secretary of DSMU will be members of Institutional Ethics Committee.

2.6.1 Membership

The Director, TRIHMS will appoint the Secretary, DSMU. All members and Jt-Secretary will be appointed by the Director TRIHMS in consultation with the Secretary, DSMU.

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 of the DSMU 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.

The following qualities are sought in DSMU 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 DSMU, TRIHMS will be appointed for the duration of 3 years.
- The appointment procedure for membership will be followed so that it allows for continuity, development and maintenance of expertise within the DSMU, 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 Member Secretary of the DSMU.
- In case of the resignation/discontinuation of member, a replacement will be appointed by the Director, TRIHMS in consultation with the Secretary, DSMU for the remaining term of the existing Data Safety Monitoring Unit.

2.6.2. b Renewal

- The membership will be renewed after the stated term of 3 years.
- The process of renewal will be as follows :
- Selection of Secretary, DSMU and other members will be done at least 3 months and 1 month in advance respectively. Secretary, DSMU designate will be inducted into the DSMU as an observer before he/she takes on the mantle in the new DSMU. Other members designate may attend the DSMU meeting as observers before starting their tenure as DSMU members.
- Designated members of the DSMU who wish to attend DSMU meetings as observers should read, understand, accept and sign the agreement contained in the Confidentiality / Conflict of Interest form **(AX2 – V1/SOP02a/V1)** at the beginning of the DSMU meeting and/or before tasks of the DSMU 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 by Secretary, DSMU.

2.6.2. c Resignation / Replacement procedure

The members who have resigned may be replaced at the discretion of the Secretary, DSMU. DSMU members who decide to resign must intimate the Member Secretary, DSMU,in writing of their proposed resignation, 30 days in advance of the forthcoming DSMU meeting. In case of resignation, Member Secretary, DSMU would appoint a new member before the next scheduled DSMU meeting.

2.6.3 Conditions of Appointment

- Members must accept the appointment in writing.
- Members must submit a one page CV and training certificates in Ethics and 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 TRIHMS SOPs.
- Members are required to sign the Confidentiality / Conflict of Interest Agreement (AX1-V1/SOP 02/V1) 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 DSMU in the course of its work. All DSMU members shall disclose in

writing to the DSMU 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 a DSMU member holds an economic interest in the research) or non-financial in nature (such as when a DSMU 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.
- None of the members of DSMU is allowed to serve on a monitoring team with a conflict of interest, indirect or direct, as previously defined, with respect to the study being monitored.

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 DSMU member in reviewing the SAEs of 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.

2.7 Office Bearers

The DSMU will have the following office bearers who have the expertise and professional qualifications to review the study related documents submitted (On-Site and Off-Site SAEs, Monitoring report, Deviation, Continue Review Applications/ Annual status reports etc)

2.7.1 Secretary

The Secretary, DSMU will be a staff member of TRIHMS, 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, finalizing the minutes and ensuring that the function of the DCMSC is conducted as per the norms and policies described in this SOPs. Secretary, DSMU will review all submitted SAE's, CRA/ASR and monitoring reports. The Secretary or Jt Secretary, DSMU will discuss the SAEs and the DSMU minutes will be ratified in the next earliest respective full board meeting of IEC. The Secretary and Joint Secretary of DSMU will be members of TRIHMS IECs.The minutes of the DSMU meeting of the month is presented to the full board IEC meeting by the DSMU Secretaries.

In the absence of the secretary of DSMU, the Jt-Secretary of DSMU will function as acting Secretary for routine DSMU work as well as for the meeting.

Jt-Secretary

The DSMU Jt-Secretary will be designated the same responsibilities as that of the Secretary so as to manage the DSMU and the matters brought before it with fairness and impartiality, in the absence of the Secretary and in matters where the member secretary has a conflict of interest.

2.7.3 Secretary

The Secretary is composed of the Secretary and Jt secretary, DSMU, and the administrative supporting staff. The supporting staff consists of staff members of TRIHMS appointed by the Director, TRIHMS.

The Secretary shall have the following functions:

- Organization of an effective and efficient tracking procedure for each SAE/status report received
- Organization of regular DSMU meetings. .
- Preparation of the agenda and the minutes of the meetings
- Maintenance of the DSMU records.
- Communication with DSMU members and PIs.
- Arrangement of training for personnel and DSMU members.
- Assign monitoring to DSMU members on regular basis or as and when needed.

The DSMU Administrative Staff: Working Rules

1. There will be DSMU Coordinator/s and attendant/s /helper/s who will help the DSMU Secretary in executing functions of the DSMU. Additional staff may be appointed and duties assigned as and when deemed necessary by the DSMU.
2. The administrative staff will be appointed by conducting formal interviews as per TRIHMS policy.

Duties of the DSMU Coordinator:

- Organizing DSMU meetings regularly.
- Preparation of the agenda and drafting minutes of the meetings.
- Updating safety / study data in the system on regular basis.
- Maintaining DSMU records.
- Communicating with DSMU members and PIs.
- Accepting CRA/ASR, on site & Offsite SAE's and monitoring reports from PI/Co-ordinators/ Members.
- Sending SAE's to the assigned reviewers
- Sending monitoring reminders to Monitors (DSMU members) and PI's on regular basis.
- Arranging training for personnel and DSMU members.
- Answering queries of the investigators.
- Sending CRA reminders to PI's on regular basis according to the due date.
- Preparation for accreditation, audits
- Participate in the development and subsequent implementation of SOPs

3. Duties of the attendant/s /helper/s

a. Assisting the Secretary in arranging the DSMU meetings.

b. Dispatching the DSMU letters to the investigators.

c. Filing study related documents.

d. Archiving and maintaining the study files

e. Corresponding with the DSMU members.

The DSMU staff will report to the Secretary, DSMU./IEC The office timings for the DSMU staff will be as per TRIHMS rules and regulations. The staff will avail leave as per TRIHMS norms.

2.8 Roles and Responsibilities of the DSMU members

The member's primary responsibilities will be reviewing serious adverse event reports and conducting regular monitoring of ongoing projects.

- Participate in the DSMU meetings.
- Monitor SAEs and recommend appropriate action(s).
- Monitor ongoing studies and provide report to the DSMU.
- Maintain confidentiality of the documents and deliberations of the DSMU meetings.
- Declare conflict of interest before reviewing the SAE and monitoring the projects, if any (as per point 2.6.3 of this SOP)
- Carry out work delegated by the 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 DSMU Secretary.

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 Secretary, the Jt-Secretary will conduct the meeting. In the absence of both, a member who is selected by secretary will conduct the meeting as the Acting Secretary.

2.9 Education for DSMU Members

All DSMU members must be conversant with ICMR Guidelines for Research involving Human Subjects, Schedule Y of Drugs and Cosmetics Act, ICH-GCP guidelines, CIOMS and CTCAE grading guideline and will undergo continuing education.

2.10 Annual activity report

The Secretary, DSMU shall prepare an annual activity report of the DSMU for submission to the Director, TRIHMS. This shall include:

• A quantitative evaluation of the activities of the unit in a year.

• List of SAE's reviewed by unit.

• List of site monitoring done by the unit.

• List of Continuing review application received by the unit.

2.11 Meetings:

DSMU will meet on the first/second Tuesday of every month at 9.00 a.m.

In case the day is a public holiday or the IEC meeting date is prior to DSMU meeting, an alternate date and time will be decided. The DSMU meeting will be usually conducted before IEC meeting. The minutes of the DSMU meeting for SAE review will be presented by the DSMU Secretary/ Joint Secretary and the decisions will be ratified in the IEC meeting.

Institutional Ethics Committee,
Tomo Riba Institute of Health & Medical Sciences
(IEC, TRIHMS)

Title: Management of Research study Submissions

SOP Code: SOP 03/V1 Date: 03/12/2019 Pages: 50 to 112

3.1 Purpose

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

3.2 Scope

The scope includes the following -

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

3.3 Responsibility

It is the responsibility of the IEC Secretary 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
- Submission of Serious Adverse Events and Deviations/Violations
- Any other documents

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

3.4.2 Verification of Submission

The IEC Secretary has created an online system (email id : iectrihms@gmail.com) for submission of protocols and other study related documents. It is mandatory to make online submission of new research proposals.

On receipt of the study related documents via email, IEC Administrators will scrutinize the documents for the completeness of the online submission. The scope of administrative review is as enlisted:

- Check the submissions for initial review as per checklist, (AX2-V1/SOP 03/V1) to ensure that all mandatory forms and documents are submitted.
    - Submission should include
        - Project submission Form (AX1-V1/SOP 03/V1)
        - Study protocol
        - Other related documents necessary for initial review (AX 2-V1/SOP03/V1)
- *Notify* the investigators, will receive an acknowledgement mail from the office of IEC TRIHMS on successful submission of Project protocol.
- *Check* completeness of hard copy of the research proposal submitted with necessary information and signatures at all designated places in the submission form.
- *Stamp*, sign & date on the cover letter confirming receipt of the documents.
- *Record* the completeness of submission on document receipt form (AX 3- V1/SOP03/V1) and inform the investigators for necessary action
- *Ensure* payment of Institutional Ethics Committee processing fees for all Pharmaceutical sponsored clinical trials.
- *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.

<u>The following points will be considered while scrutinizing a research application:</u>

- A fee of Rs. 25,000/- + applicable GST will be levied for IEC initial review of Pharma protocols.
- A fee of Rs. 5,000/- + applicable GST will be levied for review of protocol amendments (major) for ongoing study-
- The fees may be paid online via NEFT transfers, as cheque or demand draft drawn in favour of "TRIHMS".
- One hardcopy of the IEC form (duly signed) and other study related documents as per the checklist (AX 2-V1/SOP 03/V1) is requisitioned for all applications including thesis, investigator-initiated studies and pharma-sponsored studies.
- Additional hard copies if required should be submitted by the PI.
- Soft copy of vernacular versions the ICFs and questionnaires uploaded online shall be accepted only in .pdf format
- The running project number, study title, principal investigator, type of study and
- duration of project will be labeled on each project file.
- All correspondence from and with the IEC Secretary, for the project, should quote 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-V1/SOP 03/V1)

1. Project Submission Form

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

2. Essential Documents

a) Study protocol
b) Lay summary-Provide a non-scientific summary of the proposal, including a statement about the importance of the question the research application will address, the relevance of the research to your country or region, and the potential impact of the study results.
c) Case Record Form
d) Informed Consent Documents- Participant Information Sheet & Informed Consent Forms (ICFs) for adults. For studies involving children, parent information sheet and consent form and child information sheet and assent form are mandated in case of children between age 7-18 years of age.
e) English, Hindi and local language ICDs are to be mandatorily submitted to IEC. ICDs in other languages may be submitted if required by the study [Refer (AX4- V1/SOP03/V1)].
f) Application for waiver of consent (if applicable)
g) Audio video informed consent (if applicable)
h) Investigator's Brochure (if applicable)
i) Package insert/product insert (if applicable)
j) Questionnaires (if applicable)
k) Agreement to comply with national and international GCP protocols for clinical trials
l) Regulatory clearance from appropriate regulatory authorities i.e. Drugs Controller General India (DCGI) approval/ICMR/Health Ministry Screening Committee(HMSC) (if applicable)
m) For national/international collaborative study Draft/Final Memorandum of Understanding (MoU) between the collaborating institutes
n) Draft/Final Clinical Trial Agreement (CTA)(if applicable)
o) Draft/Final Material Transfer Agreement(MTA) if applicable
p) Insurance/Indemnity policies, indicating who are covered(if applicable)
q) Participant recruitment and enrollment procedures/advertisement(if any)
r) Documentation of clinical trial registration (if applicable)
s) Decision of other Ethics Committees (If required / asked for)
t) One page, recent, signed and dated curriculum vitae of the investigators indicating qualifications and relevant experience.
u) APMC / MCI registration certificate of the investigators (if applicable)
v) Good Clinical Practice Certificate/Training certificate in clinical research
w) Any other important information relevant to the study
x) Cover letter enlisting all the documents submitted.

3.6 Minor revisions of study after initial review for approval

- Minor modifications submitted after initial review of the research proposal that do not alter the risk-benefit assessment for the research and do not require substantial changes in protocol and informed consent document fall under the category of IEC decision **"revision with minor modifications/amendments"**

- PI will submit 1 copy of the revised study related documents along with justification for modification, and clearly highlighted / demarcated sections which have undergone change. The additional hard copies if required should be submitted by the PI.

- The IEC Secretariat will verify the completeness and reconfirm that the copies contains the revisions 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 Major revisions of study after initial review for approval

- Major modifications submitted after initial review of the research proposal that may alter the risk-benefit assessment for the research and require substantial changes in protocol and informed consent document fall under the category of IEC decision **"revision with major modifications for resubmission"**

- PI will submit 1 copy of the revised study related documents along with justification for modification, and clearly highlighted / demarcated sections which have undergone change. The additional hard copies if required should be submitted by the PI.

- The IEC Secretariat will verify the completeness and reconfirm that the copies contain the revisions 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

3.8 Post approval- Research Protocol Amendments and other study related documents

- Investigators who may wish to modify or amend their approved protocols and/or other study related documents must seek IEC approval

- The PI should submit 1 hard copy + soft copy of the amended documents. Additional hard copies if required should be submitted by the PI.

- The IEC Secretariat will verify the completeness of the submission.

- The PI should highlight the modification/s in the amendment, and provide a summary of changes. PI should also indicate whether these changes would entail change in the ICF as per the form.

- The Member Secretary in consultation with Chairperson will decide whether to initiate:

  - Full board review or
  - Carry out an expedited review in case of minor administrative amendment

  This process is further elaborated in SOP 06/V1.

3.9 Annual Continuing Reviews of Approved Research Studies

- The DSMU on behalf of the IEC, will send reminders for annual report to individual PI at least 90 days prior to lapse of approval.

- The DSMU will receive a copy of Annual Status/ Continuing Review Report in the prescribed format and related documents (as per SOP 07/V1) for the approved research study.

- The IEC Secretariat will verify the completeness of the Continuing Review Application Form (AX1-V1/SOP07/V1) /Progress report. The IEC Secretariat will sign and date the documents.

- The progress or continuing review application will be discussed in the Full Board meeting of IEC or expedited review meeting of the IEC.

3.10 Research study Completion/ Premature Termination / Suspension / Discontinuation of the study

- The DSMU on behalf of the IEC will send reminders for annual status report to Individual Principal Investigators.
The IEC will receive a copy of Study Completion Report / Premature Termination / Suspension / Discontinuation of the study in the prescribed format (as per SOP 12/V1 & SOP13/V1).
• The IEC Secretariat will verify the completeness of the Study Completion / Premature Termination / Suspension / Discontinuation of the study (SOP12/V1 & SOP 13/V1) filled by the PI.
• The Study Completion / Premature Termination / Suspension / Discontinuation of the study report will be discussed in Full Board/ Expedited meeting of IEC.

3.11 Submission of Serious Adverse Events and Deviations/Violations

- The IEC secretariat will receive a copy of SAE and Deviations and Violations in the prescribed format (as per SOP 9/V1 & SOP8V1)

- The IEC Secretariat will verify the completeness of the SAE/Deviations and Violations SSOP8V1 & SOP8/V1) filled by the PI.

- The SAEs will be discussed in the DSMU meeting and the Minutes of the DSMU meeting will be forwarded to the IECs.

- The SAE and Deviations and Violations will be discussed in the Full Board meeting of IEC for further action.

Tomo Riba Institute of Health & Medical Sciences
(AX1-V1/SOP03/V1)
Project Submission Form for review by IEC

A. Grouping of Project

Project No.	(Will be allotted eby IEC Office
Title:	
PI:	

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

Study Group
(Please select the option Y/N as applicable)

	Group		**Detail**	**Yes**	**No**
			Controlled Trial		
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 Trial		
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/Study involve transfer of data / material from TRIHMS		
8	A3	a	Is this a multi-centre trial / study ?	**Y**	**N**
9	A3	b	If multicentric, is TRIHMS the co-ordinating centre?	**Y**	**N**
10	A3	c	Does this trial / study involve transfer of patient's data to another site (including industry)?	**Y**	**N**
11	A3	d	Does this trial / study involve transfer of patient's blood, serum, DNA, tissue to another site ?		
			Intramural Funding		
12	A4	a	Are you seeking intramural funding	**Y**	**N**
13	A4	b	Does this trial / study use additional resources of TRIHMS beyond the usual patient's 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/study	**Y**	**N**
15	A5	b	Is this trial/study partly or wholly supported by grants from sponsored industry ?	**Y**	**N**
16	A5	c	Is this a phase IV/ marketing trial/study undertaken on behalf od industry?	**Y**	**N**
			Modification in approved trial/study		
17	A6		Are you seeking modification/s in the TRIHMS – IEC approved trial/study	**Y**	**N**
			Patient to bear the cost of trial/study		
18	A7	a	Are patients going to bear the cost of experimental intervention or drug therapy?	**Y**	**N**
19	A7	b	Will patient/participant undergo additional blood sample collection, biopsy, endoscopy, procedure etc.?	**Y**	**N**
20	A7	c	Will patient/participant bear the cost of complications arising from experimental treatment ?	**Y**	**N**
21	A7	d	For the trial/study purpose, will the patient spend Rs.5000/- or more above the usual expenses (for any reason such as drug therapy, additional investigation, prolonged stay or repeated travel) ?	**Y**	**N**
			Community or screening trial/studies		
22	A8	a	Will this trial/study be undertaken in the community?	**Y**	**N**
23	A8	b	Will this trial/study involve screening in the community?	**Y**	**N**
			Trial/study involving Vulnerable Population		

24	A9 a	Does this trial / study 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 or any other vulnerable group.	**Y**	**N**
		Trial/study involving genomics & proteomics		
25	A10	Does this trial/study involve conducting genomics or proteomics studies on patients' specimens?	**Y**	**N**
		Trial/study with conflict of interest		
26	A11	Will this trial/study involve development of a device, drug or test that would lead to profits or patent?	**Y**	**N**
		Trials involving standard treatment/procedures/ and Feasibility studies		
27	A12	Is this a prospective follow-up study (documentation of parameters only) of patients being offered standard treatment at TRIHMS?	**Y**	**N**

	Group	**Detail**	**Yes**	**No**
		Extramural Grants		
28	A13	Is this a phase II-IV trial/study restricted to standard intervention/treatments published in EBM booklet?	**Y**	**N**
29	A14	Is this a feasibility study for introduction of new treatment, practices/procedures recently shown in major national/ international studies, to be beneficial / superior and need to be started at TRIHMS?	**Y**	**N**
30	A15	Is this a review of procedures/practices routinely followed at TRIHMS?	**Y**	**N**
31	A16 i) ii)	Is this a retrospective analysis of charts and audit of procedures / tests / treatments? Is this a prospective analysis of charts and audit of procedures / tests / treatments?	**Y**	**N**
32	A17 i) ii)	Is this a retrospective review of biological material/ specimen (may involve some additional staining techniques)? Is this a prospective review of biological material/ specimen (may involve some additional staining techniques)?	**Y**	**N**
33	A18 i) ii)	Is this a retrospective review of radiology reports and their clinical correlation? Is this a prospective review of radiology reports and their clinical correlation ?	**Y**	**N**
34	A19 i)	Is this a retrospective review of laboratory reports and their clinical	**Y**	**N**

	ii)	correlation ? Is this a prospective review of laboratory reports and their clinical correlation ?		
		Procedure demonstration at workshop etc.		
35	A20	Are you demonstrating an experimental procedure which is not an established standard of care at a workshop, or a public meeting?	**Y**	**N**
36	A21	Are you performing a procedure at a workshop conducted at TRIHMS by non-TRIHMS staff member ? (Please check other requirements also)	**Y**	**N**
Signature of PI				
Date of Submission				

B. Project Fact Sheet

B1	Project No. (To be filled by the Secretariat)	
B2	Date of receipt by IEC	
B3	Project Title	
B4	Key Words title (2 -4 Options)	
B5	Principal Investigator Co-Principal Investigator Co-Investigator	
B6	Number of ongoing studies in which PI is involved ? (as PI only)	
B7	Contact Number Principal Investigator	
B8	Site/sites where study is to be conducted i.e. TRIHMS / Any other (Please specify)	
B9	Tick the type of study (multiple options if applicable)	o Investigator initiated study o Pharmaceutical sponsored study o Thesis* If *Thesis specify the name of student_____ o Investigator Initiated study +Thesis
B10	Funding Agency / *sponsor	
B11	Total Estimate budget in Rs.	
B12	Duration of the Project (months)	
B13	Total number of participants to be accrued in the study (including TRIHMS, if multi-	

	institutional study)	
B14	Number of participants from TRIHMS to be accrued	
B15	a)If this is a retrospective study, mention time frame from which data is collected b)The total number of participants whose data is being analyzed	
B16	Will biological products/data be sent out of the country ? (Yes/No) If yes attach the copy of regulatory cearance obtained [DCGI/ICMR/Health Ministry Screening Committee (HMSC)]	Yes /No
	Signature of PI	
	Date of submission	

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

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

Investigators Declaration

1	This research project (including collection of blood or tissue samples for research) will not be started until the final approval of the IEC has been obtained.
2	We agree to undertake research proposal involving human participants in accordance with the Schedule Y (Drugs & Cosmetics Act 1940), ICH-GCP and ICMR ethical guidelines. We will not modify the research protocol, consent, etc without approval by the IEC
3	We agree to obtain a properly informed and understood consent from all trial participants before their inclusion in the trial by using 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.
4	We agree to report within a week all serious adverse events (SAEs) associated with the trial in the SAE form to the IEC. In the event of a death of the trial participant, the Secretary, IEC and DSMU, will be informed within 24 hours.

5	We agree to submit status report at least annually, of the trial in the appropriate form. A final report will be submitted at the end of the trial
6	Full details on funding and a proposed budget are included with the trial proposal. The proposed budget is presented on the specific budget sheet of this form
7	We understand that the 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.
8	We understand that IEC will review and score those aspects of the budget proposal limited to, study merit, participants' rights, safety, and well-being.
9	We agree to remit service charges and Estimated Professional charges to TMC as per the existing TMC norms for clinical services. (This will not apply to intramural projects and those projects co-sponsored by TRIHMS and Projects funded by ICMR /DBT/ DST/WHO/IAEA.
10	We agree that the grant money will be spent in accordance with the budget proposal only. The funds will not be 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 for conducting intramural research, improving teaching facilities in the department, providing financial assistance to investigators for conferences, etc after obtaining permission from the IEC.
11	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 bear the expenses while participating in the trial. We 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.
12	We 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 TRIHMS Conflict of Interest Policy.
13	We will ensure that personnel performing this study are qualified, appropriately trained and will adhere to the provisions of the Institutional Ethics Committee, TRIHMS approved protocol.
14	All data and biological specimen collected during the research project, including those supported by commercial sponsors (e.g. pharmaceutical company), will remain the property of TRIHMS or as per the Clinical Trial Agreement.
15	The salaries for the staff employed for the research project will be as shown in the budget sheet and at par with the prevailing TRIHMS salary scales.
16	The study documents will be made available to members of the IEC at any time for random verification and monitoring. We will ensure that the study documents are archived for 15 years post study close out or until the sponsor confirms that the records are no longer required; whichever is earlier.

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 TRIHMS before they are released or presented elsewhere.
18	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 TRIHMS before they are released or presented elsewhere.
19	We will not issue any press release before the data and conclusions have been peer-reviewed by the TRIHMS staff or published in a peer-reviewed journal.
20	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.
21	We 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.
22	We 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, 2017. We will comply with all policies and guidelines of the TRIHMS and affiliating / collaborating institutions where this study will be conducted, as well as with all applicable laws regarding the research.
23	We understand that serious protocol violations and/or non-compliance during the trial by the investigators may result in withdrawal of project approval by the IEC.
24	We agree to comply with all other requirements, guidelines and statutory obligations as applicable to clinical investigators participating in clinical trials.

Study Team Undertaking with Duties & Delegation

Project Title							
Sr. No.	**CC No.** If available	**Investigator Name**	**Email ID**	**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 C. Screening of patients D. Selection & Recruitment and consenting of patients E. Laboratory investigations F. Laboratory report interpretation G. Treatment decision H. Patient evaluation I. AE and SAE management, evaluation and reporting	K. Data collection and monitoring of data L. Interpretation of data M. Statistical analysis & Interpretation N. Maintaining patients file and master file of project O. Drafting final report P. Publication Q. Assigning duties to the study team R. Communication with IRB. Z. Any other, please specify

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.

- o I hereby declare that I have no conflict of interest in my project.
- o I have the above conflict/s 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 name) has been discussed in (DMG /working group name) and is accepted to be submitted for Institutional Ethics Committee review.

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

DMG discussion-	
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	Pre-clinical Phase-I, Phase-II, Phase-III, Phase-IV, NA			
C.5.3	Pharmacokinetics Pharmacodynamics	Yes Yes	No No	NA NA
C.5.4	Feasibility Study Pilot	Yes Yes	No No	NA NA

	Pivotal	Yes No NA
C.5.5	Observational studies	
	➢ Prospective cohort ➢ Retrospective cohort ➢ Time series study ➢ Case-control study ➢ Nested case-control study ➢ Cross-sectional study ➢ Community survey (a type of cross-sectional study) Longitudinal study ➢ Epidemiological study ➢ Survey (others) ➢ Others (please specify	
C.6	**Study Population**	
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) **Specify Age**	
C.6.2	Does it involve vulnerable participants **Individuals may be considered to be vulnerable if they are:** • Socially, economically or politically disadvantaged and therefore susceptible to being exploited • Incapable of making a voluntary informed decision for themselves or whose autonomy is compromised temporarily or permanently, for example people who are unconscious, differently abled. • Able to give consent, but whose voluntariness or understanding is compromised due to their situational conditions. • Unduly influenced either by the expectation of benefits or fear of retaliation in case of refusal to participate which may lead them to give consent.	o Yes No o (If yes, tick the appropriate boxes) o Minors (up to 18 years) pregnant women o elderly o seriously/terminally ill o neonates o mentally challenged o handicapped o economically/socially disadvantaged o institutional employees / students
C.7	**Study methodology** Explain, in sequence, the conduct of study and all data collection procedures. Describe the involvement of human participants 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 participants from the study.	
C.7.1	How many participants/samples will be screened? How many participants/samples are likely to be accrued?	
C.7.2	**Power estimates** Describe power calculations, if the study involves statistical comparisons between two or more groups. Mention evidence to support that adequate number of participants can be enrolled during the study period by the investigators.	
C.7.3	**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.	
C.7.4	**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.8	**Adverse Events**	
C.8.1	Have you defined adverse events in your study, and what rules would be used 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.8.2	Describe all possible risks and discomfort to participants due to use of intervention and /or data collection methods proposed risks, discomfort, side effects of drug et. Describe expected degree and frequency of such c.	
C.8.3	Describe benefits to the participant/s in this study. Also describe the benefits, if any, to the society.	

C.8.4	Describe benefit/risk assessment	
C.8.5	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.8.6	If some procedures in this trial are emotionally upsetting describe what arrangements have been made for psychological counselling?	
C.8.7	Who will bear the cost of treating the complications arising from this trial?	
C.8.8	a) Have you made provision for insuring trial participants for any accidental unforeseen trial related injury? b) Does this study require institutional insurance coverage?	Yes No, **Specify** Yes No
C.9	**Informed Consent**	
C.9.1	Describe the participant recruitment strategy adopted	• OPD basis [ ] • EMR data base[ ] • Referrals[ ] • Advertisements[ ] • Any other- Please specify
C.9.2	Describe	
	(i) How, where, when and by whom the Informed Consent /assent will be obtained?	
	(ii) How much time the participant/s will be given to consider participation and decide?	
	(iii) Describe additional plans/needs for informed consent/assent 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.9.3	In what way will you ensure the confidentiality and privacy of the participants?	
C.10	Are you seeking waiver of consent? If Yes, specify reasons	Yes No
C.11	**Drug/Sponsor details**	
C.11.1	Does your study involve testing of drug/s, device/s	Yes No

	and/or biologics? If yes- 1) Please attach copy of DCGI permission/DCGI Application 2) If marketed drug, please attach copy of package insert/product insert.	
C.11.2	Are drugs already approved by the regulatory authorities and available in the market or are the new ones ?	Already approved [ ] New one [ ] NA [ ]
C.11.3	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.11.4	Who has prepared and /or is manufacturing the drug/s, device/s and biologics under investigation?	
C.11.5	Who holds the patent or IND/IDE of the drug/s, device/s and biologics under investigation?	
C.12	**Permission /Agreements**	
C.12.1	Does your study require permission from	
	1.Director, TRIHMS ?	Yes No
	2.Health Ministry's screening Committee (HSMC) ?	Yes No
	3.Drug Controller General India (DCGI) ?	Yes No
	4.Others?	Yes No
C.12.2	Does your study require you to send human biological material/data outside India?	Yes No NA
C.12.3	If yes, have you obtained/sought permission:	
	1. from the Director, TRIHMS	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.12.4	Has TRIHMS and the collaborating institution/sponsor signed CTA/MoU/MTA/ other agreement for that? If yes, attach a copy of CTA/MoU/MTA/other agreement	Yes No NA
C.12.5	If the study is to be conducted fully or partially outside the TRIHMS, please describe the need for permission from institution(s), health centre(s),local government/administrative bodies, etc.	

C.12.6	Have you made provision for insuring yourself, and TRIHMS against any legal action that may arise out of this project?	
C.13	**Trial Monitoring, Data Management and access**	
C.13.1	Does your study have provisions for monitoring the data to ensure the safety of participants?	Yes No NA
C.13.2	Who will be responsible for monitoring and ensuring the safety of participants?	
C.13.3	i. Who will be maintaining the trial records and where? ii. For how long will the data be stored? iii. Give details of where they will be stored and who will have access to the trial/study master file other trial/study documents.	
C.14	**Post research access**	
C.14.1	Post research access will be provided to the participants? I f yes, describe briefly arrangements made for post research access.	Yes No NA
C.14.2	What are the reasonable possibilities of the availability of the investigational drug(s)/ device(s) and biologics for the study participant/s, after the study completion, if found to be effective?	
C.15	**Results**	
C.15.1	How are the results of the study intended to be reported and disseminated?	Please tick o Peer reviewed scientific journals o Other Publication o Conference presentation Internal report o Submission to regulatory authorities o 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. o Other ……Please

		specify……..
C.16	**Name of PI:**	**Signature: Date:**

D. Budget Sheet for the Proposed Study

1	Title of the Project:	
2	Principal Investigator	
3	Designation and address of the PI	
4	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 Foregn
	Address, phone, fax. E-mail of sponsor with the name of the contact person	
	No funding required	
5	Total Budget for the entire project in Rs.	
6	Duration of the Project in months	
7	Proposed date of starting the project	
8	Direct payments to investigators, if any	
9	Any other benefits to the investigators	
10	**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				
3	**Equipment and Hardware-Kindly specify**				

	-				
	-				
	-				
4	**Drugs and Consumables**				
	-				
	-				
	-				
5	**Clinical Investigations**				
	-				
	-				
	-				
6	**Hospitalization**				
	-				
	-				
	-				
7	**Travel expenditure for investigators**				
	-				
	-				
8	**Travel expenditure for trial participant and one attendant**				
9	**Honorarium to doctors/technician**				
10	**Insurance**				
	I. For investigators				
	ii. any unforeseen, accidental trial related injury				
11	**Any other expenditures**				
12	**Miscellaneous**				
13	**TRIHMS Service Charge (as per current TRIHMS norms for pharma sponsored studies)**				
14	**Estimated** Professional charges for clinical				

	services **(as per current TRIHMS norms 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

Project No._____

The members of the Institutional Ethics Committee met on …… at Tomo Riba Institute of Health & Medical Sciences 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 TRIHMS 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, TRIHMS).
- 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-V1/SOP03/V1) 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-V1/SOP03/V1

Checklist of Documents

Item No.	Mandatory Documents	Yes	No	NA
1.	IEC processing fee **(applicable for pharma sponsored trials)**			
	Project Submission Form (both hard and soft copies) duly signed by the Principal Investigator			
2.	**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.	Lay summary			
5.	Participant Information Sheet & Informed consent forms (ICFs) in English (and if required any other language)			
6.	Application for waiver of consent			
7.	Participant Information Sheet & Informed consent forms (ICFs) in English & Hindi (and if required any other language)			
8.	Case Record form			
9.	Questionnaire			
10.	Investigator Brochure			
11.	Package insert/label			
12.	Insurance policy			
13.	DCGI approval letter/DCGI submission letter			
14.	NOC from DCGI/ICMR/HMSC			
15.	Appendix VII (schedule Y) Undertaking by The Investigator			
16.	Clinical Trial Agreement (CTA)/Memorandum of Understanding(MOU)/Material Transfer Agreement(MTA) if applicable			
17.	Brief resume of Principal Investigators and Co-investigators (1 Page each)			
18.	Copy of Good Clinical Practice training certificate for all investigators			
19.	APMC /MCI of Principal Investigators and Co-investigators			

20..	Any Other			

AX3-V1/SOP03/V1
Tomo Riba Institute of Health & Medical Sciences
Institutional Ethics Committee

Document Receipt Form

TRIHMS 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.	Cover letter enlisting documents enclosed.			
3.	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			
4.	Study Protocol			
5	Participant Information Sheet & Informed consent forms (ICFs) in English (and if required any other language)			
6.	Application for waiver of consent			
7.	Case Record form			
8.	Questionnaire			

9.	Investigator Brochure			
10.	Package insert/label			
11.	Insurance policy			
12.	Drugs controller General, India (DCGI) submission letter			
13.	Drugs controller General, India (DCGI) approval			
14	HMSC approval			
15.	Appendix VII (schedule Y) Undertaking by The Investigator			
16.	Clinical Trial Agreement (CTA) **If applicable**			
17.	Memorandum of Understanding (MOU) **if applicable**			
18.	Material Transfer Agreement (MTA) **if applicable**			
19	Brief resume of Principal Investigators and Co-investigators (1page each)			
20.	GCP Training certificate			
21.	MMC of Principal Investigators and Co-investigators			
Documents submitted: o Complete o Incomplete will submit on				
Comments:				
Receiver Name, Sign & Date				
Item No.	**Mandatory Documents**	**Yes**	**No**	**NA**
(IEC Secretariat)				

AX4-V1/SOP03/V1

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, , ICH- Good Clinical Practice (ICH – GCP) and the Declaration of Helsinki.

Kindly note:

- Informed consent documents in English and Hindi are mandatory and any Language if applicable
- Font: Arial & Times New Roman
- 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

- Glossary of technical words/medical terminology for participant understanding
- Schedule of investigations to be performed for the study as a chart.

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

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

Participant Information Sheet & Informed Consent Form

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

Name of the funding agency (if applicable)

Name of the sponsor (if applicable)

Address of Research Site

Introduction:

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

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

Purpose:

The purpose of this study is to

…… …… …… …… ……

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

Clear state

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

…… …… …… …… ……

Information:

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

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

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

Clearly state

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

iv. Statement of foreseeable circumstances under which the subject's participation may be terminated by the Investigator without the Subject's consent
v. Statement that the subject or subject's representative will be notified in timely manner if significant new findings develop during the course of the research which may affect the subject's willingness to continue participation will be provided
vi. Information regarding patients roles and responsibility (follow-up/ QOL assessment)

Alternative treatments:

Disclose appropriate alternative treatments available, if any.

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

Risks:

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

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

Costs:

Describe the cost for participating in the study to the subject/participant. The information must be written in clear terms regarding the cost which will be borne 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.

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

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

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

Confidentiality

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

Compensation for study related Injury or death

(As per the DCGI directive for regulated studies, it is mandatory for sponsors to comply 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 _

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].

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

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

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

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

Study Title:

Study Number:

Participant' Initials:_____ Participant's Name:_____

Date of Birth / Age:_____

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

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

Participant's name (print):	
Participant's Signature/Thumb impression & date:	
Address : Qualification (please attach supporting documentation) (if applicable) _____ Occupation: Student / Self-Employed / Service /	

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

Guidelines for developing informed consent documents for Biological sample study:

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

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

Other specifics are as follows :

a) Period of storage of the sample/data and probability of the material being used for secondary purposes.
b) Whether material is to be shared with others, this should be clearly mentioned.
c) Right to prevent use of her/his biological sample, such as DNA, cell-line, etc., and related data at any time during or after the conduct of the research.

d) Risk of discovery of biologically sensitive information and provisions to safeguard confidentiality.
e) Post research plan/benefit sharing, if research on biological material and/or data leads to commercialization.
f) Publication plan, if any, including photographs and pedigree charts.

Template of consent for Biological sample study

As part of this protocol the investigators may store your blood/tissue/serum samples for future research. The investigators may also store and use the tumor tissues that are removed as part of routine biopsy or surgery, for future research. The tissue could be either paraffin blocks or fresh tissue that is frozen at very low temperatures as part of the Hospital Tumor Tissue Repository. Such blood, plasma, serum or tissue samples could be used for pathology, 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.

Informed consent form to participate in a biological sample study
Study Title:
Study Number:
Participant' Initials:_____ Participant's Name:_____
Date of Birth / Age:_____

Do you consent to biological sample study?

YES, I consent NO, I do not consent

a) I understand that I am being invited to take part in the research study. I confirm that I have read/been read to, and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions.
b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

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

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

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

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

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

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

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

Please tailor your ICF to suit the needs of our Indian population, and if this is a multinational Pharma based project, an additional ICF specifically designed for the trial site may be used. Separate forms should be prepared when minors are used; one for the mature minors (age 7 - 18 years) and one for the parents.

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

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

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

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

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

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

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

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

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

AX5-V1/SOP 03/V1

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. Data will be stored securely for a period of _____ years. Nobody will know it except the doctor doing the research. The doctor will not tell your friends or anyone else. The information will only be accessed by the doctor the Ethics Committee and the Regulatory authority

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

Right to refuse or withdraw
You do not have to be in this study, if you do not want to be. If you do not want to be in this study, we will tell you what other kinds of treatments there are for you. If you decide that you

don't want to be in the study after we begin, that's OK too. Nobody will be angry or upset. We are discussing the study with your parents and you should talk to them about it too.

Whom to contact

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

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

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

<Name of Member Secretary of IEC >

Your responsibilities

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

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

We expect your co-operation throughout the study.

Child Assent Form

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

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

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

_____

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

_____

Name and Signature/ Thumb impression of Legally Acceptable Representative Date:

_____ Date:

Name and Signature of Impartial Witness

_____ Date:

Name and Signature of the attending Physician

AX6-V1/SOP 03/V1
Parent Information sheet and Informed Consent Form

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

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

Purpose:
The purpose of this study is to ……

Participant selection

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

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

Procedures and Protocol
Describe or explain the exact procedures that will be followed on a step-by-step basis, the tests that will be done, and the drugs that will be given. Describe very clearly which procedure is routine and which is experimental or research. Duration Include a statement about the time commitments of the research for the participant and for the parent including both the duration of the research and follow-up, if relevant.
Example: The research takes place over ___ (number of) days/ or ___ (number of) months in total. During that time, it will be necessary for you to come to the clinic/hospital/health facility (number of) days, for (number of) hours each day. We would like to meet with you six months

after your last visit for a final check-up. Altogether, we will see you and your child 4 times over a year.

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

Example: These vaccines can have some unwanted effects or some effects that we are not currently aware of. However, we will follow your child closely and keep track of these unwanted effects or any problems. We will give you a telephone number to call if you notice anything out of the ordinary, or if you have concerns or questions. You can also bring your child to this health facility at any time and ask to see [name of nurse, doctor, researcher].
We may use some other medicines to decrease the symptoms of the side effects or reactions. Or we may stop the use of one or more drugs. If this is necessary we will discuss it together with you and you will always be consulted before we move to the next step.)

Risks
A risk can be thought of as being the possibility that harm may occur. Explain and describe any such possible or anticipated risks. Provide enough information about the risks that the parent can make an informed decision. Describe the level of care that will be available in the event that harm does occur, who will provide it, and who will pay for it.
Example: By participating in this research it is possible that your child will be at greater risk than he/she would otherwise be. There is a possibility that _____may happen as a result of taking this drug. While the possibility of this happening is very low, you should still be aware of the possibility. If something unexpected happens and harm does occur, we will provide you with_____. [Explain the level of care that will be available, who will provide it, and who will pay for it. Inform the parent if there is a particular insurance in place.]

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

Example: By participating in this research it is possible that your child may experience some discomfort such as the discomfort of the injections. There may be a slight hardening and/or swelling where the needle stick goes into the skin. This should disappear in one day. Your child may also be fussier than usual or more tired. These behaviours 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 participants &/or attendant.

Emergency Medical Treatment

(If applicable, add here) In case of the physical injury to the participant during the course of research please state the name and contact details of the PI.

Describe available medical treatment in case of complications.

Benefits

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

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

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

Confidentiality

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

Example : The information that we collect from this research project will be kept confidential. Information about your child that will be collected from the research will be put away and noone 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. _____

Consent

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

_____ _____

Name and Signature /Thumb impression of Parent/Guardian Date

_____

_____

Name and Signature/ Thumb impression of Participant (when appropriate) Date

_____

_____

Name and Signature of Person Obtaining Consent/Authorization Date

_____

_____

Name and Signature of Impartial Witness Date

AX7-V1/SOP 03/V1

Consent for prospective audit study

Participant Consent for Participation in the study

Participant Information: (Should be concise and simple)
To state the purpose of the study (What the study is about and why the study is being done)

Consent

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.
Purpose of the study-

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, TRIHMS 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 my data will be stored for___ years, 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 have any queries regarding my rights I may contact,
<Name of Secretary of IEC > Phone: <0360-2350331>

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.

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

Name and Sign/Thumb impression of the participant
Date
Name and Signature/ Thumb impression of Legally Acceptable Representative Date:
Name and Signature of Impartial Witness Date: Name and Sign of the Principal Investigator Date

AX8-V1/SOP 03/V1
Consent for prospective audit study

Parental/LAR consent
Parent Information: (Should be concise and simple) To state the purpose of the study (What the study is about and why the study is being done)
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 understand that if I have any queries regarding my ward's rights I may contact, <Name of Secretary of IEC > Phone: <0360-2350331 > 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 am willing to allow the use of my ward's data for this study.

I understand that my ward's participation in the study is voluntary and that I am free to withdraw consent for my ward's participation at any time, without giving any reason, without my ward's medical care or legal rights being affected.

Name and Sign/ Thumb impression of the Guardian/Parent /LAR
Date
Name and Signature of Impartial Witness Date Name and Sign of the Principal Investigator
Date

AX9-V1/SOP 03/V1
Assent for prospective audit study

Child Information: (Should be concise and simple) To state the purpose of the study (What the study is about and why the study is being done)

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 have any queries regarding rights I may contact,

<Name of Secretary of IEC > Phone: < 0360-2350331>

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

AX10-V1/SOP 03/V1

Informed Consent Template for Audio-Visual Recording
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).

Protocol Number

Protocol Title

Sponsor
Name of Principal Investigator (Study Doctor)
Site Name & Address (Institute)
Contact Number of the Study Doctor
Alternate Numbers for Contact
Patient ID:

The Indian Regulatory Authority Drugs Controller General, India (DCGI) (an authority which approves and monitors conduct of clinical studies in India), who has approved this Study, has laid down new Rules that in addition to the requirement of obtaining written informed consent, an audio-visual recording of the informed consent process of each trial participant, including the procedure of providing information to the participant and his/her understanding on such consent is required to be done while adhering to the principles of confidentiality and such audio-visual recording and related documentation would be preserved for a period of 15 years

under the responsibility of the Institute and study doctor.

Statement by the Participant/ LAR

By signing this form, I hereby give my consent to the study doctor and Institute for an audio-visual recording of my informed consent process, including the procedure of providing information to me and my understanding on such consent, preservation/ archival of such audio-visual recording and related documentation for a period of 15 years under the responsibility ot the Institute and study doctor. The extent of this recording is understood to be limited to discussion of contents of Informed Consent Form for this study.

The study doctor and Institute will adhere to the principles of confidentiality for such an audio-visual

recording of my informed consent process, however

- I understand that such an audio-visual recording of my informed consent process may be seen by the representatives of the DCGI office and/or Ethics Committee. I understand that my consent is voluntary and is applicable to the entire duration of my participation in this study.
- If I refuse to provide an audio-visual recording of my informed consent process, in compliance with regulations I would not be able to participate in this study.
- If I have any questions about my data protection or privacy rights under this form, I understand that I may contact the Study Doctor
- I confirm that I have read and understood the contents of this Consent Form and have had the opportunity to ask questions before signing it

To be completed by Participant/ LAR/ Impartial Witness, as applicable

Participant's Name (print):	
Participant's Signature/Thumb Impression & date:	
Legal Acceptable Representative name	
Legal Acceptable Representative Signature /Thumb impression & date (if applicable):	
Impartial Witness	
Impartial Witness's signature & date (if applicable):	
Name of PI or Co-PI/Co-I:	
PI or Co-PI/Co- sign & date:	

AX11-V1/SOP 03/V5
IEC form for re-review of research proposals

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**

AX12-V1/SOP 03/V1

Instructions for Submission of Projects for Institutional Ethics Committee Approval

The latest version of IEC documents can be accessed by ONLINE @ www.trihms.org.

- All IRB submissions should be made via email to iectrihms@gmail.com
- 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 submission of hard copy of the IEC form to IEC.

After initial review of projects

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

A. **Approved-** Your study is scientifically and ethically sound and you may initiate the study subject to terms indicated in the final approval letter.

B. **Revisions with minor modifications/amendments-** 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. However, in some

cases may be referred for a full board review.

C. **Revisions with major modifications for resubmission-** 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.

D. **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 21 working days.

If your project, after initial review attains the status B or C, the following documents are to be submitted to IEC:

1. IEC form for re-review of projects **AX11-V1/SOP 03/V1**
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 TRIHMS-IEC submission form.

- **The vernacular versions of ICF (Hindi 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 TRIHMS 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 along with institutional legal advisor's comments 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 behavioural 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 participants 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 participants 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 participants.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. Crosssectional 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 randomized;
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.

Institutional Ethics Committee,
Tomo Riba Institute of Health & Medical Sciences
(IEC, TRIHMS)

Title: Full Board Review of Submitted Protocol

SOP Code: SOP 04a/V1 Date: 03/12/19 Pages:

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/ legal aspects of the study. The committee should evaluate the possible risks to the participants with proper justification as well as the expected benefits to participants/community. The adequacy of documentation for ensuring privacy & confidentiality should also be reviewed.

The purpose of this Standard Operating Procedure (SOP) is to describe how the IEC members will review an initial submission of the research study for approval using the Assessment Form. The Assessment Form AX1-V1/SOP04a/V1 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 review of revised and resubmitted protocols submitted for approval of the IEC. The specific elements in the Assessment Form must be adequately addressed in the protocol and/or protocol-related documents submitted for review. Relevant comments made during discussion and deliberation about a study should be recorded in the minutes of the meeting. The decision reached by the 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, the research proposals are categorized into three types, viz.

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

An investigator may categorize his/her protocol into the above three types. In case the PI wishes to apply for expedited review or exemption from review of the submitted research proposal, a standard request form needs to be filled out, providing justification for the same. Standard Request Forms for Expedited Review and Exemption from review are available as annexures AX1-V1/SOP04b/V1 (SOP 04b/V1) and AX1-V1/SOP04c/V1 (SOP 04c/V1) respectively.

However, the decision to accept the request for Expedited Review /Exemption from review will be made by the Member Secretary, IEC.

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

Full board Review

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

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

4a.4

- Studies involving deception of participants -Some types of research studies require deception due to nature of research design. A true informed consent may lead to modification and may defeat the purpose of research. Such research may be carefully reviewed by the EC before implementation.

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

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

- Major deviations and violations in the protocol.

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

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

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

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, competence of the investigators, informed consent and elements of the study covered in the submission form to evaluate the suitability and feasibility of the study.

The following will be considered as applicable:

4a.5.1 Scientific Design and Conduct of the Study

- Is the project original and innovative? e.g. Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this 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 predominantly, a service proposal?
    - ❖ If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced?
    - ❖ What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventive interventions that drive this field?

- Appropriateness of the study design in relation to the objectives of the study.

- The statistical methodology (including sample size calculation), and the potential for reaching sound conclusions with the smallest number of research participants.

- The available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial.

- The justification of predictable risks and inconveniences weighed against the anticipated

benefits for the research participants and the concerned communities.

- The outcome of the research should be relevant to the health problems of society
- The justification for the use of control arms.
- Potential of the work that would be conducted to lead to a larger and high impact study.
- Criteria for prematurely withdrawing research participants, and criteria for suspending or terminating the research as a whole.
- The adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a Data Safety Monitoring Board.
- 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/CTA and MTA for national and international collaborative research to safeguard the interests of participants and ensure compliance while addressing issues related to confidentiality, sharing of data, joint publications, benefit sharing, etc.

4a.5.2 Risk Benefit Assessment

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

- The EC should give advice regarding minimization of risk/ discomfort wherever applicable.

- Adequate provisions must be made for monitoring and auditing the conduct of the research, including the constitution of a Data and Safety Monitoring Board (DSMB) if applicable (for example in clinical trials)

4a.5.3 Care and Protection of Research Participants

- Qualifications and experience of the investigators for the conduct of the proposed study.

- Any plans to withdraw or withhold standard therapies for the purpose of the research, and the justification for such action.

- Plans to withdraw participants from the study by the investigator.

- Medical care to be provided to research participants during and after the course of the research.

- Adequacy of medical supervision and psycho-social support for the research participants.

- Steps to be taken if research participants voluntarily withdraw during the course of the research.

- Criteria for extended access to, the emergency use of, and/or the compassionate use of study products.

- Arrangements, if appropriate, for informing the research participant's general practitioner or family doctor, including procedures for seeking the participant's consent to do so.

- Description of any plans to make the study product available to the research participants following the research and description of any financial costs to research participants.

- Rewards and compensations for research participants (including money, services, and/or gifts).

- Provision for payment (in cash or kind or both) for incidental expenses and other inconveniences, free services and the processes involved without amounting to undue inducement.

- Provisions for compensation/treatment in case of injury/disability/death/lost wages of a

research participant attributable to participation in the research (as per institutional policy/ICMR guidelines/existing national legislation (CDSCO, DCGI).

- Insurance and indemnity arrangements.

4a.5.4 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.5.5 Informed Consent/ Consent Process

4a.5.5.1 Essential Elements:

1. Statement that the study involves research and explanation of the purpose of the research in sufficient details in layman's language

2. Statement that the study is approved by IEC after evaluation of scientific and ethical validity.

3. Expected duration of the Participant's participation and total number of participants that will be accrued on the study.

4. Description of the procedures to be followed, including all invasive procedures.

5. Description of any reasonably foreseeable risks or discomforts to the Participant.

6. Description of any benefits to the Participant or others reasonably expected from research. If no benefit is expected from the study, whether the Participant is being made aware of this through the consent document.

7. Disclosure of specific appropriate alternative procedures or therapies available to the Participant.

8. Statement describing the extent to which confidentiality of records identifying the Participant will be maintained and who will have access to Participant's medical records

9. Trial treatment schedule(s) and the probability for random assignment to each treatment (for

randomized trials)

10. Compensation and/or treatment(s) available to the Participant in the event of a trial-related injury

11. An explanation about whom to contact for trial related queries, rights of Participants and in the event of any study related injury.

12. The anticipated prorated payment, if any, to the Participant for participating in the trial. In particular, the IEC must review payments to determine that:

- The amount of payment and the proposed method and timing of disbursement neither is coercive nor presents undue influence.
- In case any amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
- 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. Participant's responsibilities on participation in the trial.

14. Statement that participation is voluntary, that the participant can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the Participant is otherwise entitled.

15. Any other pertinent information.

• **Additional elements, which may be required:**

a. Statement of foreseeable circumstances under which the Participant's participation may be terminated by the Investigator without the Participant's consent.

b. Additional costs to the Participant that may result from participation in the study.

c. The consequences of a Participant's decision to withdraw from the research and procedures for orderly termination of participation by Participant.

d. Statement that the Participant or Participant's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect

the Participant's willingness to continue in the study.
e. A statement that the particular treatment or procedure may involve risks to the Participant (or to the embryo or foetus, if the Participant 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 /authorization/consent of LAR and/or Impartial witness (if applicable).

• Assurances that research participants will receive information that becomes available during the course of the research relevant to their participation including their rights, safety, and well-being.

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

• Provision for audio-visual recording of consent process, if applicable, as per relevant regulations. The protocol meets the criteria for approval of application for consent waiver or verbal/oral consent request.

4a.5.5.2 Types of consent processes and their implications

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

recontacted for every new use of their stored samples/data if the scope of research is outside that for which they had originally given consent.

- **Delayed consent:** It may be administered in the post-medical procedure period when biospecimen or data may be collected for appropriate research from critically ill patients who may not have given prior consent for research. Consent may be taken from the participant or LAR when it is practical.
- **Dynamic consent:** This consent is different from one of static, paper-based consent and involves an ongoing engagement and interactions over time with participants to re-contact in response to changing circumstances using technology based platforms. It incorporates a flexible, configurable, technology-based design accommodating both participant and researcher needs. Modern longitudinal biobanks equipped with advanced technology strive for this type of consent.
- **Withdrawal of consent or destruction of sample:** The donor has the right to ask for destruction of her/his collected sample(s) and discontinuation/withdrawal from participation in the research. In longitudinal studies, a participant may withdraw from one component of the study, like continued follow-up/data collection when withdrawal may be referred to as partial.
- **Waiver of consent:** While using anonymised (de-identified) samples/data, researchers should seek the approval of the EC of the institution or the repository for waiver of consent from donors.
- **Re-consent:** Secondary or extended uses of stored samples/dataset: In such an instance, one of the preliminary considerations for ECs must be to identify the circumstances under which the research requires re-use of collected identifiable biological material to generate the data or utilize the pre-existing identifiable dataset. This must also include review of the informed consent obtained originally to see if reconsent is warranted. There may be situations where consent would be impossible or impracticable to obtain for such research, in which case the research may be done only after independent evaluation by an EC (Declaration of Helsinki, October 2013).
- **Paediatric donors:** In longitudinal studies once the child donor attains the legal age of consent a re-consent should be sought for the storage and use of her/his tissue or sample. In paediatric biobanks or biobanks with paediatric samples it is important to address the issue of children reaching legal age of consent. Sometimes re-contact may lead to withdrawal, resulting in limited data analysis. This may lead to bias orit could evoke emotional distress about past research. On the other hand, re-consen may give the participant the power to agree. A biobank should decide the policy it would like to adopt for re-contact.

4a.5.6 Community Considerations

- The EC should ensure that due respect is given to the community, their interests are

protected and the research addresses the community's needs.

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

4a.5.7 Recruitment of Research Participants

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

4a.5.8 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.5.9 Disclosure of Conflict of Interest

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

4a.5.10 Social values:

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

4a.6 Responsibility

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

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

4a.7 Detailed instructions

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 IEC member (IEC committee scoring Form AX2-V1/SOP04a/V1). The scores will be considered for granting intramural funds. The comments from external consultants if received on time will be considered during the IEC discussion. However, Pharma-sponsored studies, extramurally funded investigatorinitiated studies and in-house studies requiring no intramural funds 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:
  E-copies/ hard copies of study documents to be reviewed in the full board meeting would be circulated along with Agenda to the Committee members preferably 7 days in advance of the scheduled meeting.

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. Generally, 2 lead discussants will be assigned to new research proposals. However, for studies involving multiple specialties, complexity, high risk or vulnerable populations more than two lead discussants may be assigned.
- The scientific member reviews the scientific, ethical, and informed consent issues and the Social scientist/NGO representatives/Ethicist /Lay Person has the responsibility of reviewing the ethical aspects of the study and finalizing the informed consent documents which helps the PI to make the documents lucid and in simple language.
- Legal expert will review legal documents which includes CTA/ MTA/ MOU etc. and advice on any legal matters such as data sharing, IPR and compensation issues.
- The lead discussants will present the research study at a regular full board meeting of the IEC.
- The Investigator may be called for any questions or clarification required by the Committee.
    - 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 the assigned project/s 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.
- All members are expected to read all protocols and submissions before a meeting, and to participate in meeting discussions.
- The Member Secretary can invite an independent consultant (if necessary) for comments during the full board meeting.

Responsibilities of IEC members

- Check the meeting date to see if he/she is available to attend the meeting.
- Check the contents of the e-copy/ hard copy of study documents received via email or mail.
- 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 lead discussants should submit the online/ offline Study Assessment Form and 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 submitting the study assessment form and comments would be that of the respective IEC member.

- The non-medical member of the IEC shall specifically address ethical aspects of the study in the study assessment form such as study population involved, consenting process, waiver of consent etc.

4a.8 Review the Protocol:

Review all elements as per section 4a.3, 4a.4, 4a.5. The protocol will be reviewed by lead discussants as per guidelines to review a study protocol described in AX1-V1/SOP04/V1.

4a.9 Use of study assessment forms and scoring sheet

It is the responsibility of the IEC members (lead discussants) 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-V1/SOP04a/V1) helps to ensure that all elements of research study are

reviewed and are accordingly documented during the discussion / meeting. The lead discussant(s) of the research proposal shall complete the study assessment form for initial review and expedited review. The lead discussant needs to submit comments for the resubmitted projects via AX1-V1/SOP04a/V1.

All scientific IEC members shall score the studies seeking intramural funds as per scoring sheet (AX2-V1/SOP04a/V1)

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 or expedited review. The lead discussant needs to submit comments for the resubmitted projects via AX1-V1/SOP04a/V1.

4a.9.1 Collection of the assessment reports

The IEC Secretariat will collect the Assessment Forms AX1-V1/SOP04a/V1 and the comments from each lead discussant and file them in the original set of the study file.

4a.10 Guidance for addressing ethical issues related to research

4a.10.1 Role of the EC

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

4a.10.2 As per National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017 Biobanks can use the stored material/data for doing research themselves or they can outsource or supply such material/data to other researchers or institutions on a nonprofit basis.

4a.10.3 Ownership of the biological samples and data: The participant owns the biological sample and data collected from her/him and therefore, could withdraw both the biological material donated to the biobank and the related data unless the latter is required for outcome measurement and is so mentioned in the initial informed consent document. Complete anonymization would practically make the original donor lose the right of ownership. Biobanks/institutes are the custodians or trustees of the samples and data through their ECs as their present and future use would be done under supervision of the respective ECs. Researchers have no claim for either ownership or custodianship.

4a.10.4 Transfer of biospecimens: An MTA should be executed if the biospecimens are likely to be shipped from the host institution to collaborating institutions within the country or abroad.

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

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

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

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

4a.10.6 Return of research results to individual/groups

Results of the study should be communicated back to the providers of samples/ data. Wherever applicable, research findings in aggregate form (which does not reveal individual results) must be discussed with the community, especially when research involves vulnerable populations.
In the absence of an appropriate mechanism to deal with informational harm that can occur if participants are provided feedback when they are not prepared to face it or if it is not actionable or when such information is unrelated, a lot of distress could be caused to participants concerned. At the time of sample collection, it may be a good approach to offer donors the choice of receiving the results of the research whether they are beneficial or not. Participants may also choose not to be contacted about their results. Another alternative is to give participants the option of receiving an aggregate report of all the results of the study which could become a shared benefit for the community. The aforementioned options may be incorporated in a tiered consent.

4a.10.7 Benefit sharing

Biological materials and/or data have potential commercial value but the participants'

contribution and their share in this benefit is very often not known to them. The informed consent document should emphasize this aspect with necessary clauses for clarity about benefit sharing.

Annexure
AX1-V1/SOP04a/V1
Study Assessment Form

Protocol Number:	Date (DD/MM/YY):
Protocol Title:	
Prinicipal Investigator:	
Department:	
Application	
Total No. Of Participants:	
Funding agency:	
Duration of the study:	
Lead discussant Name:	
Type of Study:	**Treatment studies /Interventional Studies** ▪ Randomized controlled trial - Double-blind randomized trial - Single-blind randomized trial - Partial-Blind randomized trial - Open labeled ▪ Adaptive clinical trial ▪ Nonrandomized trial (quasi-experiment) ▪ Interrupted time series design ▪ Any other (please specify) comment:_____ ▪ Pre-clinical ▪ Phase-I, Phase-II, Phase-III, Phase-IV, NA **Feasibility Study:-** Pilot Pivotal ▪ Pharmacokinetics ▪ Pharmacodynamics

Research involves – ▪ Less than minimal risk ▪ Minimal risk ▪ Minor increase over minimal risk of Low risk ▪ More than minimal risk od High risk	
Review Type	- Full Board - Expedited
Justification for Expidited review	Comment
CTRI Registration	- Applicable - Not Applicable
Academic clinical trial to be notified to DCGI as per **GSR 313 (E)**. [i.e. clinical trials looking at any new indication or new route of administration or new dose or new dosage form and the data generated is not intended for submission to licensing authority for marketing purposes.]	- Yes - No - N/A
Does this study require permission from regulatory aithorities?	- Yes - No - N/A If Yes- - DCGI - ICMR - other govt. Departments/Agencies
Are human biological material/data sent abroad?	- Yes - No - N/A Comment: If yes, permission required - Health Ministry's Screening Committee(HMSC) - Others, please

Mark and comment on whatever items applicable to the study

1	Need for human participants	- Yes - No - N/A Comment:
2	Objectives of the study	- Clear - Unclear What should be improved?
3	Background information and data	- Sufficient - Insufficient

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

	legal, economic, and social) to subjects minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk? e) Are the risks minimized, whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes? f) Does the study define risk management plan?	- Yes - No - N/A - Yes - No - N/A
9	Inclusion Criteria	- Appropriate - Inappropriate Comment:
10	Exclusion Criteria	- Appropriate - Inappropriate Comment:
11	Discontinuation and withdrawal criteria	- Appropriate - Inappropriate comment
12	Does the study involve modified or new claims, namely, indications, dosage forms (including sustained release dosage form) and route of administration of already approved drugs and combination of two or more drugs	- Yes - No - N/A
13	Study/Data collection proforma	- Appropriate - Inappropriate Comment
14	Involvement of Vulnerable participants	- Yes - No - N/A Comment: o Children (up to 18 years); o Women in special situations (pregnant or lactating women, or those who have poor decision-making powers/poor access to

		healthcare. o Terminally ill or are in search of new interventions having exhausted all therapies o Suffering from stigmatizing or rare diseases. o Economically and socially disadvantaged (unemployed individuals, orphans, abandoned individuals, persons below the poverty line, ethnic minorities, sexual minorities – lesbian/gay/bisexual and transgender (LGBT), etc.); o Have diminished autonomy due to dependency or being under a hierarchical system (students, employees subordinates, defence services personnel, healthcare workers, institutionalized individuals, under trials and prisoners). o Unduly influenced either by the expectation of benefits or fear of retaliation in case of refusal to participate which may lead them to give consent. o Tribally and marginalized communities; o Refugees, migrants, homeless, persons or populations in conflict zones, riot areas or disaster o Situations o Afflicted with mental illness and cognitively impaired individuals, differently abled mentally and physically disabled; Comments on addressing vulnerability issues:-
15	Sufficient number of participants?	- Yes -No - N/A

		Comment:
16	Control Arms (placebo, if any)	- Yes -No - N/A Comment:
17	Are qualifications and experience of the participating investigators appropriate?	- Yes -No - N/A Comment:
18	Is the duty delegations as per investigator's expertise and study-design?	- Yes -No - N/A Comment:
19	Disclosure or declaration of potential conflicts of interest	- Yes -No - N/A Comment:
20	Facilities and infrastructure of TMC for conduct of the research	- Appropriate - Inappropriate Comment
21	Is community consultation required	- Yes -No - N/A Comment:
22	Involvement of local researchers and institution in the protocol design, analysis and publication of results	- Yes -No - N/A Comment:
23	Contribution to development of local capacity for research and treatment	- Yes -No - N/A Comment:
24	Benefit to local communities	- Yes -No - N/A Comment:
25	Has the PI applied for waiver of consent?	- Yes -No - N/A Comment:
26	Has the criteria for waiver of informed consent documentation been met?	- Yes -No - N/A Comment:
27	Is the waiver of consent granted?	- Yes - No -N/A **Specify reasons for granting waiver of consent** o Research involves 'not more than minimal risk o There is no direct contact between the researcher and participant o Rights of the participants are not violated o Confidentiality of data and privacy of research participant are protected **If No, Specify reasons for not granting waiver of consent**

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

Assessment Report

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

Assessment Report
AX2-V1/SOP04a/V1

Assessment of Resubmitted Protocol

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

investigators? -Yes - No	
Signature:	**Date:**

AX3-V1/SOP04a/V1
IEC scoring form for intramural projects
Tomo Riba Institute of Health and Medical Sciences (TRIHMS)

TRIHMS Project No. -
Principal Investigator-

Review Criteria	*Max. Marks*	IEC Reviewer 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 based proposal? * If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? * What will the 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 the Investigators?

Y/N

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

Institutional Ethics Committee,
Tomo Riba Institute of Health and Medical Sciences (IEC, TRIHMS)

Title: Expedited Review of Submitted Protocol/Documents

SOP Code: SOP 04b/V1 Date: 03/10/2018 Pages: 140 to 146

4b.1 Purpose

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

4b.2 Scope

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

4b.3 Responsibility

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

4b.4 Categorization of protocols

The 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 into the above three types. An investigator may apply for expedited review for the study protocol using Expedited Review Application Form (AX1-V1/SOP04b/V1).

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

4b.5 Expedited Review

- Expedited review is a procedure through which certain kinds of research proposals that pose no more than minimal risk may be reviewed and approved by a subcommittee (refer section 4b.6.2) without convening a meeting of the full Board for example;
- Research involving non-identifiable specimen and human tissue from sources like blood banks, tissue banks and left-over clinical samples.
- Research involving clinical documentation materials that are non-identifiable (data, documents, records).
- Modification or amendment to an approved protocol including administrative changes or correction of typographical errors and change in researcher(s), handover of trials or projects.
- Minor changes in previously approved research during the period covered by the original approval may be eligible for expedited review where:

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

- Revised proposals previously approved through expedited review, full board review or continuing review of approved proposals.
- Minor amendments/corrections in the CRF, eCRF, budget Minor deviations from originally approved research causing no risk or minimal risk;
- Continuing review of research previously approved by the convened IEC (e.g., not originally subject to expedited review) may be eligible for expedited review if
    a) The research is permanently closed to the enrolment of new subjects.
    b) All subjects have completed all research-related interventions.
    c) The research remains active only for long-term follow-up of subjects.
    d) Where no subjects have been enrolled and no additional risks have been identified.
    e) Where the remaining research activities are limited to data analysis.
- Expedited review of SAEs/unexpected AEs of minor nature will be conducted by SAE subcommittee.
- For multicentre research where a designated main EC among the participating sites has reviewed and approved the study, a local EC may conduct only an expedited review for site specific requirements in addition to the full committee common review.
- Premature Termination/ Discontinuation/ Suspension/Withdrawal of study before site initiation.
- Research on interventions in emergency situation – When proven prophylactic, diagnostic, and therapeutic methods do not exist or have been ineffective, physicians may use new intervention as investigational drug (IND) / devices/ vaccine to provide emergency medical care to their patients in life threatening conditions. Research in such instance of medical care could be allowed in patients –
    I. When consent of person/ patient/ responsible relative or custodian/ team of designated doctors for such an event is not possible. However, information about the intervention should be given to the relative/ legal guardian when available later;
    II. When the intervention has undergone testing for safety prior to its use in emergency situations and sponsor has obtained prior approval of DCGI;
    III.Only if the local IEC reviews the protocol since institutional responsibility is of paramount importance in such instances.
    IV.If Data Safety Monitoring Board (DSMB) is constituted to review the data;

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.
4. When the research involves no more than minimal risk to the subjects but require funding

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/V1

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-V1/SOP 03/V1)] 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 board review (as per SOP04a). After deciding that the study or study documents qualify for an expedited review, Member Secretary informs the Chairperson. Member Secretary in consultation with the Chairperson forms a subcommittee comprising of the Member Secretary of the IEC, an external IEC member and one or two IEC members from TMC. The external member will chair the meeting. The project documents will be provided to the lead discussant. Two lead discussants will be assigned. Review may be made either by circulation of comments, email, telephone discussion or meeting. The lead discussant should complete the online study assessment form **(AX1-V5/SOP04a/V5)**.

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 the same 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.
In reviewing the research, the lead discussants may exercise all the authorities of the IEC except that the lead discussants may not disapprove the research. If that is the case, it must go through full board review. The decision of the full board meeting will be communicated to the PI.

The lead discussants while reviewing the projects meeting the criteria for expedited review are required to document in the study assessment form the justification for using the expedited procedure for initial and continuing review of research, actions taken by the reviewer and any findings required by laws, regulations, codes, and guidance.
The lead discussant using expedited procedures should complete the online study assessment form to document protocol-specific reasons justifying a waiver of consent.

The expedited review process should ordinarily be completed within 5 working days after it has been accepted and categorized for expedited review by the Member Secretary of the IEC. Although the project qualifies for expedited review, it may be reviewed in the full board meeting due to logistics or any other reason.

Research proposals that have undergone expedited review/undergone subcommittee review should be ratified by the full committee, which has the right to reverse/or modify any decision taken by the subcommittee or expedited committee.

4b.6.3 Communication between the IEC and the investigator

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

Annexure 1
AX1-V1/SOP04b/V1
Expedited Review Application Form

TRIHMS Project No. :_____(*To be filled by IEC Secretariat*)
1. Principal Investigator's Name: _____

2. Department : _____
3. Title of Project: _____
4. Name of study team members: _____
_____

5. Brief description of the project:
_____
_____

6.State reasons why expedited review from IEC is requested? (Tick applicable)

- Risks to subjects is no more than minimal
- Research involving non identifiable specimen and human tissue from sources like blood bank, tissue banks, left over clinical samples
- Research involving materials (data, documents, records, or specimens) which are non-identifiable that have been collected, for non-research (clinical) purposes

Are children included in the study? Yes / No
Does the research involve vulnerable population? Yes / No

Any other reasons: _____

Principal Investigator's signature: _____ Date_____

Recommendations by the IEC Member Secretary:

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

Final Decision: Expedited Review / Full Board Review

Signature of the Member Secretary:

Date- _____

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Exemption from the Review for Research Projects

SOP Code: SOP 04c/V1 Date:03/10/2018 Pages: 147 to 156

4c.1 Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe the IEC review exemption process and delineate the research studies that can be exempted from full board/expedited IEC review. The Exemption Form AX1-V1/SOP04c/V1 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. This SOP describes exemption from review in detail. The specific points in the Exemption Form shall guide the Member Secretary to determine whether the study qualifies for exemption from review. The decision should be taken by the 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, the letter conveying the decision. AX01-V1/SOP04c/V1.

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 may also apply for exemption from IEC review of the study protocol using Review Exemption Application Form (AX1-V1/SOP04c/V1).However the decision to accept the request will be made by the Member Secretary, IEC with permission from the Chairperson.

4c.5 Exemption from review

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

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

- Research conducted on data available in the public domain for systematic reviews or meta-analysis.
- Observation of public behavior when information is recorded without any linked identifiers and disclosure would not harm the interests of the observed person.
- Quality control and quality assurance audits in the institution.
- Comparison of instructional techniques, curricula, or classroom management methods.
- Public health programmes by Govt. agencies such as programme evaluation where the sole purpose of the exercise is refinement and improvement of the programme or monitoring (where there are no individual identifiers).

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.

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

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

2.No research can be considered as minimal risk if it involves but is not restricted to the following:

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 behavior(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.

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 AX1V1/SOP04c/V1, 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.5.

4c.6.3 Exemption Process

- If the protocol and related documents satisfy the criteria as listed in 4c.5, 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 full board/expedited meeting as appropriate. .
- Exempt research should fulfil organization's ethical standard, such as:
    - ❖ The research should hold less than minimal risk to participants.
    - ❖ Selection of participants should be equitable.
    - ❖ If there is recording of identifiable information, there should be adequate provisions to maintain the confidentiality of the data. If there are interactions with participants, the 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.
- The Member Secretary will inform the IEC of the decision at the forthcoming regular meeting and minute it in the meeting notes.

Annexure 1
AX1-V1/SOP04c/V1
Review Exemption Application Form

TRIHMS 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, study population, and procedures/methods to be used in the project.

Please check that your application / summary includes:

- Procedures for voluntary, informed consent
- Privacy & confidentiality
- Risk to participants
- Needs of dependent persons
- Conflict of interest

- Permission for access to participants from other institutions or bodies
- Inducements

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

- o Audit of educational practices
- o Observation of public behaviour when information is recorded without any linked identifiers and disclosure would not harm the interests of the observed person;
- o Quality control and quality assurance audits in the institution;
- o Comparison of instructional techniques, curricula, or classroom management methods;
- o Research on microbes cultured in the laboratory
- o Research on immortalized cell lines
- o Research on cadavers or death certificates which reveals no identifying personal data
- o Analysis of data freely available in the public domain for systematic reviews or meta-analysis;
- o Consumer acceptance studies related to taste and food quality; and
- o Public health programmes by Govt agencies such as programme evaluation where the sole purpose of the exercise is refinement and improvement of the programme or monitoring (where there are no individual identifiers).
- o Any other (please specify) ----------

Principal Investigator's signature: _____ Date _____

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

Forwarded by the DMG Convenor/Secretary:
Name: _____
Signature: _____
Date: _____

Recommendations by the IEC Member Secretary:

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

- Discussion at full board

Signature of the Member Secretary: _____ Date _____

Final Decision:

- Exemption
- Cannot be exempted,
- Reasons _____
  _____

- Discussion at full board

Signature of the Chairperson: _____ Date _____

Final Decision at Full Board meeting held on _____

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.

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Tittle: Agenda Preparation, Meeting Procedures and Recording of Minutes

SOP Code:SOP05/V1 Date: Pages: to

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 three months. The IEC will meet on first Monday of every month at 10.00 a.m. (unless otherwise notified).

Meeting Venue: For IEC : Meeting room, 1st Floor, MEU office, TRIHMS, Naharlagun, Pin 791110.

5.2Scope

This SOP applies to procedures to conduct the IEC meeting.

5.3Responsibility

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

5.4Detailed 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.
- Lead discussants will be assigned as necessary taking into account conflicts of interests of members. In addition, the IEC Administrator will check the agenda prior to the meeting to identify IEC members who may have a conflict of interest due to their participation as key personnel on a current or proposed research project. If a conflict of interest is identified, the study is assigned to another member who does not have a conflict of interest. An IEC member who has a conflict of interest with regard to a research project that will be reviewed at a convened IEC meeting must notify the IEC office of the conflict prior to the meeting. Once the IEC office receives notice of recuse, the IEC Member Secretary will seek an alternate IEC member to join the meeting for the review of that project if necessary to meet quorum.
- It is general practice (but not required policy) that IEC Chairs are not assigned lead discussant responsibilities except in circumstances when their expertise is the most appropriate.

5.4.2 Distribution of Study/Documents Packages to the IEC Members

- A hard copy/ soft 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 cancelled 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 02/V1 section no. 2.9) is fulfilled. This should be maintained throughout the meeting and at the time of decision making.
- 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 Member Secretary should discuss the minutes of the previous full board/expedited 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 list of protocols that were exempted should be notified.
- The IEC may invite investigators to attend the full board meeting related to their studies, and clarify doubts, if any
- All proposals that are determined to undergo full board review must be deliberated and decision about the proposal taken at a full board meeting.
- Time allotted for the meeting should be reasonable to allow ample discussion on the each agenda item.
- 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.
- The Member Secretary may identify subject experts to review the proposal as per need. The comments of an independent consultant (if applicable) could be presented by the Member Secretary or these experts may be invited to the EC meeting or join via video/

tele conference but will not participate in final decision making. However, her/his opinion must be recorded.

- 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/V1) 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 of the IEC including the Chairperson and the Member Secretary present in the room have the right to vote/express their decision and should exercise this decision. If there is equality of votes, the chair will have a casting vote.
3. The concurrence / voting of the members will be recorded in the minutes as - Agreed / Disagreed / Abstained /Recused.

- Agreed: in favour
- 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
- **Revision with minor modifications/amendments -** refers to minor modifications that do not alter the risk-benefit assessment for the research and do not require substantial changes in protocol and informed consent document. The revisions will be reviewed by the Member Secretary, IEC or in some cases by the respective lead discussant on behalf of the full board. Such revised proposals may not be taken up for the full board review, however in some cases may be referred for a full board review. If revisions are found satisfactory, approval will be granted.

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

- **Revision with major modifications for resubmission -** Extensive revisions are necessary. Principal Investigator has to comply with the changes suggested by IEC and respond to the queries. The revised project will then be reviewed in the next full board meeting.

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

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

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

An IEC may decide to reverse its positive decision on a study if it receives information that may adversely affect the risk/ benefit ratio/ safety of participants.

- Any advice by the IEC that is non-binding will be appended to the decision.
- The discontinuation of a trial will be recommended if the IEC finds that the goals of the trial have already been achieved midway, unequivocal results are obtained or if the IEC feels the continuation of the trial may potentially harm participants.

- If necessary, the investigator may be invited to present the protocol or offer clarifications in the meeting. Representative of the patient groups or community can be invited during deliberations to offer their viewpoint.
- Subject expert/s may be invited to offer their views or their review comments would be considered. The expert/s should not participate in the decision making process. However, his / her opinion must be recorded.
- The proceedings of the IEC meetings will be documented and the meeting minutes will be signed by the Chairperson/Member Secretary, IEC.

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 will be circulated to all the members for comments before final approval by Chairperson/Co-Chairperson.
- The minutes of the IEC meeting will be approved and signed by Chairperson/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 and relevant stakeholders, preferably within a period of 15 working days of the IEC meeting at which the decision was made.

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

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

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

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

Calculation of

Expiration Date

Initial Approval

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

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

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

  Date of IEC approval +364 days= Date of expiry

  01/05/2020 + 364 days =) Valid till

  30/04/2021

- 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
- The date of approval of a study is the date of issuance of the IEC approval letter.
- In the case of a positive decision, the PI is notified of the following requirements through an

approval letter (AX2-V1/SOP05/V1)

- Responsibilities of the PI
- Submission of annual status reports/progress report(s) is decided on case to case basis, usually yearly.
- The need to notify the IEC in the case of amendments to the recruitment material like the potential research participant information, or the informed consent form
- The need to report serious and unexpected adverse events related to the conduct of the study
- The need to report unforeseen circumstances, the termination of the study, or significant decisions by other IECs or DSMBs
- The information the IEC expects to receive in order to perform on-going review
- The final summary or final report
- The schedule/plan of ongoing review by the DSMB of sponsored trials

- IEC shall intimate the licensing authority about the approval of clinical trials intended for academic purposes such as use of approved drug formulation to study new indication or new route of administration or new dose or new dosage .The IEC shall await for comments from the DCGI for a period of 30 days from the date of receipt of communication from the IEC. If no communication from DCGI is received in the specified time frame, IEC shall presume that no permissions are required from the licensing authority and will issue the final approval letter for the study.
- 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.

AX1 –V1/SOP05/V1

Agenda/Minutes format

I. Minutes-IEC &DSMU

II. SAEs

III. Deviations

IV. Projects for Initial Review

V. Resubmission of projects after initial review

VI. Post approval amendments a)Protocol b) ICF c)IB d)CRF

VII. Status Reports

VIII. Monitoring Reports

IX. Letters

X. Any other

AX2 –V1/SOP05/V1

Approval Letter Format

FORMAT FOR APPROVAL LETTER OF IEC

To,
Dr.
Principal
Investigator,
TRIHMS,
Naharlagun..

Ref:

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

The waiver of consent was granted since_____

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**
- **Submission of DCGI approval to IEC (if applicable).**

Following points must be noted:

1. **IEC has approved recruitment/review of_____participants/samples on this study.**
2. **IEC has approved the conduct of the study at TRIHMS**
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 unit (DSMU), 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/ICHGCP
9. In the events of any protocol amendments, IEC must be informed and the amendments should be highlighted in clear terms as follows:

    a) The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)

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

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

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

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

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

10. Any Serious Adverse Events (SAEs) occurring on the study should be reported to IEC

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

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

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

14. Principal Investigator should comply with regulations and guidelines as applicable

Thanking You,
Yours Sincerely,
Member Secretary,
IEC - TRIHMS.

AX3 –V1/SOP05/V1

Letter Format for project / Amendments

Dr…

Principal Investigator,
TRIHMS.

Ref: Project No. Title Dear

Dr…

The following documents of the above referenced project was reviewed and discussed during the IEC meeting held on date/time/place
The following members of the IEC were present:
IEC comments were as follows-

a.

b.

c.

Status-

i. **Approved**
ii. **Revision with minor modifications/amendment, Revision with major modifications for resubmission. Kindly comply with the above suggestions of the IEC and submit the one copy of revised proposal or documents within six months for review. If you fail to submit within six months, this project will be closed by IEC and you will have to submit a new project.**
i. **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
sincerely,
Member Secretary,
IEC TRIHMS

AX4 –V1/SOP05/V1

Format for Documents Date

Dr. ,
Principal Investigator,
TRIHMS

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. **Revision with minor modifications/amendments, Revision with major modifications for resubmission. Kindly comply with the above suggestions of the IEC and submit the one copy of revised proposal or documents within six months for review. If you fail to submit within six months, this project will be closed by IEC and you will have to submit a new project.**
iii. **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- TRIHMS.

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Review of post approval amended protocol / Protocol related documents

SOP Code:SOP06/V1 Date: Pages: to

6.1 Purpose

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

6.2 Scope

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

6.3 Responsibility

PIs are responsible for obtaining IEC approval of proposed amendments to an IEC approved protocol before implementing them.

Amendment is a revision, modification, addition to or deletion from an approved research protocol.

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

Receipt of the Amendment Package

- The amendment /documents along with the appropriate soft copy forwarded by the PI is received by the secretariat. The amendment /documents along with the covering letter should be accompanied by Amendment Reporting Form(AX2-SOP06/V1)
- The secretariat will confirm that the: changes or modifications in the amended version are underlined or colour 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/V1 (Procedures for Management of protocol submission)

The Member Secretary, IEC, classifies the amendments into minor or major and tables the major amendments on the agenda of the subsequent scheduled meeting (for major amendment refer 6.4.1 and for Minor amendments refer to 6.4.2). The amendments and other documents which need full board review are processed as per the SOP04a/V1.

6.4 Review amended protocols/documents/letters: Review as per Section 4a.3 SOP 04a/V1.

6.4.1 Review process for major protocol amendment:

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

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

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

a) Change in study design
b) Additional treatments or the deletion of treatments

c) Changes in inclusion/exclusion criteria.

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

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

f) A significant decrease or increase in dosage amount

g) Change in risk/benefit ratio

6.4.2 Minor amendments and notifications:

Minor amendments (those that do not increase the risk or decrease the potential benefit to subjects) and minor changes in previously approved research during the period covered by the original approval: Where the research is permanently closed to the enrolment of new subjects; all subjects have completed all research-related interventions may be reviewed in the expedited review subcommittee meeting (Refer SOP No.04b/V1.).

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

This may include but may not restrict to:

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

6.5 Decision

- If the IEC approves the amendments, the decision is communicated to the PI.
- If the IEC does not approve the amendments, the secretary should immediately notify the investigator in writing of the decision and the reason for not approving the amendment.
- If the IEC recommends or suggests modifications to any of the documents, or the amendments, the secretariat sends a written communication to the investigator about the specific changes asking him or her to make the necessary changes and resubmit the documents to IEC.
- Member Secretary will issue an approval letter to the Principal Investigator, if response from the PI found to be satisfactory

6.6 Storage of Documents:

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

AX1-V1/SOP06/V1

Amendment/Document Amendment Approval letter

Format for Approval for amended documents

Date

Dr. ,
Principal Investigator,
TRIHMS

Ref: Project No. Title

Dear Dr.

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

The following members of the IEC were present:

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

This decision was taken by consensus.

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

Thanking you,

Yours truly,

Member-Secretary,
IEC- TRIHMS

AX2-V1/SOP06/V1

Post approval Amendment Reporting Form (Kindly tick in the boxes provided)

Project No.:	
Title:	
Principal Investigator:	
Date of IEC Approval:	
Start Date of Study: Status of Study: Validity of IEC approval-	
No. of amendment: Have the changes modifications in the amended versions been highlighted/ underlined? ☐ Yes ☐ No Nature of amendment ☐ Major ☐Minor	
Does this amendment entail any changes in Informed Consent Form (ICF)	☐ Yes ☐No
If yes, whether amended ICFs are submitted pl. specify ICF Version No. & Date and its IEC approval	
Please mention version no. and date of amended Protocol / Investigators Brochure / ICF Addendum/ Case Record Form / Any other documents	
• Does the revision entail any change in the Risk vs Benefit Analysis	☐ Yes ☐No
• Target accrual of trial (entire study) _____ • Total patients to be recruited at TRIHMS (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:

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Continuing review of study protocols

SOP Code: SOP 07/ V1Date: Pages: to

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 Principal Investigators regarding the submission of Continuing Review Application/Annual Status Report.
All IEC approved studies will be reviewed annually. IEC is responsible for determining the date of submission of continuing review application of the IEC approved projects including those that are reviewed more frequently in the year based on specific criteria. (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 rate of accrual of participants, the occurrence of unexpected events or problems along with protocol deviation/violation and non-compliance, any new information pertaining to the research and assess final reports of all research activities. 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 DSMU.

7.4 Detailed Instructions

7.4.1Determine the date of continuing review

- The secretariat will identify the list of IEC approved projects that are due for continuing review on a regular basis.
- The Secretariat should receive the continuing review application well in advance i.e. 10 months after IEC final approval and at least annually.

7.4.2 Notify the Principal Investigator or the study team

- Reminder emails are sent from the IEC secretariat to the Principal Investigators for submission of continuing review applications for projects, 3 months prior to the expiry of study approval/CRA approval validity date. Principal Investigators are required to submit one signed hard copy of the CRA to the DSMU.

- First reminder will be sent 3 months in advance to the lapse in validity/annual review
- Failure to submit the CRA within the due date after the 1st reminder will result in issuance of warning letter and necessary action.
- IEC may close the study if PI fails to submit CRA on time.

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 review the application for its completeness and forward it to the DSMU Member Secretary for further scrutiny. 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 in which 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.

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 DSMU 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 DSMU 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 DSMU 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-V5/SOP07/V5) 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
2. Revision with minor 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. Query – The IEC and/or DSMU has raised queries against the continuing review application submitted.
4. Deferred/On-hold-The IEC has postponed the decision on approval of continuing the study due to reasons such as awaiting expert opinion, awaiting site monitoring reports from the DSMU etc.
5. Not approved-The IEC feels that there are major concerns in the conduct of the study.

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 by the Member Secretary and maintained 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 application 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 of the IEC. If IEC has recommended modifications, the decision will be notified to the Principal Investigator and he/she will be requested to comply to IEC recommendations/ respond to IEC queries within 1 week of receipt of the IEC decision letter. In case the IEC decision is to put the study on-hold, then the subject recruitment or enrollment is suspended, however in case of safety concerns the project is completely suspended.

7.4.10 Lapses in IEC Approval

Investigators must plan ahead to meet IEC determined dates of submission of continuing review application. 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 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.

AX1-V1/SOP 07/V1

Form A
Continuing Review Application
SECTION A

1) TRIHMS Study No:
2) CTRI No (if applicable):
3) Date of Registration:
4) Protocol title:
5) Principal Investigator:
6) Phone No:
7) Email Id:
8) Institute:
9) Source of funding: Please tick
   - ☐ Intramural
   - ☐ Extramural – Please specify_____
   - ☐ Pharma – Please specify_____
   - ☐ Others- Please specify_____
   - ☐ Not applicable
10) Account No (If Applicable):
11) Date of IEC approval:
12) Date of lapse of IEC approval (for the full duration of the study):
13) Mention overall duration of study (in years/months) approved by IEC at the time of study approval:
14) Start Date of study:
15) If the start date is > 6 months from the IEC approval date kindly provide the reasons for the same
16) Date of approval of last CRA (if applicable):
17) CRA approval valid till date :
18) Period of report of the current CRA : _____/___/_____ to _____/__/_____
19) Study was initially reviewed by expedited review (Please tick) –Yes / No

20) Is the study expected to extend beyond the projected duration: Yes / No

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

22) Are you applying for extension for the same: Yes / No

23) If yes- period of extension requested?_____

24) How many prior extensions sought? (in number) _____

Section B

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

1. No of study arms (If Applicable):
2. Project Status (In case of studies on blocks/samples/retrospective case series please give the following information with respect to amount of work completed)

    ☐ Ongoing (Kindly select one option from below)

    ☐ Active Enrollment

    ☐ Accrual completed

    ☐ Target accrual reached-Yes / No / NA

    If No – provide reasons_____

    ☐ Follow-up

    ☐ Analysis

    ☐ 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)

a) Target accrual of trial (entire study) including healthy volunteers, patients and biomedical samples/blocks)_____

b) Total patients/samples to be recruited at TRIHMS (IEC ceiling)_____

c) Screened: _____

d) Screen failures: _____

e) Total participants/samples accrued since protocol began_____(should be equal to sum of i to n)

f) Date of accrual of first subject/sample:

g) New participants accrued since last review _____

h) Date of accrual of last participant: _____

i) Active on intervention- (exclude subjects who have completed intervention)05

j) No of participants who have completed intervention and are onfollow-up:02

k) Patientslosttofollowup:_(includessubjectswhohavecompletedintervention)

l) Consent Withdrawn: Reason and state at which phase of the study–before /during/after completion of intervention (Specify TRIHMS case number/Sub Id)

m) Withdrawn by PI: Reason and state at which phase of the study –before /during/after completion of intervention(Specify TRIHMS case number/Sub Id)

n) Deaths: State at which phase of the study – before /during/after completion of intervention (Specify TRIHMS case number/Sub Id)

Sub id	**Phase- Before /during/after completion of intervention**	**Whether notified to IEC- Yes/No** **If No- provide reasons**

o) Any other:_____

p) Any Impaired participants

- o None_____
- o Physically_____
- o Cognitively_____
- o Both _____

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

☐ Yes ☐No ☐NA

If 'Yes', attach in format below

TRIHMS Case No/Sub Id	SAE Event	Report type	Arm	Date submitted to DSMU

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

TRIHMS 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 ☐NA

If 'YES', please provide in format below

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

1) 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

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

☐Yes ☐No ☐NA

If 'YES', fill in format below

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

3) 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

4) Is the recruitment on schedule?

☐ Yes ☐No ☐NA

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

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

☐ Yes ☐No ☐NA

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

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

☐ Yes ☐No ☐NA

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

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

☐ Yes ☐No ☐NA

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

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

12)Does the protocol have an inbuilt monitoring plan?

☐ Yes ☐No ☐NA

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

13)Has the study been monitored?

☐ Yes ☐No ☐NA

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

Date of monitoring _____

Monitored by _____

Number of subjects monitored _____

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

☐ Yes ☐No ☐NA

(If 'YES', submit as an attachment)

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

☐ Yes ☐No ☐NA

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

16)Is the report on interim data analysis available?

☐ Yes ☐No ☐NA

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

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

☐ Yes ☐No ☐NA

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

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

☐ Yes ☐No ☐NA

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

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

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

Total budget proposed for the project _____

Total budget sanctioned for the project _____

Total budget utilized for the project _____

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

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

☐ Yes ☐No ☐NA

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

22)Any other information:___

SIGNATURES:
Principal Investigator:
Date

AX1-V1/SOP 07/V1
Form B

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

TRIHMS Project No:
PROTOCOL TITLE:
Principal Investigator: **Co- Investigator (s) :** **Phone no:** **Email Id:** **Institute**: ACTREC/TMH **Date of TRIHMS IEC approval:_____Approval validupto: _____** **Mention overall duration of study (in years/months) approved by IEC at the time of study approval:** **Start Date of study:** If the start date is > 6 months from the IEC approval date kindly provide the reasons for the same **Duration of study:** **Period of Report of the current CRA:_____/_____/_____to _____/_____/_____** **Funding Source:** **Account no:**

1) Project Status

□ Ongoing

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

□ Not started/Not initiated

If 'Not started' state reasons

2) Provide the date of last status review report submitted to TRIHMS- 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 TRIHMS- IEC?

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

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

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

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

5) Summary of Protocol participants:

o Total patients/samples to be recruited at TRIHMS (IEC ceiling)_____
o Total number of samples screened since protocol began :_____
o Total Screen failures since protocol began: _____
o Total participants accrued / samples collected since protocol began_____
o New participants accrued /samples collected since protocol began: _____
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 / NA
(If 'NO', please attach a sheet giving reasons and your plans to improve accrual)

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

Yes (Kindly attach a sheet explaining the changes) / No / NA

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 TRIHMS- 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 TRIHMS- 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 TRIHMS office?

Yes / No / NA

14) Has any information appeared in the literature, OR evolved from this OR similar research that might affect the TRIHMS- 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 / NA

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

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

If Yes, When was study last monitored?

Date of monitoring _____
Monitored by _____
Number of subjects monitored _____

16) Is the DMC report available?
Yes (If 'YES', submit as an attachment) / No / NA

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

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

18) Scientific and Technical Progress

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. How many prior extensions sought? (in numbers)

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

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

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

Total budget proposed for the project: Rs. _____

Total budget sanctioned for the project: Rs. _____

Total amount utilized for the Project: Rs _____

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

Funding Source: _____

Amount : Rs. _____

SIGNATURES:

Principal Investigator

Date:

AX2-V1/SOP 07/V1

Reminder letter to investigator

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

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

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

Thanking you for your co-operation,

Yours truly,

Signature with date
Secretary, DSMU

AX3-V1/SOP 07/V1

IEC decision letter for Continuing Review of projects

Date

Principal Investigator,
TRIHMS

Ref: Project No./ Title

Dear Dr.

The continuing review application for the above referenced project was reviewed 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 till (valid date). The Principal Investigator should submit continuing review application/annual status report on or before. In order to ensure that there is no lapse in the IEC approval period, it is mandatory to submit study status report prior to lapse of study validity.

Status: Revisions with minor modifications/ Query/Deferred/On-hold/Not approved. Kindly respond to IEC at the earliest.

This decision was taken by consensus/unanimously/voting.

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

Thanking you,

Yours faithfully,

Member Secretary,
Institutional Ethics Committee

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

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

SOP Code:SOP08/V1 Date: Pages: to

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–V1/SOP08/V1) 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 wilful or voluntary misconduct on the part of a Principal Investigator or a member of the research team.

Examples:

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

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 wilful or voluntary misconduct on the part of an Investigator or a member of the Investigator's study team.

Examples:

- Sample collections at different time points than specified in the protocol.
- Participant following up on days not specified in the protocol.

c) Protocol Waiver

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

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

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

Examples of waivers are:

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

d) Non-compliance

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

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

ii. Serious Non-compliance: An action or omission, non-compliant with national regulations or IEC policy, taken by an investigator that any other reasonable investigator would have foreseen as increasing risks or compromising the rights and welfare of a participant or other 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 protocol deviation/ violation /noncompliance in studies that enrol 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.b 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 TRIHMS are required to report all suspected noncompliance to the IEC

8.4.1.c 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, TRIHMS informing IEC about an alleged protocol violation/ protocol deviation/non-compliance

8.4.2 Noting protocol deviation / violation / waiver / non-compliance by the Secretariat

- The PI will report the protocol deviation/violation as per Annexure 1AX1V1/SOP08/V1
- The IEC members who have performed monitoring of a particular trial and detect protocol deviations/non-compliance/violations will inform the Secretariat inwriting.
- 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

i. 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 IEC will undertake an inquiry. Chairperson, IEC may temporarily suspend the study, pending review in IEC.

ii. Member Secretary IEC in consultation with Chairperson, IEC undertakes an inquiry of the allegations within 7 working 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.

iii. Qualified IEC staff documents and compiles the information and Member Secretary IEC presents the findings to the IEC.

iv. 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 infact.

v. 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.

vi. 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.

1. National regulatory agencies are notified, if applicable.
2. In case of externally funded studies, notice is sent to the sponsor and to the concerned regulatory bodies.
3. 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:

i. The issue is resolved by a subcommittee of IEC (comprising of member Secretary, IEC, DSMSC Secretary, one IEC member). Principal investigator and concerned staff may be called for the discussion.
ii. Member Secretary IEC documents the outcome of all communications in writing. This report includes any actions to be taken by IEC or corrective actions required on the part of the investigator and the timelines for resolution.
iii. A copy of this report is sent to the principal investigator(s) involved in the noncompliance, associated research staff and others as deemed appropriate within 21 working days.
iv. A written response from the principal investigator acknowledging the report and describing corrective actions is required within 07 working days from the date of the corrective report.
v. The complainant will be provided information as deemed appropriate by the IEC Chair.
vi. All communication is documented in a restricted IEC confidential file.
vii. 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.

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- E-mail: OHRP@hhs.gov

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, but not limited to

- 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 if required to the Department Head(s) and Institutional Officials.

- 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

AX 1-V1/SOP08/V1

Deviation (D)/Violation (V)
Reporting Form

Please report single event in one reporting form
Specify ifD/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.

IEC Project No.:
Project Title:
Participant Case No. :
Trial Id :
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: Phase of

Study i.e Active Intervention/Completed Intervention/Follow up:

Study status:
IEC approval Date-
Target recruitment -
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**
- ☐ **Protocol procedure**
- ☐ **Laboratory assessment**
- ☐ **Investigational Product**
- ☐ **Safety Reporting**
- ☐ **Source documentation**
- ☐ **Staff**
- ☐ **Participation-compliance**
- ☐ **Others (Please specify)**

Complete Details of D/V:

Impact on (if any):

Trial participant ☐ **Yes** ☐**No If yes, please specify**

Quality of data ☐ **Yes** ☐**No If yes, please specify**

Action taken by PI/Co-PI/Co-I:

Are any changes to the project/protocol required?

☐ **Yes** ☐**No**

If yes, please specify the changes of Protocol

Name of PI:

Sign of PI:

Date:

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Review of Serious Adverse Events (SAE) Reports

SOP Code: SOP 09/V1 Date: Pages:

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 benefit /risk 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 and safety of study participants.

9.2 Scope

This SOP applies to the Data Safety Monitoring Unit (DSMU) and IEC review of SAEs and unexpected events reports, both onsite and offsite, including follow up reports submitted by investigators. The detailed instructions regarding SAE review are described in the following section 9.4.

Investigators, IEC members and DSMU members must follow the procedure as per current regulations. This prescribes procedures for reporting of SAEs and the provision of compensation in case of injury or death during clinical trial.

9.3 Responsibility

The primary responsibility of the DSMU/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/SUSARS/CIOMS reports and directing them to DSMU for detailed review. Following the DSMU meeting, the Secretary, DSMU will then forward the minutes of the DSMU meeting to the IEC. DSMU minutes are discussed in the subsequent IEC meeting.

Notifying the IEC/DSMU 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

- **The initial reports of all serious adverse event of Death/ other than death** should be reported by the PI along with the justification for the causality assessment **within 24 hours** of the occurrence to-
    1. IEC
    2. Sponsor or its representative
    3. CDSCO (in case of studies that require approval of the CDSCO)

- **The follow up report of the serious adverse event of Death/ other than death** along with the justification for the Principal Investigator's causality assessment shall be forwarded by the Investigator within **fourteen calendar days** of the occurrence of the serious adverse event of death to-
    1. IEC
    2. Sponsor or its representative
    3. CDSCO (in case of studies that require approval of the CDSCO)
    4. Head of the Institution (in case of studies that require approval of the CDSCO)

- In case the event is Death due to disease progression, the event should be notified in the SAE reporting format unless it is specified in the IEC approved protocol that such events will not reported.

- If the patient is out of trial and on survival follow up the event should be notified unless it is specified in the IEC approved protocol that such events will not reported

- SAE reports are received by DSMU - 01 signed hard copy (original) + soft copy

- Serious Adverse Event should be graded as per CTCAE Ver. 5.0

- 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 14 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, 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 DSMU Office.
- The IEC Secretariat will verify if the reports are complete, signed and dated by the PI/Co-PI/Co-I and will check for dates and typo errors in the SAE report such as SAE description, SAE term and CTCAE grading
- In case the IEC Secretariat notes that the report is incomplete or incorrect, the report will be returned to the PI with the consent of Secretary, DSMU
- 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 or any other justified reasons, SAEs may be reported as email notifications or soft copy attachment of SAE form in order to meet SAE reporting timelines. Email notifications should include patient trial id, patient case number, SAE event and a brief description of the SAE. However duly signed hard copies of the SAEs along with the email notification (hard copy) should be submitted to DSMU 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, DSMU, 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, DSMU within 1 working day for immediate action either as hard copy or via email. If deemed necessary, Member Secretaries of IECs and Secretary, DSMU 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 discussion, necessary action may be taken by the DSMU Secretary/IEC Member Secretary
- SAEs received from 1st – 31st of every month are reviewed in the scheduled DSMU meeting

- Two lead discussants are assigned by Secretary DSMU 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, DSMU 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 DSMU members via email for review.

9.4.4 After the DSMU review of SAE

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

9.4.5 Responsibilities of the IEC in case of studies that are approved by licensing authority (DCGI):

- In case of SAE (any) report, IEC after due analysis will send its opinion on compensation to the licensing authority within 30 calendar days of the occurrence of the serious adverse event

9.4.6 During the IEC meeting

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

- Note the SAE report in the IEC records if information submitted is found to be adequate
- Direct the PI to inform participants already enrolled in the study about the SAE and request them to undertake additional visits, additional procedures, additional investigations, etc. as per recommendation

- Direct the PI to re-evaluate the event as to whether it is AE/SAE and report to IEC.
- Direct the PI to inform participants already enrolled in the study about the SAE and obtain their consent regarding continuation in the research study, if necessary.
- Request further follow up information
- Request additional details
- Recommend an amendment to the protocol, the ICD, Participant information sheet, investigator brochure and/ or any other document.
- Recommend whether or not compensation should be paid to the patient /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

9.4.7 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 DSMU, 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.

- For-cause monitoring

- 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-V1SOP09/V1) 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-V1 SOP09/V1) will be reported to IEC Secretariat, and forwarded to Member Secretary, IEC and Secretary, DSMU.
- If the IEC and DSMU 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 needs to be reported by the PI and action on such reports will be taken by the Member Secretary, IEC and Secretary DSMU, as per 9.3-9.4
- The IEC Secretariat will timely accept the complete set of "Off site SAE reports" and/ or the log.

Off site SAEs (PSUR)

- The PSUR/Line listings submitted by PI on a monthly/quarterly/biannual basis are filed by DSMU as a detailed review of the same is out of the scope of IEC/DSMU.
- It is the PI's responsibility to review the listings in detail and report if a trend is observed and communicate the same to DSMU.
- 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 DSMU/Noted & File' and then forwarded to IEC for signature/review
- Any queries raised by the IEC Secretary 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
  - 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, ifnecessary.
  - 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 were already discussed in DSMU and ratified in previous IEC meetings will be answered based on the opinion and findings of the DSMU 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. 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.

AX1-V1/SOP09/V1

AX-V1/SOP9/V1 **SERIOUS ADVERSE EVENT REPORT** **TRIHMS**	**TRIHMS 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**

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.	Date of Occurrence of SAE:	
4.	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 _____	
	If report is delayed, provide reasons- _____	
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: (Kindly refer to CTCAE V5.0 where applicable) B] CTCAE Grade: (where applicable)
10.	Does the Principal Investigator feel this SAE is related to participation in the trial ☐ Yes ☐ No ☐ NA 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 ☐ NA		
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 ☐ NA 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/DSMU 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 15 days or earlier (of occurrence of the SAE) to the IEC
For IEC use only	

Final Assessment of DSMU/ 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 borne by: Institute/ Sponsor/participant
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. DSMU Reviewer_____ date: _____ Explanation:

AX2-V1/SOP09/V1

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-V1/SOP 09/V1). This log should be timely submitted to the IEC Secretariat

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-V1/SOP09/V1

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 timely submitted to the IEC Secretariat. 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.
4. 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 ☐ NA

Name and Signature of Principal Investigator: Date:

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Maintenance of Active Project Files, Archival / Disposal of closed files and Retrieval of documents

SOP Code: SOP 10/V1 Date: Pages:

10.1 Purpose

To provide guidelines for preparation and maintenance of study files and other related documents for all IEC approved ongoing projects as well as storage/archival/disposal of study files and other study related documents for projects which are completed and closed

10.2 Scope

This SOP applies to all active/closed protocol/study 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 the 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 of all essential documents and correspondence related to the study/protocol. Study master file 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 archive the closed project files 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 Secretariat, auditors and the regulatory authorities would have access to these files.
- The records are stored by ITS on servers and 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–V1/SOP10/V1). 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 requested 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- V1/SOP 10/V1) will be maintained, providing details of the documents being written off / disposed off.

Annexure
AX1 –V1/SOP10/V1
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: Provide reason for non-availability of the requested document in the PI master file:	
Principal Investigator / Requesting person’ s sign & date	
Permission of the Secretariat: Yes/No Signature of IEC Secretariat:	

AX2 –V1/SOP10/V1

Format of written off/disposal register

Project No	Title	PI	No. of Files	IEC Approval Date	Study Initiation Date	Status	Study Closure Date	Name & Sign of Authorized Individual

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Documentation of the IEC activities

SOP Code: SOP 11/V1 Date: Pages:

11.1 Purpose

To describe the procedures for documenting the IEC activities.

11.2 Scope

This SOP will apply to all research proposals submitted to IEC for review and approval.

11.3 Responsibility

It is the responsibility of the IEC staff to maintain the IEC files in the IEC office.

11.4 Detailed Instructions

11.4.1 IEC records will include the following

1. IEC member records
    a. Appointment and Acceptance letters of each member
    b. Terms of Reference
    c. Signed and dated confidentiality agreements/ Conflict of Interest and financial disclosure form
    d. Updated Curriculum vitae /MMC (if applicable)/ Good Clinical Practice certificate
    e. Training records of each IEC member
    f. Documentation of resignations/terminations
    g. Terms of Reference

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 are maintained in the "master file."

10. IEC records of initial and continuing review of research by the full board procedure include:

- Study assessment forms submitted by the lead discussants on review of research proposals.
- Scoring sheets of proposals that has sought intramural funding.
- Any other findings required by laws, regulations, codes, and guidance to be documented.

11. IEC records of initial and continuing review of research by the expedited procedure include:

- The justification for using the expedited procedure.
- Study assessment forms submitted by the lead discussants on review of research proposals.
- Any other findings required by laws, regulations, codes, and guidance to be documented.

12. IEC audit files
13. IEC Member/Staff evaluation file
14. IEC records document the justification for exempt determinations. Maintains files on Exemption Requests and Emergency Use Notification.
15. Registration/accreditation documents, as required
16. Regulatory correspondence
17. A copy of national and international guidelines and applicable regulations
18. 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.

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Review of study completion reports

SOP Code: SOP 12/V1 Date: Pages:

12.1 Purpose

The purpose of this SOP is to provide instructions on the review of Study Completion Report for the 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-V1/SOP12/V1) 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/V1 (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/V1).

12.4.2 Before and during Board Meeting

- IEC member(s) should review 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 will be 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 15 days. This update will be tabled in the Full Board Meeting ofIEC.

- 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/V1 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.

Annexure

AX1-V1/SOP12/V1

Study Completion Report
TRIHMS Project No. - Study Title: - Principal Investigator: -
Sponsor - Funding Source - Account No -
Duration of the study -
Date of IEC Approval 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 TRIHMS (IEC ceiling)_____ o Screened: _____ o Screen failures: _____ o Enrolled: _____ o If total target accrual could not be achieved – Kindly provide reasons o Consent Withdrawn:_____TRIHMS Case No& Reason for withdrawal o Withdrawn by PI:_____TRIHMS 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 the funding agency/ TRIHMS-IEC - 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 TRIHMS -IEC (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 field**

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Management of Premature Termination / Suspension / Discontinuation of the study / Withdrawal of study before site initiation

SOP Code: SOP 13/V1 Date: Pages: to

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 but not limited to:
  - When research is not conducted in accordance with IEC policies.
  - When research is associated with unexpected serious harm to participant
  - Failure to submit status report
  - For e.g. - Frequency of SAEs occurring at the institution or other sites in case of multicentre studies may require the study to be prematurely terminated for the safety of the patients.
  - If protocol non-compliance/violation is detected
- **Suspension/Termination/ Discontinuation By Investigator/Sponsor:**

  An investigator may also put on hold a previously approved research when in the judgment of the investigator this is appropriate to protect the rights or welfare of participants or when new safety information appeared in the literature, or evolved from this or similar research

- Withdrawal of study before site initiation. An investigator may withdraw a study before site initiation due to reasons such as regulatory delays, logistic and budgetary infeasibility etc.
- Reports of Suspension/Termination/ Discontinuation/ by 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- V1/SOP13/V1) 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- V1/SOP13/V1) 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 / TRIHMS IEC 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.

AX1- V1/SOP13/V1

Premature Termination / Suspension / Discontinuation Report

TRIHMS Project No.:	
Protocol Title:	
PI:	
E-Mail:	
Study Site:	
Sponsor/Funding agency:	
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 TRIHMS (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 _____

Total number of SAEs reported (if applicable):

Type of SAEs reported:

Have any adverse events or outcomes reported to the IEC- □ Yes □ No □ NA

Have any Protocol deviation/ violation reported to the IEC- □ Yes □ No □ NA

If yes, please provide the list of reports in tabular form.

Have there been participant complaints or feedback about the study

□ Yes □ No □ NA If yes Describe _____

Had there been any suggestions from the DSMSC

□ Yes □ No □ NA

If yes, have you implemented that suggestion

□ Yes □ No □ NA

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): □ Yes □ No □ NA

If No- provide reasons-

Summary of Results (if any) :

Budget sanctioned-

Budget utilized-

(Please enclose UC duly signed by Accounts officer)

PI Signature:	Date:

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title :Review of Request for waiver of Written Informed Consent

SOP Code: SOP 14/V1 Date : Pages:

14.1 Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe the type of research 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-V1/SOP 14/V1 is designed to standardize the process of applying for consent waiver.

14.2 Scope

This SOP applies to the protocols with a request for granting consent waiver submitted for IEC review.

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. The decision to grant waiver of consent should be taken by the IEC members at the expedited subcommittee meeting or during full board meeting.

14.4 Detailed instructions

- The PI can apply to the IEC for a waiver of consent; if the research involves less than minimal risk to the participants and the waiver will not be adversely affect the rights and welfare of the participants.
- When a request for waiver of consent is submitted by the Principal Investigator along with the study documents to the IEC secretariat, in the given format AX1-V1/SOP 14/V1 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 IEC will document its findings justifying the waiver or alteration of the consent process.
    - ✓ The IEC minutes will document required determinations and protocol-specific findings justifying those determinations for:
        - Waiver or alteration of the consent process.
        - Research involving participants with diminished capacity
    - ✓ The decision regarding approval/disapproval of waiver is informed to the Principal Investigator in writing. If the waiver is not granted, the 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 2017guidelines) must be met for a research project so that it can qualify for granting a waiver of both written and verbal consent.

The researcher can apply to the EC for a waiver of consent if the research involves less than minimal risk to participants and the waiver will not adversely affect the rights and welfare of the participants (5.7-ICMR 2017)

1. The EC may grant consent waiver in the following situations:
   - Research cannot practically be carried out without the waiver and the waiver is scientifically justified;
   - Retrospective studies, where the participants are de-identified or cannot be contacted;
   - Research on anonymised biological samples/data;
   - Certain type of public health studies/surveillance programmes/programme evaluation studies;
   - Research on data available in the public domain; or
   - Research during humanitarian emergencies and disasters, when the participant may not be in a position to give consent. Attempt should be made to obtain the participant's consent at the earliest.

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

e.g. conducting interviews with citizens about their religious beliefs/ people with HIV and AIDS/conducting phone interviews with homosexuals.

The only record linking the participant and the research would be the consent document and when there is a possible legal, social or economic risk to the participant entailed in signing the consent form as they might be identified as such by signing the consent form, the requirement for obtaining consent can be waived of by the 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 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 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 pre-empt 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 that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

2) In cases in which the documentation requirement is waived, the IEC may require the investigator to provide subjects with a written statement regarding the research.

3) An IEC may waive the requirement for the investigator to obtain a signed consent form if an appropriate well documented mechanism is substituted for protecting the children who will participate in the research.

4) The IEC is allowed to waive parental consent 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.

14.6 Consent in public health research may be waived:

- On routinely collected data under programme conditions, including research involving linkage to large anonymous databases of information that has been routinely collected such as administrative data and through surveillance activities. However, at the time of collection people concerned may have been told that the data would be used for other purposes, including research.
- In circumstances where obtaining consent is impractical, such as for stored anonymous data/ biological samples, surveillance and administrative data or personal non-identifiable data/ material available from public health programmes.
- For studies performed within the scope of regulatory and public health authorities, such as process and impact evaluations of national policies and programmes, including neonatal screening programmes or diabetes screening as part of national programme activities may be exempt from the requirement for informed consent.
- When the primary purpose is refinement and improvement of the public health programmes;
- For studies using health-related registries that are authorized under national regulations; or
- When it is not practical or meaningful to obtain consent in large geographical clusters in cluster randomization trials and several Implementation Research (IRs).

AX1-V1/SOP14/V1

Application form for requesting waiver of consent

1. **Principal Investigator's name:**
2. **Designation:**
3. **Department:**
4. **Title of project:**
5. **Names of other Co-investigators:**
6. **Request for waiver of informed consent:**

- **Please tick the reason(s) for requesting waiver (in boxprovided)**

1. **Research involves 'less than minimal risk'** ☐
2. **There is no direct contact between the researcher and participant** ☐
3. **Retrospective studies, where the participants are de-identifiedor cannot be contacted-** ☐
4. **Certain types of public health studies/surveillance programmes/programme evaluation studies-** ☐
5. **Research on anonymized biological samples/data** ☐
6. **Research on using data available in the public domain** ☐
7. **Any other (please specify)- [PI to provide justification for the waiver of consent]**

- **Statement assuring that the rights of the participants are notviolated**
- **State the measures described in the protocol for protecting confidentiality of data and privacy of research participant**

Principal Investigator's signature with date

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Site Monitoring

SOP Code: SOP 15/V1 Date: Pages:

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 Safety and Monitoring Unit 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 DSMU Secretary assigns the DSMU members /independent experts to monitor the trials. The monitoring is conducted by at least 2 members of the DSMU 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.

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 but not limited to :

  - 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 DSMU 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 DSMU 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. DSMU 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-V1/SOP15/V1).

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-V1/SOP15/V1 and write the comments.

15.4.4 After the visit

- The monitor will complete the report (use the form AX1-V1/SOP15/V1) describing the findings of the monitoring visit and submit the same to the DSMU office. After the form is received at DSMU office, it is checked for completeness. The preliminary comments will be shared with the PI.
- Form is reviewed by DSMU secretary, and the form is forwarded to IEC Secretary for action
- The IEC Secretary/DSMU member representative/lead discussant for the project presents the monitoring visit findings including briefing about the study protocol, performance, SAE and previous monitoring reports if any in the IEC full boardmeeting.
- 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 **15 days of the meeting**.
- Grounds for recommending suspension or termination of a clinical trial to the IEC 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. Safety issues
5. Compliance issues
6. 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.

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Annexure
AX1-V1/SOP15/V1
Study Monitoring Visit Report

1) TRIHMS Project No:

2) Title:

3) Principal Investigator:

4) Institute:

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

6) a) Date of IEC approval:
b) Is the period of IEC approval valid : □ Yes □ No □ NA

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
- □ Any complaints related to the research
- □ Non Compliance / Suspicious conduct
- □ Other _____

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

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/samples to be recruited - _____
- Screened: _____
- Screen failures: _____
- Enrolled: _____
- Withdrawn: _____ Reason:_____
- Discontinued: _____ Reason: _____
- Completed: _____
- Active: _____
- Follow up: _____

14) Is the recruitment on schedule?

□ Yes

□ No If 'No' is it acceptable? □ Yes □ No □ NA

If 'No' State reasons/Steps taken by PI to improve recruitment:

_____

_____

_____

_____

15) Protocol

a) Have there been any amendments to the Protocol? □ Yes □ No □ NA

If Yes then state changes leading to amendment:

_____

b) Is the Protocol version approved by IEC? □ Yes □ No □ NA

c) Is the latest version of the protocol being used for the study? □ Yes □ No □ NA

16) Informed Consent

a) Is Informed consent obtained from all enrolled participants? □ Yes □ No □ NA

b) Have there been any amendments to the ICF? □ Yes □ No □ NA

If Yes then state changes leading to amendment:

_____

_____

_____

_____

c) Is the Informed consent form version approved by IEC? □ Yes □ No □ NA
d) Is the latest version of the ICF being used for the study? □ Yes □ No □ NA
e) Is there source documentation of the ICF process? □ Yes □ No □ NA
f) Is ICF signed by PI /Co-Principal Investigator/Co-I? □ Yes □ No □ NA
g) Is ICF signed by Participant? □ Yes □ No □ NA
h) Is ICF signed by LAR? □ Yes □ No □ NA
j) Is ICF signed by Impartial Witness? □ Yes □ No □ NA

17) Any Protocol Deviations/Violations noted? □ Yes □ No □ NA Have all the deviations/violations notified to IEC? □ Yes □ No □ NA Comments (If Any)

18) Have the eligibility, inclusion exclusion criteria been adhered to? □ Yes □ No □ NA

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 DSMU 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

Is the utilization of sanctioned funds appropriate? □ Yes □ No □ NA
If 'No' kindly state the issues:

_____

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 DSMU member_____

Signature and Date _____

Name of DSMU member_____

Signature and Date _____

Name of study team member present: _____

Signature and Date: _____

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Tittle: Dealing with participants / patients queries, requests and complaints

SOP Code: SOP 16/V1 Date: Pages:

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.

This SOP provides guidelines for dealing with queries/requests/complaints of participants/patients regarding their rights as a participant in any approved research study.

16.2 Scope

This SOP applies to all queries, requests and complaints 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

Informed Consent document of the research study provides the contact details of IEC. In case of any queries/concerns/complaints, participants can directly contact the IEC.

When the IEC member/ administrative staff receives an inquiry or query or request from a research participant/ research participant's representatives/patient via phone/email/letter -

- The query, request and information will be recorded in the Query/Request/Complaint record (Form AX1- V1/SOP 16/V1)
- The Member Secretary will inform the Chairperson about the query/complaint received via phone/email/letter.
- The Chairperson / Members designated by the Chairperson will provide the information required by the research participant.
- 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-V1/SOP 16/V1 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.

AX1- V1/SOP 16/V1

Query/Request/Complaint record

□ **Query** □ **Request** □ **Complaint** Date Received:
Received by – Name of IRB staff-
□ Telephone call No…… □ Fax No…… □ Letter / Date…… □ E-mail / Date…….. □ Walk-in / Date / Time…… □ Other, specify ……...
Participant's Name:_____Anonymous ☐
Contact Address: Phone:
P.No./Title of the Study:
Starting date of participation:
Specify details- **Query:** **Request:** **Complaint:**
Action taken:
Outcome:

Name of the Chairperson/ Member Secretary -

Signature of the Chairperson/ Member Secretary_____Date -_____

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Reviewing Research Studies Involving Vulnerable Populations

SOP Code: SOP 17/V1 Date : Pages:

17.1 Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe procedures to review research protocol involving vulnerable populations. The SOPs provides clear, unambiguous instructions so that the related activities of the Ethics Committee are conducted in accordance with Indian laws and relevant, National and International Guidelines. It describes the requirements concerning review of research that involves groups that could be potentially vulnerable to coercion 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.

17.2.1 Guidelines for review of research involving vulnerable population

The word vulnerability is derived from the Latin word vulnarere which means 'to wound'. Vulnerable persons are those individuals who are relatively or absolutely incapable of protecting their own interests because of personal disability, environmental burdens, social injustice, lack of power, understanding or ability to communicate or are in a situation that prevents them from doing so.

Vulnerable groups: Effort may be made to ensure that individuals or communities invited for research be selected in such a way that the burdens and benefits of the research are equally distributed.

a. Research on genetics should not lead to racial 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:

1. Socially, economically or politically disadvantaged and therefore susceptible to being exploited.
2. Incapable of making a voluntary informed decision for themselves or whose autonomy is compromised temporarily or permanently, for example
    a) people who are unconscious,
    b) differently abled,
    c) able to give consent, but whose voluntariness or understanding is compromised due to their situational conditions/ contexts.
    d) Unduly influenced either by the expectation of benefits or fear of retaliation in case of refusal to participate which may lead them to give consent.

Following are some examples of vulnerable populations or groups:

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

Principles of research among vulnerable populations

Vulnerable populations have an equal right to be included in research so that benefits accruing from the research apply to them as well. If any vulnerable group is to be solely recruited then the research should answer the health needs of the group. Participants must be empowered, to the maximum extent possible, to enable them to decide by themselves whether or not to give assent/consent for participation.

In vulnerable populations, when potential participants lack the ability to consent, a Legally Authorized Representative (LAR) should be involved in decision making. Special care must be taken to ensure participant's privacy and confidentiality, especially because breach of confidentiality may lead to enhancement of vulnerability.

If vulnerable populations are to be included in research, all stakeholders must ensure that additional protections are in place to safeguard the dignity, rights, safety and wellbeing of these individuals.

Additional safeguards/protection mechanisms

When vulnerable individuals are to be recruited as research participants additional precaution should be taken to avoid exploitation/retaliation/reward/credits, etc., as they may either feel intimidated and

incapable of disagreeing with their caregivers, or feel a desire to please them. In the first case, they may be subjected to undue pressure, while in the second, they may be easily manipulated. If they perceive that their caregivers want them to participate in research, or if the caregiver stands to benefit from the dependant's participation, the feeling of being pressed to participate may be irresistible which will undermine the potential voluntariness of the consent to participate.

Researchers must justify the inclusion of a vulnerable population in the research. ECs must satisfy themselves with the justification provided and record the same in the proceedings of the EC meeting. Additional safety measures should be strictly reviewed and approved by the ECs. The informed consent process should be well documented. Additional measures such as recording of assent and reconsent, when applicable, should be ensured. ECs should also carefully determine the benefits and risks of the study and examine the risk minimization strategies. As potential participants are dependent on others, there should be no coercion, force, duress, undue influence, threat or misrepresentation or incentives for participation during the entire research period. Vulnerable persons may require repeated education/information about the research, benefits, risks and alternatives, if any.
Research on sensitive issues such as mental health, sexual practices/preferences, HIV/AIDS, substance abuse, etc. may present special risks to research participants. Researchers should be cognizant of the possibility of conflicting interests between the prospective participant and LAR and should be more careful. Participants may be prone to stigma or discrimination, specifically when the participant is enrolled as a normal control or is recruited from the general population in certain types of research. Efforts should be made to set up support systems to deal with associated medical and social problems. Protection of their privacy, confidentiality and rights is required at all times – during conduct of research and even after its completion. Whenever possible, ancillary care may be provided such as setting up of a facility, school for unattended children of the participants or a hospital, or counseling centre.

Stakeholders Obligations / duties

Researchers

- Recognize the vulnerability of the participant and ensure additional safeguards are in place for their protection
- Justify inclusion/exclusion of vulnerable populations in the study.
- COI issues must be addressed.
- Have well defined SOPs to ensure a balanced benefit-risk ratio.
- Ensure that prospective participants are competent to give informed consent.
- Take consent of the LAR when a prospective participant lacks the capacity to consent.
- Respect dissent from the participant.
- Seek permission of the appropriate authorities where relevant, such as for institutionalized individuals, tribal communities, etc.
- Research should be conducted within the purview of existing relevant guidelines/regulations.

Ethics Committees

- During review, determine whether the prospective participants for a particular research are vulnerable.
- Examine whether inclusion/exclusion of the vulnerable population is justified.
- Ensure that COI do not increase harm or lessen benefits to the participants.
- Carefully determine the benefits and risks to the participants and advise risk minimization strategies wherever possible.

- Suggest additional safeguards, such as more frequent review and monitoring, including site visits.
- Only the full committee should do initial and continuing review of such proposals. It is desirable to have empowered representatives from the specific populations during deliberations.
- ECs has special responsibilities when research is conducted on participants who are suffering from mental illness and/or cognitive impairment. They should exercise caution and require researchers to justify cases for exceptions to the usual requirements of participation or essentiality of departure from the guidelines governing research. ECs should ensure that these exceptions are as minimal as possible and are clearly spelt out in the Informed Consent Document (ICD).
- ECs should have SOPs for handling proposals involving vulnerable populations.

Sponsors

- The sponsor, whether a government, an institution or a pharmaceutical company, should justify the inclusion of vulnerable groups in the protocol and make provisions for protecting their rights/safety.
- The sponsor must enable monitoring and ensure that procedures are in place for quality assurance (QA) and quality control (QC).
- The sponsor should ensure protection of the participants and research team if the research is on sensitive topics.

The following is required when children are enrolled in research:

As per the National Commission for Protection of Child Rights, a child is defined as a person from 0 to 18 years of age

Research proposals should be scientifically sound.

• Risk or harm is a very important consideration in research involving children. Risk refers to a potential harm that can occur to the child as a direct or indirect consequence of the research procedure. The risks entailed in research procedures need to be considered when they are over and above the routine care of the participant.

Research may include any procedure the participant undergoes for research including questionnaires, investigations such as blood sampling, bone marrow aspiration, liver biopsy etc., or therapeutic interventions such as medication or surgery, over and above the routine standard of care for the patient. Harm occurring from participating in research may be physical (such as pain from a needle prick for blood sampling), psychological (such as fear of separation from parents) or social (such as missing school and friends etc). Risks must be assessed in relation to benefits.

A benefit is a good outcome. The benefit is usually potential, which means positive but uncertain outcome. The benefit may be direct, as in a direct benefit to the participant; or indirect.

Examples of direct benefits include the possibility of recovery, reduction in pain, improvement in disease severity, etc. Indirect benefits include the opportunity to understand more about the disease, develop social relationship with other patients, etc. Payments for participation should not be considered in the benefit-risk- ratio. Also, patients and participants may consider other benefits such as better access to doctors, access to investigations which are not otherwise freely available, being special patients as part of research, etc. These indirect benefits may be more misunderstood by illiterate patients from poor socioeconomic strata.

The equation between the potential benefit and the risk or potential harm should be at least as favorable for the proposed research procedure as for the alternatives available to the children.

- There should be benefit to children in general and, in most cases, to the individual child subject. Interventions intended to provide direct diagnostic, therapeutic, or preventive benefit for the individual child participants must be justified in relation to potential risks involved in the study and potential benefits to society. The risk presented by interventions not intended to benefit the individual child participant is low when compared to the importance of the knowledge that is to be gained.
- The need for the study should be justified by a thorough review of literature.
- The research should be conducted by a team of investigators who have the requisite expertise. One or more members of the team should be a paediatrician and/or have prior experience of conducting research involving children.
- Research involving children should take into consideration the unique physiology, anatomy, psychology, pharmacology, social situation and special needs of children and their families.
- Research involving children must be conducted in a child-friendly environment, as far as possible. The settings of the research provide the child and parent adequate medical and psychological support. Both pain and emotional discomfort should be prevented as much as possible. When unavoidable, it should be adequately managed and reduced. To do this, non-invasive procedures should be preferred.
- In general, drugs should be tested for safety, pharmacokinetics, and at least initial indications of efficacy in adults established before they are tested in children. It may often be appropriate to defer paediatric testing until adult testing has reached Phase III or beyond, when substantial data are available on the safety and efficacy of a drug in adults. However, there may be situations where studies involving children would be needed without prior adult studies, for example, surfactant use in premature babies with respiratory distress syndrome. For studies prior to phase III the drug has a therapeutic value in a primary disease of the children.
- Children will not be involved in research that can be carried out equally well with adults.
- The purpose of the research is to obtain knowledge relevant to health needs of children. For clinical evaluation of a new drug the study in children should always be carried out after the phase III clinical trials in adults.
- Interventions that are intended to provide therapeutic benefit are likely to be at least as 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.
- Investigators must seek to involve children in discussions about research and obtain their assent to participation as in accordance with their developmental level and decision making capacity. The parental/LARs' permission for the child's participation in the research is termed as 'consent', whereas the child's agreement to participate is termed as 'assent'.

Consent process for illiterate parents /LARs

- When a participant is willing to participate but not willing to sign or give thumb impression or cannot do so, then verbal/oral consent may be taken on approval of the EC, in the presence of an impartial witness who should sign and date the document. This can be documented through audio or video recording of the participant, the PI and the impartial witness, all of

whom should be captured in the frame. However, verbal consent should be an exception for specific reasons carried out with the approval of EC and not to be followed routinely.

- In non-regulatory, observational studies, sometimes literate or illiterate, parents /LARs may verbally agree to participate but refuse to give their thumb impression. In such cases, again, the documentation of the consent process needs to be done by a literate impartial witness.

In some cases, fresh or re-consent may need to be taken, such as when:

- New information becomes available which would necessitate amendment/deviation of protocol (excluding any new safety related information which can harm the participant if not immediately implemented by the investigator).
- A research participant regains consciousness from an unconscious state or becomes mentally competent to understand the study (procedures to address such a possibility should be spelt out in the informed consent form).
- Long term follow-up or study extension is planned at a later stage.
- There is change in treatment modality, procedures, site visits.
- Attains 18 years of age, or the legally acceptable representative has changed.
- There is possibility of disclosure of identity through data presentation or photographs (which should be camouflaged adequately) in an upcoming publication.
- Future research may be carried out on stored biological samples if not anonymized.

Determinants of risk

1. *Age and developmental status*: Risk assessment in children must take into account their age, developmental status and maturity. For example, taking 10 ml blood sample may be low risk for a 10-year-old but high risk for a preterm neonate.

2. *Underlying medical condition*: In some cases, a research procedure that may be of minimal or low risk to a healthy child could be of high risk to a child with underlying medical condition. For example, intramuscular injections that may be safe for healthy children are risky for children with clotting disorders. **Ethics committees should ensure that children with underlying medical conditions that place them at risk due to research procedures are excluded from the study.**

3. *Cumulative characteristics of risk during research*: Determinations about risk should consider the cumulative characteristics of research interventions or procedures and the time period for which they are done. For example, a single chest X-ray is a minimal risk procedure, but if the child has to undergo multiple chest X-rays over a short duration of time, the risk category should be higher.

Type of assays and sample collection

In research involving children, due consideration should be given to the number and type of body fluid assays and investigations.

- Blood samples should be age and/or bodyweight appropriate. Depending on the nature of the study the ethics committee may obtain an independent opinion from a pediatrician regarding the safety of blood volumes proposed to be drawn for the purpose of the study.
- The samples should be obtained using appropriate facilities and materials.
- Alternative sampling (for example, urine or salvia sampling) for pharmacokinetic studies should be preferred when possible. However, the ability to use alternative samples may depend on the validation of the analytical methodology and clinical utility of measurements made in these matrices.
- For blood and tissue assays, micro volumes and micro-assays should be used, whenever possible.
- For painful and/or invasive procedures standard pain relief methods should be employed.
- Timing of sampling should be coordinated with the routine standard of care sampling of the patients to avoid repeated needle pricks.
- Sampling should be performed by trained staff.
- The number of attempts for sampling should be limited. Timing of sampling and number of sampling attempts should be defined in the protocol. For example, it is recommended that after one unsuccessful attempt, another experienced person should take over the procedure.

Paediatric formulations to be used in paediatric studies

Formulations used in a study should be described in the protocol. Age-appropriate formulations should be used to avoid the risk of adverse reactions (for example, young children choking on tablets), the risk of dosing errors or inaccuracy. Whenever available, paediatric formulations should be used. Excipients used for the formulation should take into consideration the age of the children included in the study (for example, benzyl alcohol is contraindicated in neonates). Conditions to avoid bacterial contamination and degradation of the medicinal product should be specified in the protocol.

Guidelines for ethical approval based on degree of risk

For research procedures that are intended to provide potential direct diagnostic, therapeutic or preventive benefit for the individual child participant, a risk category higher than minimal risk may be justified. For studies having interventions not intended to directly benefit the individual child participant, the risk-levels should be minimum risk or low risk.

Concerns regarding informed consent

1. The process of obtaining consent and assent should not be a mere formality, limited to getting the participants' signatures on the forms. Instead this should be a process, wherein the onus is on the investigator to ensure that the parents and children (as far as their developmental level and maturity permits) understand what is going on in the research. This process should also include opportunities for the parents and children to ask questions. The consent process is not a one-time process but should be an ongoing interaction between the researcher and the participant, to help resolve the queries which may arise in the participant's mind during the course of the study.

2. The language of the patients/participant information sheet (PIS) should be simple and easily understood by the parents. Many times, in order to protect themselves from any future litigation, investigators fill PIS with technical terms (medical and legal) which the parents find difficult to understand. While translating to a local language difficult technical words must be avoided, and simple daily-use words that the participant is able to understand should be used.

3. When checking that parents understand all the aspects of research participation, a particular concern is whether they understand that they will be participating in research and that the purpose of research differs from the purpose of normal clinical care. The purpose of research is to generate knowledge, usually for the benefit of patients or individuals in the future. The misbelief that the purpose of research is treatment is termed as therapeutic misconception.

Children's assent

Assent is defined as a child's affirmative agreement to participate in research. A mere failure of the child to object should not be interpreted as assent. The assent process should take into account the children's developmental level and capability of understanding. Cultural and social factors also play an important role. Children vary considerably in the ability to understand abstract concepts depending on their age and maturity. The assent form chosen should be appropriate for the child's age and reading ability. Children with chronic illness may have been challenged to develop increased capacity to make independent judgments based on previous experiences. The other important issue here is the child's general level of independence and autonomy.

Content of the assent form has to be in accordance with the developmental level and understanding capacity of the child. For example, a child aged 8 years should be told what exactly she/he is going to undergo, although they may not understand the concept of research Younger children are better able to grasp the more practical aspects of research (e.g., what they are expected to do or what will happen) than they are to understand the abstract concepts such as randomization. For a 15-year-old, however, the assent process should be similar to the informed consent process. If the study is of a long duration study, the researchers may have to repeat the assent process with more information, as the child grows older.

Age and method of obtaining assent

For children between 7 (84 months and above) and 11 years of age, oral assent must be obtained in the presence of parent/LAR. For children between 12 and 18 years of age, written assent must be obtained. If a child becomes 13 years old during the course of the study, then written assent must be obtained in addition to parent/LAR consent. This is a joint decision-making process between the child and the concerned adult. In cases of verbal assent, the parent /LAR's counter-signature must be obtained confirming that the child's verbal assent has been taken. Re-assent must be taken in all the same situations as re-consent as mentioned above. For children less than 7 years of age, parental consent is sufficient. As assent is part of the informed consent process, the regulations as per the CDSCO guidelines for regulatory clinical trials apply for assent as well.

Content of assent form - The type and amount of information given needs to be simplified as per the child's cognitive and developmental level. The information should be simple, and age-appropriate.

Waiver of assent

Waiver of assent may be provided by the ethics committees in the following situations:

1. If the research has the potential of directly benefiting the child and this benefit is available only in the research context. In such situations, the child's dissent may be overruled.

2. Waiver of assent may also be considered if the research involves children with mental retardation and other developmental disabilities, where the children may not have the developmental level and intellectual capability of giving assent.

3. Assent may also be waived under the same conditions in which adult's informed consent maybe waived.

Dissent or refusal of a child to participate must always be respected. Explanation must be given to ensure that to the child understands that she/he may withdraw her/his assent at any time during the study.

Data and Safety Monitoring Board (DSMB)

The need for a DSMB may be determined as an additional safeguard by the EC depending on the anticipated risks to the children involved in the research. Data and Safety Monitoring Board evaluating research performed in children should have members with appropriate *expertise* in reviewing clinical studies in children.

When studies have a significant safety concern, the establishment of a DSMB can enhance the safety of study participants. An independent review of research data may be essential to ensure the ongoing safety of study participants. Those involved in the study design and conduct of a study may be biased in reviewing the data. Hence, there is a need for a group of expert advisors to ensure that such concerns would be addressed in an unbiased way.

Data and Safety Monitoring Boards are traditionally established for large, multicentric, randomized, studies that evaluate interventions intended to prolong life or decrease an adverse health outcome.

Factors to consider while establishing a DSMB for a particular study;

- The study endpoints are such that a highly favorable or unfavourable result or even a finding of futility, during an interim review might make the continuation of the study unethical.
- The indicators for safety concern due to the intervention (for example, an invasive procedure, or potentially toxic drug).
- The study is being performed in a potentially vulnerable population such as neonates or other vulnerable individuals.
- The study involves a population at heightened risk of death or other serious adverse health outcomes.
- The study includes a large number of individuals, is of long duration, or is multi-centric.

In studies with one or more of the above characteristics, the additional oversight provided by a DSMB can further protect the study participants.

If the study is likely to be completed in a short span, the DSMB may not be effective. In such situations, mechanisms should be in place a priori to expedite DSMB reviews and inputs. Alternatively, the study could build in periods of pauses to allow the DSMB to review interim data before any further enrolment of participants.

A DSMB can also enhance the scientific validity of a study by reviewing accumulating data of the study (for example, overall event rates) and suggest modifications in the protocol such as change in the inclusion criteria, the study endpoints, or the size of the study.

Finally, any independent DSMB evaluating studies performed in children should have members with appropriate expertise in the evaluation of clinical studies in children.

Research in neonates

Neonates represent the most vulnerable group within the paediatric population. Study protocols in this population should take into account this, and the potential long-term effects of interventions, including developmental effects. ECs' reviewing any research proposed in neonates should have an advisory member with expertise in neonatal research/care.

ECs' should carefully scrutinize all research proposed in neonates for potential risks. Risks if any should be carefully weighed against possible benefits in this fragile population. ECs' should ensure a proper scientific review of the protocol by a competent person/s to remove any risks resulting from poor methodology. Neonates should be researched when the findings of the study will have potential implications for neonatal healthcare. All measures to reduce risks should be undertaken. When possible, older children should be studied before conducting studies in younger children and infants. Within neonates, those who are critically ill should be considered for research even more carefully. Parents or caretakers of these babies face stresses that may interfere with their ability to make an informed decision on behalf of their baby. Strategies such as continuous consent can to some extent reduce such problems. The consent of one parent is required for studies in neonates with research exposing them to no or minimal risk or in studies that offer the prospect of direct benefit to the participant. However, for studies that do not offer the prospect of direct benefit or are high risk, consent from both parents is required. The exception being when only one parent has legal responsibility for the care and custody of the child, one parent is deceased, unknown, incompetent, or not reasonably available. In such cases, it is the duty of the investigators to provide adequate justification.

If one of the parents is a minor, then consent should not be taken from her/him. If both parents are minors, then enrolment of such a baby should be avoided as far as possible. To enrol such neonates for research, the investigators should provide adequate justification to the EC. A legally acceptable representative should provide an informed consent in such situations.

When adults are unable to consent, the 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 foetus 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 4aV5). 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 lead discussants (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
- ✓ Before requesting assent/ surrogate consent to participate in clinical trial the Investigator must provide the LAR and/or impartial witness with the following information in a language that is non- technical and understandable by the LAR and/or impartial witness and the same shall be recorded through audio-visual means.
- ✓ Assent/surrogate consent of the participants is a requirement wherever possible, and, if so, whether the plan for assent/ surrogate consent is adequate.
- ✓ There is adequate room for ensuring the involvement of the LAR and/or impartial witness in the consenting process.
- ✓ Details of such questions if any, asked by the LAR/ or impartial witness and his/her understanding on consent are also to be recorded through the audio video means. The process of signing/putting thumb impression by the LAR/ or impartial witness should also be video recorded.
- ✓ When a research participant regains consciousness from unconscious state or is mentally competent to understand the study. If such an event is expected then procedures to address it should be spelt out in the informed consent form.

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 lead discussants 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 lead discussants 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) and opine.

17.6 IEC Meeting

- The details of review procedures and communication of decision is described in detail in SOP05/V1
- Document review of risk assessment in IEC minutes for the protocols involving vulnerable population.
- IEC Member Secretary will minute the discussions

Annexure 1

AX1- V1/SOP 17/V1

Checklist 01 –Requirements for Research Involving Children

Investigator IEC :

Study Title:

RISK DETERMINATION	BENEFIT ASSEMENT	IEC ACTION
Minimal risk	With direct benefit □ without direct benefit □	Approved □ Not Approved □
	Potential to child	Approved □ Not Approved □
	No direct benefit to individual but offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	Approved □ case by case (With special safeguards Not Approved □
Less than minimal risk	With direct benefit □ without direct benefit □	Approved □ Not Approved □
	Potential to child	Approved □ Not Approved □
	No direct benefit to individual but offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	Approved □ case by case (With special safeguards Not Approved □
Minor increase over minimal risk or Low risk	With direct benefit □ without direct benefit □	Approved □ Not Approved □
	Potential to child	Approved □ Not Approved □
	No direct benefit to individual but offer general knowledge	Approved □ case by case (With special

	about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	safeguards Not Approved □
□ More than minimal risk or High risk	With direct benefit □ without direct benefit □	Approved □ Not Approved □
	Potential to child	Approved □ Not Approved □
	No direct benefit to individual but offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	Approved □ case by case (with special safeguards Not Approved □

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

(ii) Risk may not be more than a minor increase over minimal risk, consent of both parents required under normal circumstances.

(iii) Approval to proceed with this category of research must be made by the IEC with input from selected experts

	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?	□	□	□
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?	□	□	□

	Yes	No	NA
If Yes- please justify			
Will efforts be made to ensure that parents' permission to involve their children in research studies is free from coercion, exploitation, and /or unrealistic promises?	☐	☐	☐
Are provisions made to obtain the assent of children over 7 and, where appropriate, honoring their dissent?	☐	☐	☐
Are provisions made to protect participants' privacy and the confidentially of information regarding procedures?	☐	☐	☐
Are there special problems that call for the presence of a monitor or IEC member during consent procedures?	☐	☐	☐
Are special needs of adolescents such as counseling and confidentiality accounted for in the research design?	☐	☐	☐
Are there any special problems such as confidentiality and reporting that might arise in sensitive research about child abuse or sexual practices of teenagers?	☐	☐	☐
Does the research involve implications for other family member ?(for example, genetic risk , HIV infection , Hepatitis C)	☐	☐	☐
If Yes: Are adequate mechanisms in place to deal with other members of the family?	☐	☐	☐
Should parents be required to be present during the conduct of the research? (Are proposed participants very young ? Are the procedures involved painful? Must subject stay overnight in the hospital when they otherwise would not have to?)	☐	☐	☐

Comments: _____

_____

Name & Sign of Lead discussant :

Date:

Annexure 2

AX2- V1/SOP 17/V1

Checklist 02 - Requirements for Research Involving Pregnant or nursing women, Fetuses & nursing infant

Investigator:

Study Title:

Research Involving Pregnant or nursing women, Fetuses & nursing infant

RISK DETERMINATION	BENEFIT ASSESSMENT	IEC ACTION
□ Minimal	With or without direct benefit	Approvable
□ Less than minimal risk	With or without direct benefit	Approvable
□ Minor increase over minimal risk or Low risk	With or without direct benefit	Approvable
□ More than minimal risk or High risk	Potential benefit	Approvable
□ More than minimal risk or High risk	No direct benefit to individual but offer general knowledge about disorder and may benefit to the society or future generations are likely to benefit.	Approvable on case to case basis with special safeguards

	Yes	**No**	**NA**
Where scientifically appropriate, has preclinical studies including studies on pregnant animals, and clinical studies including studies on non- pregnant women been conducted and data made available for assessing potential risks to pregnant or nursing women, nursing infant and fetuses	□	□	□
The risk to the fetus or nursing infant is not greater than minimal, or any risk to the fetus which is greater than minimal is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus or nursing infant;	□	□	□
Any risk, is the least possible, for achieving the objectives of the research	□	□	□
The woman's consent or the consent of her legally authorized representative is obtained in accordance with the informed consent provisions , unless altered or waived in accord with SOPs	□	□	□
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:

Name & Sign of Lead discussant :
Date:

Annexure 3
AX3- V1/SOP 17/V1
Checklist 03- Research Involving Cognitively Impaired Adults

- **The purpose of this checklist is to provide support for IEC members or the Designated Lead discussant when reviewing research involving cognitively impaired adults as participants.**

For review, this checklist is to be completed by the Designated Reviewer to document determinations required by the regulations and protocol specific findings justifying those determinations.

1. **Research Involving Cognitively Impaired Adults in which there is Anticipated Direct Benefit to the subject** (All items must be "Yes")		
☐ Yes	☐ No	One of the following is true (Check the box that is true) • The risk to the participants is presented by an intervention or procedure that holds out prospect of direct benefit for the individual subject. • More than minimal risk to participants is presented by monitoring procedure that is likely to contribute to the participants well – being.
☐ Yes	☐ No	The risk is justified by the anticipated benefit to the participants.
☐ Yes	☐ No	The relation of anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.
☐ Yes	☐ No	The proposed plan for the assessment of the capacity to consent is adequate.
☐ Yes	☐ No	Assent is required of: (One of the following must be "**Yes**") One of the following is true (**Check box that is true**) < All Participants < All Participants capable of being consulted. < None of the participants
☐ Yes	☐ No	The consent document includes a signature line for a legally authorized representative.

2. **Research Involving Cognitively Impaired Adults in which there is No Anticipated Direct Benefit to the subject** (All items must be "Yes")		
☐ Yes	☐ No	The proposed plan for the assessment of the capacity to consent is adequate.
☐ Yes	☐ No	The objectives of the trial cannot be met by means of study of participants who can give consent personally.
☐ Yes	☐ No	The foreseeable risks to the participants are low.

☐ Yes	☐ No	The negative impact on the subject‘s well-being is minimized and low.
☐ Yes	☐ No	The trial is not prohibited by law.
☐ Yes	☐ No	Participants have a disease or condition for which the procedures in the research are intended.
☐ Yes	☐ No	Participants will be particularly closely monitored.
☐ Yes	☐ No	Participants will be withdrawn if they appear to be unduly distressed.
☐ Yes	☐ No	The proposed plan for the assessment of the capacity to consent is adequate.
☐ Yes	☐ No	Assent is required of (One of the following must be “**Yes**”) One of the following is true (**Check box that is true**) < All Participants < All Participants capable of being consulted. < None of the participants
☐ Yes	☐ No	The consent document includes a signature line for a legally authorized representative.

Comments-

Name & Sign of Lead discussant :
Date:

Annexure 4

AX4- V1/SOP 17/V1

Checklist 04-Research Involving Students, Employees or Residents

Participants who are students, employees or residents require special considerations.

The proposed plan for the assessment of the capacity to consent is adequate.	☐ Yes	☐ No
Have the participants been assured that their status (education, employment, and/or promotion) will not be affected by any decision to participate or not?	☐ Yes	☐ No
Have the risks to participants been minimized?	☐ Yes	☐ No
Have participants been assured that participation is voluntary (no signs of coercion)?	☐ Yes	☐ No
Have participants been assured that confidentiality will be protected or maintained?	☐ Yes	☐ No

Comments-
Name & Sign of Lead discussant :
Date:

Annexure 5

AX5- V1/SOP 17/V1

Checklist 05 - Considerations for Genetic Research

Investigator:

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-
Name & Sign of Lead discussant :
Date:

AX6- V1/SOP 17/V1

Checklist –Requirements for Research involving terminally ill patients

Principal
Investigator Proj.
No.-
Study Title:

RISK DETERMINATION	BENEFIT ASSEMENT	IEC ACTION
▪ Minimal	□ With direct benefit □ Without direct benefit	□ Approved □ Not Approved
	□ Potential benefit	□ Approved □ Not Approved
	□ No direct benefit to individual but offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	□ Approved case by case (with special safeguards □ Not Approved
▪ Less than minimal risk	□ With direct benefit □ Without direct benefit	□ Approved □ Not Approved
	□ Potential benefit	□ Approved □ Not Approved
	□ No direct benefit to individual but offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	□ Approved case by case (with special safeguards □ Not Approved
▪ Minor increase over minimal risk or Low risk	□ With direct benefit □ Without direct benefit	□ Approved □ Not Approved
	□ Potential benefit	□ Approved □ Not Approved
	□ No direct benefit to individual but offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	□ Approved case by case (with special safeguards □ Not Approved
▪ More than minimal risk or High Risk	□ With direct benefit □ Without direct benefit	□ Approved □ Not Approved

	□ Potential benefit	□ Approved □ Not Approved
	□ No direct benefit to individual but offer general knowledge about the child's condition or disorder and may benefit to the society or future generations are likely to benefit.	□ Approved case by case (with special safeguards □ Not Approved

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

	Yes	**No**	**NA**
Does the research pose greater than minimal risk to patients?	□	□	□
If yes: Are convincing scientific and ethical justification given?	□	□	□
If yes: Are adequate safeguard in place to minimize these risks?	□	□	□
Are appropriate studies that have been conducted on animals and adults justified?	□	□	□
If No: Is the lack of appropriate studies conducted on animals and adults justified?	□	□	□
Do the anticipated benefits justify requiring the subjects to undertake the risks	□	□	□
Is inclusion of vulnerable population warranted?	□	□	□
Can the research question be answered by using a non-vulnerable population?	□	□	□
Will efforts be made ensure that participants are free from coercion, exploitation, and /or unrealistic promises?	□	□	□
Are provisions made to obtain the consent?	□	□	□
Are provisions made to protect participants' privacy and the confidentially of information regarding procedures?	□	□	□
Are there special problems that call for the presence of a monitor or IEC member during consent procedures?	□	□	□
Are special needs of counseling and confidentiality accounted for in the research design?	□	□	□
Are there any special problems such as confidentiality and reporting that might arise in this research	□	□	□

Comments-

Name & Sign of Lead Discussant:

Date:

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Review of Academic Clinical Trial

SOP Code: SOP 18/V1 Date : Pages:

18.1 Purpose

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

The purpose of this Standard Operating Procedure (SOP) is to describe the procedures for submission, review, IEC communications for academic clinical research.

18.2 Scope

This SOP applies to the submission, review and IEC communications of all academic clinical trials submitted for initial review and review of revised and resubmitted protocols submitted for approval of the IEC. The specific points/items in the Assessment Form must be adequately addressed in the protocol and/or protocol-related documents submitted for the review. Relevant comments made during discussion and deliberation about a study should be recorded in the minutes of the meeting.

18.3 Detailed instructions

Academic Research

Clinical trial intended for academic purposes in respect of approved drug formulation for any new indication or new route of administration or new dose or new dosage form where –

(a) The trial is approved by the Ethics Committee; and

(b) The data generated is not intended for submission to licensing authority.

As per **GSR 313(E) dated March 16, 2016**, no permission is required for conduct of academic clinical trials from the licensing authority. However the Ethics Committee shall inform the licensing authority about the cases approved by it and also about cases where there could be an overlap between the clinical trial for academic and regulatory purposes and where the said authority does not convey its comments to the Ethics Committee within a period of **thirty** days from the date of receipt of communication from the Ethics Committee, it shall be presumed that no permission from the licensing authority is required.

In such trials, the investigator has the dual responsibility of being an investigator as well as the sponsor. Financial arrangements must be made by the institution/investigator for the conduct of the study as well as to pay for free management of research-related injury and compensation, if applicable. Funds should be made available or appropriate mechanisms be established.

The trials must be registered in CTRI and there should be mechanism for appropriate methods for informed consent, conduct of trial and proper follow-up of patients.

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

Submission

- PI should submit mandatory documents as per checklist AX1-V1/SOP18/V1
- In case of clinical trials involving drugs/devices, it is mandatory to submit drug safety and toxicity profile, adverse events data (incidence, DSMB reports etc.), Technical specifications of devices, risk – benefit assessment

Full board Review

All academic clinical trials submitted for IEC approval will be reviewed in the full board meeting.

IEC has to approve such studies after due consideration of benefits and risks and all other ethical aspects and inform to the licensing authority.
Refer SOP 04a and SOP05 for detailed review process.

Communicating Decision

IEC shall intimate the licensing authority about the approval of clinical trials intended for academic purposes such as use of approved drug formulation to study new indication or new route of administration or new dose or new dosage .The IEC shall await for comments from the DCGI for a period of 30 days from the date of receipt of communication from the IEC. If no communication from DCGI is received in the specified time frame, IEC shall presume that no permissions are required from the licensing authority and will issue the final approval letter for the study.

AX1-V1/SOP18/V1

Checklist of Documents

Item No.	Mandatory Documents	Yes	No	NA
1	Project Submission Form (both hard and soft copies) duly signed by the Principal Investigator			
	A. Grouping of Project			
	B. Project Fact 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			
2	Study Protocol			
	Participant Information Sheet & Informed consent forms (ICFs) in English, Marathi & Hindi (and if required any other language)			
3	Back translations of ICFs (not mandatory for Hindi and Marathi)			
4	Case Record Form			
5	Questionnaire (if applicable)			
6	Questionnaire Validation certificates (if applicable)			
8	Investigator Brochure			
9	Package insert/label			
10	Insurance policy			
11	NOC from ICMR/HMSC			
12	Clinical Trial Agreement (CTA) / Memorandum of Understanding (MOU) / Material Transfer Agreement (MTA) if applicable			
13	Brief resume of Principal Investigators and Co-investigators (1 Page each)			
14	MMC registration of Principal Investigators and Co- investigators			
15	Copy of Valid Good Clinical Practice training certificate for all investigators			
16	Cover letter from the investigator			

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Training of IEC

SOP Code: SOP 19/V1 Date : Pages:

Purpose
This SOP defines the procedure for training IEC members/IEC Secretariat to ensure optimal review of research protocols submitted to IEC.

Scope
This SOP is applicable to all members of the IEC and administrative staff of IEC.

Responsibility
The Chairperson and Member Secretary of the respective Committees will be responsible for ensuring trainings of IEC.

Procedure

- At the time of reconstitution of the IEC, the latest SOPs will be circulated to all members of the IEC via e-mail. Members will be encouraged to familiarize themselves with the SOPs before attending the IEC meeting.
- Member Secretary and other members will be selected at least 3 months and 1 month in advance respectively. Member Secretary designate will be inducted into the IEC as an observer before he/she takes on the mantle in the new IEC. Other member- designates may attend the board meeting as observers before starting their tenure as IEC members.
- At the time of appointment to the IEC, each member should have a valid GCP (Good Clinical Practice) certificate as a pre-requisite to induction in the IEC as GCP certificate is the universal standard in Clinical Research.
- The members will be required to update their GCP certification periodically.
- The Chairperson and/or Member Secretary will conduct a presentation of the TRIHMS IEC SOPs in the first meeting of the newly constituted IEC. Regular trainings will be conducted on the various SOPs through the term of the IEC.
- In addition to the SOP and GCP training, the IEC Secretariat will organize regular training for the IEC members. An annual training calendar will be prepared by the IEC Secretariat.
- The topics of training will be finalized by the Chairperson/Member Secretary. The training will be conducted by Chairperson, or any other member of the IEC specialized in a given topic. The IEC may also request a non-IEC member specialized in a topic of importance to impart training to the IEC members. The training programme will be scheduled and spread over the year.
- The topics of training will be selected to help members understand their roles and responsibilities while reviewing the research protocols. The topics will also include, but are not limited to regulatory guidelines, advancements in health research that could impact review of research protocols, research ethics, and concept of fairness and equity in research participation, conflict of interest, Informed consent and its significance, privacy and confidentiality matters, IPR etc.
- On finalization of the training calendar, the IEC Secretariat will circulate the same to all members of the IEC.
- The IEC Secretariat will also maintain logs of the training and certificates attended by the IEC members.
- Members will also be encouraged to attend training in Research Ethics, Bioethics Conferences, Workshops, Seminars conducted at other organizations. The members should submit the certificates of such Ethics Conferences/Workshops/Seminars to the IEC Secretariat for IEC record.

List of Annexures

- **Training Calendar**
- **Training Log**

AX1-V1/SOP19/V1

IEC Training Calendar

Sr. No.	Training Session	Speaker	Date	Target Audience
1.				
2.				

AX2-V1/SOP19/V1

Training log

Topic:

Training date:

Training

Time: Venue:

Training conducted by:

Target Audience:

Trainees:

Sr. No	Name	Designation	Signature and date
1.			
2.			

Institutional Ethics Committee, Tomo Riba Institute of Health & Medical Sciences (IEC, TRIHMS)

Title: Assessment and Audit of IEC

SOP Code: SOP 20/V1 Date: Pages:

20.1 Purpose

This SOP outlines the procedure for the self-assessment of the IEC members/staff and internal audit of the IEC to maintain high standards of research conducted at TRIHMS

20.2 Scope

This SOP is applicable to the IEC members and staff

20.3 Responsibility

Chairpersons, Member Secretaries and IEC staff will be responsible for the assessment and audit of IEC.

20.4 Procedure

20.4.1 Assessment of IEC members and IEC Secretariat

- The Chairperson will perform assessment of the IEC members annually. This assessment will cover regularity in attendance to IEC meetings, quality of review, time taken to review documents, completion of study assessment forms, etc.
- The Chairperson will also perform self-assessment annually.
- The Member Secretary will perform assessment of the Administrative Staff of the IEC annually. Evaluation forms will be circulated to individual members and the respective IEC staff via email and a copy of the same will be maintained in the IEC records.

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20.4.2 Internal Audits

20.4.2.a - Periodicity of Self-Assessment / Internal Audit

- 03 to 04 internal audits will be conducted in a year
- IEC staff will conduct quarterly internal audits as per the checklist AX5- V1/SOP20/V1
- IEC staff will conduct annual internal audit as per checklist AX4-V1/SOP20/V1 which involves standard and objective element of NABH Accreditation Standards For Ethics Committee.

20.4.2.b - Preparation for the audit

- On receipt of written/ mailed communication regarding audit, the IEC Staff will prepare and make necessary arrangements.
- The information and files requested by the auditors should be made available by the Secretariat.

20.4.2.c - Audit Procedure

- The audit involves review of IEC records, minutes, membership files, protocols, IEC correspondence etc

20.4.2.d - Report of Internal Audit

- The internal audit report will be prepared by the auditors. A signed copy of the report will be forwarded to the IEC Member Secretary.

20.4.2.e - Correction of deficiencies observed at audit

- The audit report will be discussed in the IEC meeting. Based on the IEC recommendations corrective/preventive action plan will be implemented within 2 months of receipt of the IEC recommendations.
- Action plan will be communicated by the Member Secretary to the Auditor.

20.4.2.f - Records of the Audit

- The Member Secretary/ designated IEC member/ Secretariat must keep record of the audit reports and action plans in a separate audit file.

List of Annexure

1. AX1-V1/SOP20/V1- IEC Evaluation Form of Chairs & Co- chairs
2. AX2-V1/SOP20/V1- IEC Evaluation Form of IEC Member Secretary/Members
3. AX3-V1/SOP20/V1- IEC Evaluation Form of Staff
4. AX4-V1/SOP20/V1- IEC Audit NABH Checklist
5. AX5-V1/SOP20/V1- IEC Internal Audit Checklist

AX1-V1/SOP20/V1

IEC Evaluation Form of Chairs & Co- chairs

Part A

1. **Mention (□) the individual who is performing the evaluation: Self – evaluation : ☐**
2. **Name of the person who is evaluated :**

   _____

3. **Number of Meetings attended out of total meetings : /**
4. **Number of exempt determination made :**
5. **Number of new protocols reviewed by the expedited procedure :**
6. **Number of new protocols reviewed that went to the convened full board IEC:**
7. **Number of continuing review completed as the primary reviewer :**
8. **Completion of educational requirements : ☐ Yes ☐ No**
9. **Attendance at educational sessions (Make tick (□) in the column)**

   ☐ **Regular**

   ☐ **Irregular**

10. **Number of educational sessions conducted :**

Evaluation of Chairs & Co- chairs

Part B

i) Preparedness for meetings Scale

Poor	Fair	Average	Good	Excellent
1	2	3	4	5

ii) Contribution to IRB meetings Scale

Poor	Fair	Average	Good	Excellent
1	2	3	4	5

iii) Quality of reviews Scale

Poor	Fair	Average	Good	Excellent
1	2	3	4	5

iv) Communication with IRB staff Scale

Poor	Fair	Average	Good	Excellent
1	2	3	4	5

Feedback- _____

_____

_____

_____

Signature:

Date:

AX2-V1/SOP20/V1

IEC Evaluation Form of IEC Member Secretary/Members

Part A

1. Mention (□) the individual who is performing the evaluation:

   Self – evaluation : □

   Member secretary IEC : □

2. Name of the person who is evaluated: _____

3. Number of Meeting attended out of total meetings : □/□

   □ Poor (1-4) □ Average (5-8) □ Good (9-10) □ Excellent (11-12)

4. Preparedness for meetings : (tick (□) in the box)

   □Good □ Average □Poor

5. Contribution to IEC meetings: (tick (□) in the box)

   □Good □ Average □Poor

6. Quality of Reviews : (tick (□) in the box)

   □Good □ Average □Poor

7. Time taken to respond to modification sent

   □Good (1 week) □ Average (2 weeks) □Poor (above 2 weeks)

8. Number of exempt determination made : □ □ NA

9. Number of new protocols reviewed by the expedited procedure : □ □ NA

10. Number of new protocols reviewed that went to the convened full board IEC : □

11. Number of continuing reviews completed as the primary reviewer : □

12. Number of reviews completed as the primary reviewer for study amendments: □

13. Completion of study assessment forms: (tick (□) in the box)

    □ Yes (__ out of__) □ No (out of)

14. Completion of educational requirement : (tick (□) in the box)

    □ Yes □ No

15. Attendance at educational sessions : (tick (□) in the box)

    □ Regular (__ out of__) □ Irregular (out of)

16. Number of educational sessions conducted: □ □ NA

17. Communication with IEC staff : (tick (□) in the box)

    □Good □ Average □Poor

IEC Evaluation Form of IEC Member Secretary/Members

Part B

Name of the person who is evaluated- _____

Period –

i) Preparedness for meetings Scale

Poor	Fair	Average	Good	Excellent
1	2	3	4	5

ii) Contribution to IRB meetings Scale

Poor	Fair	Average	Good	Excellent
1	2	3	4	5

iii) Quality of reviews Scale

Poor	Fair	Average	Good	Excellent
1	2	3	4	5

iv) Communication with IRB staff Scale

Poor	Fair	Average	Good	Excellent
1	2	3	4	5

Feedback- _____

Signature:

Date:

AX3-V1/SOP20/V1

IEC Evaluation Form of Staff

1. Mention (□) the individual who is performing the evaluation:
   Member secretary IEC :
   Name of the person who is evaluated :

   _____

2. Handles workload efficiently : (tick (□) in the box)

   Yes: ☐ No: ☐

3. Number of new protocol processed that were reviewed by the expedited procedure : ☐
4. Number of new protocols processed that went to the convened IEC :
5. Completion of required checklists and documentation : (tick (□) in the box)

   Yes: ☐ No: ☐

6. Maintains paper files efficiently and correctly : (tick (□) in the box)

   Yes: ☐ No: ☐

7. Drafting Agenda and Minutes in timely manner : (tick (□) in the box)

   Yes: ☐ No: ☐

8. Maintain IEC rosters efficiently and correctly : (tick (□) in the box)

   Yes: ☐ No: ☐

9. Prepare IEC records efficiently and correctly : (tick (□) in the box)

   Yes: ☐ No: ☐

10. Completion of educational requirement : (tick (□) in the box)

    Yes: ☐ No: ☐

11. Attendance at educational sessions : (tick (□) in the box)

    Yes: ☐ No: ☐

12. Number of educational sessions conducted : NA
13. Preparedness for meetings : (tick (□)in the box)

    Good: ☐ Average: ☐ Poor: ☐

14. Quality of pre-reviews : (tick (□) in the box)

    Good: ☐ Average: ☐ Poor: ☐

15. Communication with IEC chair and vice-chair : (tick (□) in the box)

    Good: ☐ Average: ☐ Poor: ☐

16. Communication with supervisor: (tick (□) in the box)
    Good: ☐ Average: ☐ Poor: ☐
17. Communication with investigators : (tick (□) in the box)
    Good: ☐ Average: ☐ Poor: ☐
18. Ability to help investigator :
    Good: ☐ Average: ☐ Poor: ☐

Feedback- _____

_____

_____

_____

Name of Member Secretary

Signature:

Date:

AX4-V1/SOP20/V1

IEC Audit (NABH Checklist)						
Auditors:						
Date of Audit Conducted:						
Standard 1	**Authority for formation of Ethics Committee: There shall be documented procedures to establish the authority for formation of Ethics Committee as per applicable rules and regulations.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
	Tick the box to indicate the requirement is met:					
1.1	Does IEC follow procedures to specify the authority under which the Ethics Committee is established and administratively governed?	SOP				
1.2	Is there any documented policy to ensure the independence of the Ethics Committee in its functioning and decision making?	SOP				
1.3	Does Ethics Committee function as per applicable rules and regulations	SOP				
	Compliance					
Standard 2	**Standard Operating Procedures (SOPs): The Ethics Committee has and follows written SOPs for its different functions as per applicable rules and regulations.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
2.1	Do the IECs have procedures in place and well defined for the development, review and revision of SOPs?	SOP				
2.2	**List of mandatory procedures for EC**					
A	**Terms of reference for EC**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Is the composition (names and qualification of the members) as per DCGI: for new induction, resignation, replacement or removal of members.	SOP, roster, circular, membership files				
ii)	Is there a clause for Declaration of Conflict of Interest and Confidentiality Agreement?	SOP/member file				

iii)	Frequency of ethics committee meetings.	SOP				
iv)	Is there any policy regarding training for new and existing committee members?	SOP, training records				
v)	Is there any policy of communication with different stake holders?	SOP				
	Compliance					
B	**Protocol Submission**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Is there any procedure for receipt of applications – original, revised, amended with supporting annexes?	SOP/Manual				
	Compliance					
C	**Ethical review**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Is appropriate review and decision making of proposals done by IEC?	• Minutes • IEC decision letters				
ii)	Is there any procedure to be followed for vulnerable population?	• SOP • Study assessment form • Minutes				
iii)	Is there any procedure for risk-benefit analysis?	• SOP • Study assessment form • Minutes				
iv)	Is there any procedure for review of Informed Consent Document (subject Information Sheet and Informed Consent Form) and informed consent process?	• SOP • ICF assessment • Minutes				
	Compliance					

D	Decision making, Minutes recording , post meeting activities including monitoring					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Is there any procedure for deliberations and maintaining minutes?	• SOP • Minutes				
ii)	Is there any procedure for reporting, analysis of SAEs and making opinion on compensation?	• SOP • Procedure for report of any onsite/offsite SAEs • Minutes				
iii)	Is the CRA reviewed by IEC? • Conduct of on-site monitoring in the past	• SOP • Minutes				
iv)	Procedure for handling issues related to non-compliance, protocol violation, negligence, complaints by the participants and other stake holders.	• SOP Review of deviation/violation/non compliance reports • Minutes				
v)	Procedure for review of protocol amendments.	• Procedure for filing an amendment review appropriate - How is the amendment reviewed by IEC?				
	Compliance					
E	**Documentation and archiving**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Procedure for control and archiving of records with confidentiality.	• Procedure for control and archiving of records with confidentiality •Does EC maintain an Archival record?				
	Compliance					

Standard 3	**Ethics Committee Composition: The Ethics Committee meets the requirement for membership as per applicable rules and regulations. Procedures are documented and followed.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Is the Composition of IEC multidisciplinary, multisectorial and appropriate for its functioning?	• IRB Roster • Circulars • SOP/manual				
ii)	Are any Subject Experts and representatives of vulnerable subjects invited as required with prior intimation?	• IRB Roster • Minutes of IEC meeting • SOP/manual				
iii)	Are Membership, appointment, reconstitution and resignation defined as per terms of reference.?	• Does the Membership File have proper documentation of reconstitution, appointment and resignation of EC members • SOP				
iv)	Are the roles and responsibilities of members well defined?	• SOP • TOR (Do appointment letters mention roles and responsibility of member)				
v)	Are the Ethics Committee members trained (initial and ongoing) in applicable rules and regulations and Ethics Committee SOPs?	• SOP • Training Calendar				
vi)	Are Conflict of Interest and Confidentiality addressed at the time of composition?	• Membership file				
	Compliance					
Standard 4	**Protection of subject rights, safety and wellbeing: The Ethics Committee follows documented procedures for subject protection.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Are the rights and responsibilities of subjects documented and specified in the SOP/ ICF template?	• SOP/ ICF template • ICF review/assessment form				
ii)	Subject's participation and withdrawal from the trial shall be voluntary and with prior intimation?	• SOP/ ICF template • ICF review/assessment form				

iii)	Subjects shall be informed and should comprehend (initial and ongoing) the associated risks and benefits of the trial.	• SOP/ ICF template • ICF review/assessment form				
iv)	Are Confidentiality and Privacy of Subjects protected?	• SOP/ ICF template • ICF review/assessment form				
v)	Monitoring of trials shall be done to ensure equitable selection of Subjects, with special attention to vulnerable and high risk	SOP				
vi)	Is compensation provided to Subjects for participation in the trial appropriate and as per the rules and regulation and is reflected in the contract?	• SOP/ ICF template • ICF review/assessment form Insurance				
vii)	Is the review of Serious Adverse Events adequate with provision for medical care and an appropriate reporting mechanism is followed as per applicable rules and regulations?	DSMU/IEC minutes				
viii)	Is the Compensation for injury to the subject as per the rules and regulations and are they monitored for compliance?					
ix)	How are Complaints and concerns of subjects addressed and managed appropriately, if the need arises?	SOP				
	Compliance					

Standard 5	**Administrative support: The Ethics Committee follows documented procedures / terms of reference (TOR) to ensure that administrative support for its activities is adequate.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Are adequate finance, human resource allocation and Secretariat for administrative work and record keeping with due care and confidentiality provided?	• HRPP manual • SOP				
ii)	Is there adequate financial transparency of Ethics Committee activities and functioning?	• HRPP manual • SOP				
iii)	Is there any procedure for communication between ethics committee, investigator/ relevant site staff, institution and regulatory authority?	• HRPP Manual • SOP				
	Compliance					

Standard 6	Review Process: The Ethics Committee follows documented procedures for initial review of the trial related documents, review of amendments and periodic review.					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Is the review done in a formal meeting within a reasonable time by the Ethics Committee following appropriate submission of documents by investigator as per rules and regulations and Ethics committee requirement?	• SOP				
ii)	Does the initial review of proposed clinical trial evaluate the scientific validity of the protocol, risk to subjects, expected benefit and ethical standards as per applicable rules and regulations?	• SOP • Study assessment Forms • Minutes of meeting				
iii)	Are Informed consent document, assent form (as applicable) and translations reviewed for appropriateness of language, accuracy and completeness of information?	• SOP •ICF assessment Form, • Minutes of meeting				
iv)	Does Ethics Committee review the informed consent processes proposed to be followed at the site for a particular trial to ensure that subject/LAR/ impartial witness are provided appropriate information, adequate time is given and impartial witness used as applicable?	• SOP				
v)	Recruitment strategies	• SOP				
vi)	Proposals involving special group and vulnerable population shall be evaluated as per rules and regulations.	• SOP • Study assessment Form • Minutes of meeting				
vii)	Is Contract and budget evaluated, for indemnity, compensation, roles and responsibilities as per applicable rules and regulations.	• SOP				
viii)	Are the amendments to the originally approved protocol, consent forms and investigators brochure reviewed in formal meetings to evaluate the risk to trial subjects.	• SOP • Minutes of meeting				

ix)	Periodic review of trial shall be done for continuation, risk evaluation and adverse event monitoring.	• SOP • DSMSC/IEC minutes				
	Compliance					

Standard 7	**Decision making and post meeting activities: The Ethics Committee follows documented procedures for decision making process and post meeting activities.**					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Are decision making process (approval/disapproval/pending/revoking) as per applicable rules and regulations, ensuring quorum and consensus/voting requirements fulfilled.	• SOP • Decision letters				
ii)	Does SOP mention statement that the subject shall be recruited into the trial only after written approval from Ethics Committee and approval by regulatory authority.	• SOP				
iii)	Do minutes capture about declaration of Conflict of Interest prior to the review and voluntary withdrawal during decision making process.	• SOP • Minutes of meeting				
iv)	Whether decisions are based on risk assessment, scientific validity and adherence to ethical principles for the initial and periodic approvals.	• SOP • Minutes of meeting				
v)	Are deliberations and decisions made during the meetings documented, approved, signed and maintained as minutes of meeting.	• SOP • Minutes of meeting				
vi)	Are Protocol deviations and non-compliances reviewed and appropriate actions taken as per rules & regulations.	• SOP • Minutes of meeting				
vii)	Are serious adverse events analyzed and compensation amount assessed and reported to Regulatory Authority as per rules and regulations.	•SOP • DSMSC/IEC minutes				
viii)	Does PI notify all decisions/opinions in writing.	• SOP • IEC decision letters				
	Compliance					

Standard 8	Monitoring: The Ethics Committee follows documented procedures for monitoring and for- cause assessment.					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Are subject's rights, safety and wellbeing monitored appropriately.	• SOP • Study assessment Form				
ii)	Is adequacy and continuity of consent process ensured.	• SOP • Study assessment Form				
iii)	For-cause assessments shall be conducted following non-compliance and/or complaints for the trials approved by the ethics committee.	• SOP • DSMSC/IEC minutes				
iv)	Have any opportunities for improvement identified and appropriate actions initiated.	• SOP • DSMSC/IEC minutes				
Compliance						

Standard 9	Self-assessment: The Ethics Committee has and follows documented procedures for self- assessment.					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Does periodic self assessments conducted.	• SOP • Member Evaluation File				
Compliance						

Standard 10	Record keeping and archival: The Ethics Committee follows documented procedures for record keeping and archiving.					
Sr. No.	**Check Parameters**	**Documents /evidence to be checked against the parameter**	**Yes**	**No**	**NA**	**Comments**
i)	Are security, confidentiality and integrity of all proposals and associated documents reviewed from time to time and administrative communication and maintained as per regulatory requirement and with confidentiality.	• SOP				
ii)	Are documents and records archived after completion /termination of trial as per applicable rules and regulations.	• SOP • Archival Log				
iii)	Are record retrieval policies and procedures in place to ensure access to information for inspection and audit and continual protection of trial subjects, post trial closure with prior permission in writing.	• SOP • Document request form				

	Institutional Ethics Committee Internal Audit						
	Auditors:						
	Date of Audit Conducted:						
	IEC:						
	Date of Meeting Minutes:						
	A.	**Documentation of Attendance**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate the requirement is met:					
	1	Name of members present					
	2	Name of members absent					
	3	Name of alternate members and the members they are replacing					
	4	Inclusion of consultants or permanent members, with competence to review issues that require additional expertise					
	5	Researchers or other guests resent					
	Compliance						
	B.	**Documentation of Quorum:**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate whether the requirement is met:					
	1	Statement that a quorum is met					
	2	a lay (non-scientist) person from the community.					
	3	a basic medical scientist/clinical pharmacologist.					
	4	a non-affiliated member*					
	5	a clinician (if research falls under FDA regulations, the physician must be licensed)					
	6	a legal expert					

	7	a philosopher, ethicist, theologian (or similar person), social scientist, representative of a non-government agency					
	Compliance						
	C.	**Quality of protocol review**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate the requirement is met:					
	1	Incomplete assessment form					
	2	Unsuitable reviewer					
	3	Appropriate independent expert (if required)					
	4	Independent expert comments documented					
	5	Appropriate review of recruitment strategies					
	7	Failure to assess PI competence/Conflict of interest					
	8	Failure to recognize vulnerability					
	9	Failure to address vulnerability					
	10	Inappropriate risk/benefit assessment					
	11	Inappropriate study design					
	12	Appropriate review of ICD					
	13	Appropriate review of parent ICF					
	14	Appropriate review of assent form					
	15	Whether criteria for expedited has been met					
	16	Whether criteria for waiver of consent has been met					
	17	Documentation of IEC deliberations as per SOP					
		Compliance					
	D.	**Documentation of Conflict of Interest**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate the requirement is met:					

	1	Minutes specify Conflict of Interest declaration by members					
	2	When members report conflicts, they do not participate in discussion or vote, except to provide information to the IEC					
	3	Minutes list criteria for Conflicts of Interest that organization should declare					
		Compliance					
	E.	**Membership / Experts file review**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate that all IEC membership files have following elements:					
	1	Latest CV signed and dated					
	2	GCP training certificate					
	3	GCP certificate valid					
	4	Confidentiality agreement					
	5	SOP training and other training documentation					
	6	COI declaration					
	7	Letter of resignation if applicable					
	8	Resignation intimation within specified period as per SOP 02					
	9	Letter of replacement /removal with reasons (if applicable)					
	10	Confidentiality agreement (Independent expert)					
		Compliance					
	F.	**Documentation of whether files contain additional information for continuing review of ongoing studies**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate whether IEC records also include the following additional information at the time of continuing review:					
	1	Mandatory documents submitted					

	2	Records of continuing review activities					
	3	Modifications to previously approved research					
	4	Unanticipated problems involving risks to participants or others					
	5	Documentation of non-compliance (whether there is non-compliance in fact, whether non-compliance is serious, whether non-compliance is continuing)					
	6	Significant new findings					
	7	Documentation of patient complaints/concerns if any addressed adequately					
	8	All correspondence between the IEC, researchers/ site staff, institution, regulatory authorities (e.g., approval letters and other correspondence)					
		Compliance					
	G.	**IEC Records**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate the requirement is met:					
	1	all minutes					
	2	all attendance records, if kept separately from minutes					
	3	the Constitution and composition of the IEC					
	4	standard operating procedures of the IEC					
	5	agenda of all IEC meetings					
	6	record of all notification issued for premature termination of a study with a summary of the reasons					
	7	Members Evaluation form					
	8	CV and GCP of IEC staff					
	9	Archival log &shredding log					
	10	Procedures followed for record retrieval					
		Compliance					

	H	**Review of Records (Random records reviewed)**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
	1	IEC approval letter					
	2	Has the study undergone continuing review?					
	3	Does an amendment/s have IEC approval?					
	4	Has there been a premature termination / suspension of the study and whether reason for the same is documented					
	5	Schedule Y regulated study					
	6	DCGI approval					
	7	Import/export license					
	8	Recruitment methods and materials are approved by IEC					
	9	Protocols or research plans					
	10	Investigator brochure					
	11	Insurance validity					
	12	CTA available					
	13	HMSC approval					
		Compliance					
	I.	**Authority for IEC Formation**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate that all IEC records for each study include:					
	1	Letter of Authority (sign and dated)					
	2	Valid period of Authority					
	3	Terms of reference (sign and dated)					
	4	Valid period of TOR					
		Compliance					

	J.	**Quality of Initial/Ongoing Review of Submission**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate the requirement is met:					
	1	Mandatory documents submitted					
	2	IEC fees collected					
	3	Document Receipt form present					
		Compliance					
	K.	**Review of protocol deviation/violation**					
	Sr. No.	**Check Parameters**	**Yes**	**No**	**NA**	**Comments**	
		Tick the box to indicate the requirement is met:					
	1	Protocol deviation/violation Review in IEC meeting					
	2	Action taken on deviation /violation (Noted, Warning to the PI, etc)					
		Compliance					
	L.	**SAE Review**					
		Check Parameters					
	Sr. No.	Tick the box to indicate the requirement is met:	**Yes**	**No**	**NA**	**Comments**	
		Review in DSMSC					
	1	DSMSC minutes ratified in the IEC meeting					
	2	Causality assessment **appropriate**					
	2	IEC reporting to DCGI					
	3	**Reporting** timelines met for **forwarding** IEC assessment to CDSCO/DCGI					
	4	DCGI orders for SAE compensation					
	5	IEC intimation to PI for payment of compensation					

	6	Documentary evidence submitted for compensation/reimbursement paid by the sponsor **to IEC**					
		Compliance					
	M	**CRA Review**					
		Check Parameters					
	Sr. No.	Tick the box to indicate the requirement is met:	**Yes**	**No**	**NA**	**Comments**	
	1	CRA reminder timelines met					
	2	Is the CRA delayed (Has submission timelines as per SOP met by PI)					
	3	Action taken by IEC for delayed submission of CRA					
	4	Review by DSMSC Member Secretary					
	5	Appropriate CRA review					
	6	Action taken by IEC incase of lapse in IEC approval					
	7	Whether CTRI registration done for the studies which are applicable for CTRI					
		Compliance					
	N	**Completion Report Review**					
		Check Parameters					
	Sr. No.	Tick the box to indicate the requirement is met:	**Yes**	**No**	**NA**	**Comments**	
	1	IEC review of Completion Report					
	2	Action taken by IEC incase of any adverse findings					
	3	Study file archived as per SOP					
		Compliance					
	O	**Monitoring Review**					
		Check Parameters					
	Sr. No.	Tick the box to indicate the requirement is met:	**Yes**	**No**	**NA**	**Comments**	
	1	Is the monitoring sample size as per the SOP i.e.≥ 10%					
	2	ICF monitoring					
	3	Risk evaluation and SAE					

		monitoring					
	4	Protocol deviation/violation reported by the PI to IEC					
	5	For cause monitoring done					
	6	Study Monitoring Visit Report completed					
	7	Report reviewed by DSMSC secretary					
	8	Report reviewed by IEC					
	9	Findings communicated to PI					
	10	PI response review by IEC					
		Compliance					

References

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2. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), E6 (R2), Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice, 9th November 2016.
3. Good Clinical Practices for Clinical Research in India, CDSCO, 2005
4. National Ethical Guidelines for Biomedical And Health Research involving Human Participants, Indian Council Of Medical Research, 2017
5. National Ethical Guidelines for Biomedical Research involving Children, Indian Council Of Medical Research, 2017
6. National Guidelines for Stem Cell Research, Indian Council Medical Research & Department of Biotechnology, 2017
7. Accreditation of Clinical Trials (Ethics Committee), National Accreditation Board for Hospitals, December 2016
8. NABH accreditation standards for ethics committee
9. The Nuremberg Code (1947)
10. The Belmont report: Ethical principles and guidelines for the protection of human subjects of research, United States. (1978).
11. WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects, (adopted in 1964, final amendment 2013)
12. "CFR Title 21". US Food and Drug Administration. Published on 09th June 2018
13. Protection of Human Subjects, Title 45 CFR Part 46, Amended on January 2018. Office of Human Research Protection & Department of Health and Human Services, USA
14. European Convention on Human rights and Biomedicine (1997).
15. WHO Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants 2011
16. International Ethical Guidelines for Health related research involving Human Subjects, CIOMS, Geneva, 2016.
17. International Ethical Guidelines for Epidemiological Studies, CIOMS, Geneva, 2009.
18. Handbook for Good clinical research Practice(GCP), WHO
19. FERCI Guideline http://ferci.org/sops

Glossary

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

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. The review process is by IEC subcommittee and the decision is ratified in the full board meeting

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

IEC members: Individuals serving as regular members of the Institutional Ethics Committee, TRIHMS. The Committee has been constituted in accordance with the EC membership requirements set forth in Schedule Y

Master SOP files: An official collection of the Standard Operating Procedures SOP) of IEC, TRIHMS 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 pre planned 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, TRIHMS 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, TRIHMS SOPs

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 TRIHMS.

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

Data Safety and Monitoring Unit (DSMU): The DSMU is the unit of IEC which is charged with the mission of developing and enacting quality assurance procedures to monitor the overall progress of institutional clinical trials and ensuring adherence to procedural requirements.

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.

Amendment: A written description of a change(s) to protocol, post approval

Case Record Form: A printed, optical, or electronic document designed to record all of the protocol required information on each trial participant

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. This is a legally binding document.

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 participant 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 participant'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 participants

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): A LAR is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure as per research protocol.

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 describe 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

Clinical trial: Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes

Clinical trial interventions include but are not restricted to:

- experimental drugs
- cells and other biological products
- vaccines
- medical devices
- surgical and other medical treatments and procedures
- psychotherapeutic and behavioural therapies

- health service changes
- preventive care strategies and
- educational interventions.

Central Drugs Standard Control Organization- CDSCO is a national regulatory body for Indian pharmaceuticals and medical devices.

Health Ministry's Screening Committee - The Health Ministry's Screening Committee (HMSC) is a high level committee, which was constituted by the Ministry of Health and Family Welfare (MOHFW), Government of India. The Committee takes decision on the international research proposals in the field of health research requiring foreign collaboration and/or assistance from foreign funding agencies.

Investigator initiated studies- Academic institutions routinely carry out investigator initiated clinical trials. In such trials, the investigator has the dual responsibility of being an investigator as well as the sponsor.

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.

Closed Study File: Any protocol, supporting documents, communication records and reports of the study which is completed or terminated or discontinued or suspended or not initiated.

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 TRIHMS

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/in cap

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

Exemption from Review: Proposals that can exempt from review includes those with less than minimal risk where there are no link identifiers which does not require the IEC approval

Expedited review/meeting: An expedited review is an accelerated review for minor changes to the approved protocol, research proposal with no more than minimal risk and documents of minor nature.

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

Full Board/ Regular Review: The proposals presenting more than minimal risk to research participants may be subjected to Full Board Review**.** Initial, resubmitted, continuing review, amendments of protocols, ICFs and any other documents are reviewed 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 lead discussants (IEC members) during the formally convened IEC meeting.

Intramural- The studies funded by the institution

Less than minimal risk- Probability of harm or discomfort anticipated in the research is nil or not expected. For example, research on anonymous or non-identified data/samples, data available in the public domain, meta-analysis, etc.

Minimal risk- Probability of harm or discomfort anticipated in the research is not greater than that ordinarily encountered in routine daily life activities of an average healthy individual or

general population or during the performance of routine tests where occurrence of serious harm or an adverse event (AE) is unlikely. Examples include research involving routine questioning or history taking, observing, physical examination, chest X-ray, obtaining body fluids without invasive intervention, such as hair, saliva or urine samples, etc.

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

More than minimal risk or High risk: Probability of harm or discomfort anticipated in the research is invasive and greater than minimal risk. Examples include research involving any interventional study using a drug, device or invasive procedure such as lumbar puncture, lung or liver biopsy, endoscopic procedure, intravenous sedation for diagnostic procedures, etc.

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: begins after drug approval. Therapeutic use studies go beyond the prior demonstration of the drug’s safety, efficacy, and dose definition. Studies in Phase IV are all studies (other than routine surveillance) performed after drug approval and related to the approved indication. They are studies that were not considered necessary for approval but are often important for optimizing the drug's use. They may be of any type but should have valid scientific objectives. Commonly conducted studies include additional drug-drug interaction, dose-response or safety studies and studies designed to support use under the approved indication, e.g. mortality/morbidity studies, epidemiological studies.

Scoring Sheet : 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 participants: 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. capacity, congenital anomaly/birth defect.

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

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: Minimum number of IEC members required to take decision at a meeting.

Monitor - DSMU/IEC member/Expert 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