Title: Human Research Protection Program Manual

Tata Memorial Centre

TMH: Tata Memorial Hospital,
Dr. E Borges Road, Parel, Mumbai - 400 012, India

ACTREC: Advance Centre for Treatment, Research and Education in Cancer
Kharghar, Navi Mumbai – 410 210, India

Table of Content

1.	**Title of the Policy : Human Research Protection Program Manual:**
	This Human Research Protection Program (HRPP) policy is provided in an effort to give comprehensive information about the organization and focus of the human research protection program to the members of the research community at Tata Memorial Centre. All members of the Tata Memorial Centre who engage in research involving human subjects must be knowledgeable about the requirements of the HRPP.
2.	**Definitions / Abbreviations :**
	• AAHRPP: Association for the Accreditation of Human Research Protection Programs • ACTREC : Advanced Centre for Treatment, Research and Education in Cancer • ADR : Adverse Drug Reaction • AE: Adverse Event • AIIMS : All India Institute of Medical Sciences • ASU: Ayurveda, Siddha, Unani. • BA : Bio-availability • BARC: Bhabha Atomic Research Centre • BE :Bio-equivalence • BIS :Bureau of Indian Standards • CRI : Cancer Research Institute • CTC :Clinical Trial Centre • CRC :Clinical Research Coordinator (CRC) or Trial Coordinator (TC) • CIOMS :Council of International Organizations of Medical Sciences, • CRM : Clinical Research Methodology • CDSCO :Central Drugs Standard Control Organization • CFR: Code of Federal Regulations • CoI: Conflict of Interest • CONSORT :Consolidated Standards of Reporting Trials • CRF: Case Record Form • CRO: Contract Research Organization • CRS :Clinical Research Secretariat • CTA :Clinical Trial Agreement • DHHS: Department of Health and Human Services • DSMB: Data Safety Monitoring Board • DSMSC :Data Safety Monitoring Subcommittee • DM : Data Manager • DEO : Data Entry Operator • DCGI: Director Controller General (India) • DAECTC : Department of Atomic Energy Clinical Trial Centre • DAE: Department of Atomic Energy • DBT :Department of Biotechnology • DCR: Drugs and Cosmetic Rules, 1945 • DGFT :Directorate General of Foreign Trade • EM : Extramural • ELSI :Ethical, Legal and Social Issues • FWA: Federal Wide Assurance

- FDF : Financial Disclosure Form
- FERCAP: Forum for Ethical Review Committees in Asia and the Western Pacific Region.
- FDA: Food and Drug Administration
- GCP :Good Clinical Practice
- GMP: Good Manufacturing Practices
- HEC : Human Ethics Committee
- HBNI: Homi Bhabha National Institute
- HRPP: Human Research Protection Program
- HIPAA : Health Insurance Portability and Accountability Act
- IAEA :International Atomic Energy Agency
- ICMR: Indian Council for Medical Research
- IM: Intramural
- IP: Investigational Product
- IB : Investigator's Brochure
- ICD : Informed Consent Document
- ICF: Informed Consent Form
- ICH: International Conference on Harmonization
- IDE : Investigational Device Exemption
- IEC : Institutional Ethics Committee
- IND : Investigational New Drug (IND)
- LAR : Legally Acceptable Representative
- MOU: Memorandum of Understanding
- MTA : Material Transfer Agreement
- NAC-SCRT: National Apex Committee for Stem Cell Research and Therapy
- NCE : New Chemical Entity
- NDA : New Drug Application
- NIH: National Institutes of Health
- NOC : No-objection Certificate
- NSR: non-significant risk
- OHRP: Office for Human Research Protections
- PI : Principal Investigator
- PHI :Protected Health Information
- RN : Research Nurse
- RF : Research Fellow
- RCT: Randomized Controlled Trial
- SAE : Serious Adverse Event
- SOPs: Standard Operating Procedures
- SRC: Scientific Review Committee
- TF: Terry Fox
- TMC: Tata Memorial Centre
- TMH : Tata Memorial Hospital
- TRAC : TMC-Research Administration Council

- WCI : Women Cancer Initiative
- WHO : World Health Organization
- WMA : World Medical Assembly
- UICC :Union for International Cancer Control

1. **Adverse Drug Reaction (ADR):** All noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase responses to a medicinal product means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.

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

3. **Approval (in relation to Institutional Ethics Committee):** The affirmative decision of the IEC that the clinical research has been reviewed and may be conducted at the institution site within the constraints set forth by the IEC, institution, Good Clinical Practice (GCP), and the applicable regulatory requirements in the context of the reviewed protocol.

4. **Clinical Trial/Study:** Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

5. **Clinical Trial/Study Report:** A written description of a trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report.

6. **Compliance (in relation to trials):** Adherence to all the trial-related requirements, Good Clinical Practice (GCP) requirements, and the applicable regulatory requirements.

7. **Confidentiality:** Prevention of disclosure, to other than authorized individuals, of a sponsor's proprietary information or of a subject's identity.

8. **Conflict of Interest:** Conflict of interest is a situation in which a person has a private or personal interest sufficient to appear to influence the objective exercise of his or her official duties as, say, a public official, an employee, or a professional." A potential or actual conflict of interest occurs whenever a trustee or employee is in a position to influence a decision that may result in any direct or indirect personal gain for him or herself, any other trustee or employee, or an immediate family member.

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

10. **Documentation:** All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records, and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken.

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

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

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

14. **Good Clinical Practice (GCP):** A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

15. **Human Subject/Trial Subject:** Human subject is defined as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. For device research, a subject is also an individual on whose specimen an investigational device (IDE) is used or as a control

16. **Identifiable Private Information:** Identifiable private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., a medical record).Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

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

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

19. **Institutional Ethics Committee (IEC):** An independent body constituted of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of the trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

20. **Interim Clinical Trial/Study Report:** A report of intermediate results and their evaluation based on analyses performed during the course of a trial.

21. **Intervention:** Intervention includes both physical procedures by which data is gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that is performed for research purposes

22. **Intramural:** The studies funded by the Institution

23. **Investigation:** Investigation is defined as a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a drug or intervention or device. Clinical Investigation is any experiment that involves a test article and human subjects.

24. **Investigational Product:** A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

25. **Investigational New Drug:** Investigational New Drugs mean substances with potential therapeutic actions during the process of scientific studies in human in order to verify their potential effects and safety or human use and to get approval for marketing.

26. **Investigator:** A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

27. **Investigator's Brochure:** A compilation of the clinical and nonclinical data on the

investigational product(s) which is relevant to the study of the investigational product(s) in human subjects

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

29. **Monitoring:** The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

30. **Monitoring Report:** A written report from the monitor to the sponsor after each site visit and/or other trial-related communication according to the sponsor's SOPs.

31. 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.

32. **Opinion (in relation to Institutional Ethics Committee):** The judgment and/or the advice provided by a Institutional Ethics Committee (IEC).

33. **Protocol:** A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents.

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

35. **Protocol Deviation:** Changes or alterations in the conduct of the trial which do not have a major impact on the subject's rights, safety or well-being, or the completeness, accuracy and reliability of the study data.

36. **Quality Assurance (QA):** All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirement(s).

37. **Quality Control (QC):** The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.

38. **Quorum:** Number of IEC members required to act on any proposal presented to the committee for action.

39. **Regulatory Authorities:** Bodies having the power to regulate. In the ICH GCP

guideline the expression Regulatory Authorities include the authorities that review submitted clinical data and those that conduct inspections.

40. **Research:** Research is defined as a systematic investigation, including development, testing and evaluation, designed to develop or contribute to generalized knowledge.

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

    - Results in death,
    - is life-threatening,
    - requires inpatient hospitalization or prolongation of existing hospitalization,
    - Results in persistent or significant disability/incapacity,
    - is a congenital anomaly/birth defect

42. **Sponsor:** An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.

43. **Standard Operating Procedures (SOPs):** Detailed, written instructions to achieve uniformity of the performance of a specific function and actions undertaken 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.

44. **Unexpected Adverse Drug Reaction:** An adverse reaction, the nature or severity of which is not consistent with the applicable product information.

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

46. **Well-being (of the trial subjects):** The physical and mental integrity of the subjects participating in a clinical trial.

3. Introduction:

The Tata Memorial Centre is a tertiary cancer centre involved in the prevention, treatment, education and research in Cancer and is recognized as one of the leading cancer centers in Asia.

TMC has two wings, Tata Memorial Hospital (TMH) and Advanced Centre for Treatment, Research and Education in Cancer (ACTREC)

The Tata Memorial Hospital (TMH) was commissioned by the Sir Dorabji Tata Trust on 28 February 1941 as a center with enduring values and a mission for concern for the Indian people.

In 1952 the Indian Cancer Research Centre was established as a pioneer research institute for basic research - later called the Cancer Research Institute (CRI). In 1957 the Ministry of

Health took over the Tata Memorial Hospital. The transfer of the administrative control of the Tata Memorial Centre (Tata Memorial Hospital & Cancer Research Institute) to the Department of Atomic Energy in 1962 was the next major milestone. The Tata Memorial Hospital and Cancer Research Institute merged as the two arms of the Tata Memorial Centre (TMC) in 1966 as a classic example of private philanthropy augmented by Government support with a mandate for Service, Education & Research in Cancer.

Every year nearly 43,000 new patients visit the clinics at TMC from all over India and neighboring countries. Nearly 60% of these cancer patients receive primary care at the Hospital. Over 70% of these patients are treated almost free of charge. Over 1000 patients attend the OPD daily for medical advice, comprehensive care or for follow-up treatment.
Nearly 6300 major operations are performed annually and 6000 patients treated with Radiotherapy and Chemotherapy annually in multi-disciplinary programs delivering evidence based treatments. Apart from patient care and service, clinical research programs contribute increasingly to improved delivery of care and highest standards of work ethics.

Many advances have taken place in every specialty. Supportive care in the form of total rehabilitation and counseling of patients are widely recognized to be important aspects of therapy. Excellent work is being carried out in areas of rehabilitation, physiotherapy, occupational therapy, speech therapy, psychology and medical social work.

Service/Research related to Cancer

At the TMC Cancer care is delivered as a part of specialist, multidisciplinary care, specialized to different sites of the body. The care and specialization is divided into various disease management group (DMG's).Cancer care is becoming increasingly complex with a multitude of rapid advances in technology and biology. In addition a wide range and numbers of health-care professionals are involved providing their specific inputs for effective management of patients. It has been recognised that cancer outcomes improve with early detection, uniformity of management protocols and multi-disciplinary focussed management. The purpose of the **DISEASE MANAGEMENT GROUPS (**DMGs) is to encourage all team members to see themselves as part of a team, with everyone informed of the overall picture and included in treatment decisions for the patients. The combined effort is also essential for formulating strategy and vision for enhancing research output and continuing education. The effort in any DMG should have a reductionist's approach in delivery of care and a unifying one for research.

Mandate of DMG

To ensure that designated specialists work effectively together in teams so that decisions regarding all aspects of diagnosis, treatment and care of patients and decisions regarding the team's operational policies are multidisciplinary decisions. Each member is expected to contribute independently to the diagnostic and treatment decisions about the patient.

The DMGs are required to ensure:

(i) Effective systems are in place among various services for providing coordinated care to patients.

(ii) Monitoring compliance with agreed upon evidence based guidelines, patient pathways

(iii) Efforts to identify priorities for specific improvement in a particular service/area as

deemed appropriate collectively by the DMG by clinical/medical audit

(iv) Audits of identified key areas that impact outcomes

(v) Efforts to continue education, training and capacity building amongst members

(vi) Look after information needs of patients

The following DMGs have been constituted

- ADULT HAEMATO LYMPHOID
- BONE AND SOFT TISSUE
- BREAST
- GASTRO INTESTINAL (G I)
- GYNECOLOGY
- HEAD & NECK SERVICES
- NEURO ONCOLOGY
- PAEDIATRIC HEMATO LYMPHOID
- PEDIATRIC SOLID TUMOURS
- THORACIC
- UROLOGY

Institutional Ethics 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 in compliance with the appropriate laws, and welfare of subjects.

The Data Safety Monitoring Subcommittee (DSMSC) is a subcommittee of the IEC, and is essentially responsible for monitoring patient safety and assessing data during the course of the study in a manner that contributes to the scientific and ethical integrity of the study**.**

The Tata Memorial Centre is a recognized training Centre for cancer education and research by national and international organizations such as WHO, IAEA and UICC. Tata Memorial Hospital is a post-graduate teaching centre and is affiliated to the Homi Bhabha National Institute (HBNI) (Deemed University) under Department of Atomic Energy, Government of India, and National Board of Examinations. Every year about 80 students register with the Centre for doing their Master's or Doctorate courses. There are about 450 students undergoing training every year in medical, non-medical and technical fields at the centre in long and short term courses.

In line with recent advances in Information Technology, the Tata Memorial Centre has established a comprehensive computerization of Medical Records, Material Management and Administration and also improved communication by broadening the Electronic mail and Internet facilities.

The Human Research Protections Program (HRPP) exists to promote high quality, ethical research. HRPP does this by serving as the advocate for the rights and welfare of persons who participate in research programs.

4. Mission:

The mission of Tata Memorial Centre (TMC) is to promote, restore and maintain the health of all the people we serve. This is to be accomplished through excellence in patient care, education, and research. Consideration for the safety and welfare of every patient or healthy volunteer who agrees to participate in a research project is the highest concern of the Research Program, and it was for the purpose of protecting these subjects that the Human Research Protections Program (HRPP) was established, including an Institutional Ethics Committee (IEC) duly constituted in accordance with applicable regulations. The Institute adheres to the highest ethical standards in protecting human research participants.

- Promote quality in clinical research
- Facilitate partnership between hospital, academia and industry
- Education and training of investigators in clinical research methodology, and good clinical research practice
- Facilitate partnerships between research networks.
- With the resultant product of sound scientific research based on good ethical principles protecting the rights and health of the trial subjects.

5. Scope:

The Institutional Ethics Committee will evaluate and approve:

A. All research involving patients and volunteer subjects at Tata Memorial Centre, including, but not limited to that conducted, supported, or otherwise subject to regulation.

B. The use of all investigational drugs/devices and procedures in patients and volunteers at Tata Memorial Centre.

C. All humanitarian use device and emergency use requests for Tata Memorial Centre. **Research** is defined by regulations as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge". **Human subjects** are defined by the regulations as "living individual(s) about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information".

6. Purpose:

The purpose of the Tata Memorial Centre HRPP is to ensure subject safety in all investigations covered under its scope of activities.

7. Institutional Ethics Committee:

7.1 Institutional Relationship:

The Hospital Ethics Committee of TMC was established in the year 1996. TMC being a premier cancer institute in the country, it has become a hub for oncology based trials. Over the years its scientific rigor and research culture led to a significant increase in the number of clinical trials being conducted. This gave rise to the need for impeccable and efficient management of its clinical trials to ensure the protection of human rights as mandated by Indian law (Schedule Y Drugs & Cosmetic Act 1940), and to satisfy public scrutiny.

In view of the above, the Hospital Ethics Committee of TMC was established in the year 1996. All research proposals after scientific evaluation and approval by the Scientific Review Committee were subjected to ethical review by Hospital Ethics Committee. Together, the

Scientific Review Committee and the Hospital Ethics Committee constituted the Institutional Review Board (IEC). Timely review and the safeguarding of high ethical standards formed the basis of the IEC review process. These are essential for clinical research including student research, investigator initiated research, extramural, intramural funded research and multi-centric multinational research.

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

However, as per the decision of the TMC-Research Administrative Council (TRAC), in order to manage the review process more efficiently, the TMC Scientific Review Committee and the Human Ethics Committees viz HEC-I & HEC-II, were merged to form the Institutional Review Board. In view of the large number of projects to be reviewed, three Institutional Review Boards (IECs) were instituted and designated as IEC-I , IEC-II and IEC-III. Each IEC reviews both the scientific and ethical aspects of the study. The IECs became functional in February 2012.IEC-III located at ACTREC was established in Dec 2009.
The Data Safety Monitoring Subcommittee (DSMSC) is a subcommittee of the IEC, and is essentially responsible for monitoring patient safety and assessing data during the course of the study in a manner that contributes to the scientific and ethical integrity of the study**.**

Tata Memorial Centre- IECs are registered with Drug Controller General India.

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

As the DCGI registration dated May 2013 is in name of Institutional Ethics Committee (IEC). Institutional Review Boards (IECs) are renamed as Institutional Ethics Committees (IEC-I,II,III).

The Institutional Ethics Committees (IECs) are constituted by the Director, Tata Memorial Centre (TMC) under authority vested by the Governing Council of the TMC. This refers to all Institutional Ethics Committees (IECs) constituted under TMC. Currently TMC has 3 IECs. In case the number of IECs increase or reduce, this IEC SOPs applies to all IECs.Institution has a Federal Wide Assurance (FWA) with the Department of Health and Human Services (DHHS) through the Office for Human Research Protections (OHRP). The assurance number is **FWA00006143**. This is periodically renewed as required.

IECs are also registered with HHS and have IORG Nos. IEC00003414, IEC00007802, IEC00009642 for IEC-I, IEC-II & IEC-III respectively. This is periodically renewed as required.

WHO/The Strategic Initiative for Developing Capacity in Ethical Review (SIDCER) in collaboration with the Forum for Ethical Review Committees in Asia and the Western Pacific Region Forum for Ethical Review Committees in Asia and the Western Pacific Region

(FERCAP) have awarded recognition to the Tata Memorial Centre Human Ethics Committees-I & II (TMC-HEC) in November 2009. The recognition of IECs-I & II was renewed in Nov 2012.

7.2 Composition

Each IEC will be multidisciplinary and multi-sectorial in composition

Each IEC is composed of a minimum of 7, and maximum of 15 members. The members are selected so as to have an equitable representation of all specialties in TMC. It includes scientific and non-scientific members, clinicians and non - clinicians, a clinical pharmacologist, members of the community, a lawyer-expert in ethics, a social worker / layperson / patient representative to represent different points of view.

Each committee will comprise of a Chairperson, Co-Chairperson, a Member Secretary, and other active members who represent an appropriate balance of professional, ethical, legal, cultural, educational, and community interests

The committee should have adequate representation of age, gender, community, etc. to safeguard the interests and welfare of all sections of the community / society. Members are expected to be aware of local, social and cultural norms, as this is the most important social control mechanism

The members should have various backgrounds to promote complete and adequate review of research activities commonly conducted by TMC.

Composition of IEC

The composition should be as follows:-

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

IEC Records

IEC records will include the following

1. IEC members' records
    a. Appointment and Acceptance letters of each member
    b. Signed and dated confidentiality agreements
    c. Updated Curriculum vitae (hard copy or soft copy)
    d. Training records for each IEC member
    e. Documentation of resignations/terminations
2. IEC membership roster/mandate
3. IEC attendance roster
4. IEC meeting agenda and minutes
5. Standard Operating Procedures
6. Annual reports

7. Copies of all original research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved consent documents, applications for study re-approval, study progress reports and interim reports, modifications, serious adverse event report forms submitted by investigators, and other reports, IEC letters. These are maintained in the "master file."
8.Files -Workshops & Conferences organized by IEC (Continuing education for members and staff
9.SOP Training Logs
10. Any other correspondence

Access to IEC records
IEC records will be made available for inspection to authorized representatives or regulatory authorities after receiving the request in writing

7.3 Membership:

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

Criteria for selection of members:

- Members are selected on their personal capacities, based on their interest, ethical and/or scientific knowledge and expertise, experience in the domain field and profile.
- The members representing medical scientist and clinicians should have post graduate qualification & adequate experience in their respective fields
- Conflict of interest will be avoided while making appointments, but where unavoidable, there will be transparency with regard to such interests.
- Directors, Head of Institution, Superintendents, Administrative officers who are responsible for business development will not serve as members or ex-officio members.
- New members will be identified according to the requirement i.e. as per the composition specified in Section 2.6. of the IEC SOP and provided the potential member fulfils the conditions of appointment as defined in 2.6.3 of the IEC 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

7.4 Responsibility:

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

- ✓ To ensure the competent review and evaluation of all ethical and scientific aspects of research projects received are in compliance with the appropriate laws, and welfare of subjects.
- ✓ Consultations for clinical science and ethics;.
- ✓ Education of professional, administrative, and support staff about ethical issues.
- ✓ Creation, development, revision and implementation of guidelines for the IECs

(SOPs).
- ✓ Initiate research studies in ethics.
- ✓ Continuing education and training programs to ensure that IEC members are qualified to perform their specific duties.

7.5 Clinical Research Secretariat (Office Of Research Administration)

7.5.1 Responsibilities

1. The HRPP will:
   a. Act as the Signatory Official for the institution.
   b. Provide a current Financial Disclosure form.
   c. Establish and implement the HRPP and policies
   d. Develop an annual budget for the HRPP.
   e. Review and evaluate reports and results of HRPP performance measurement and quality improvement activities
   f. Implement needed improvements and follow-up on actions, as appropriate
   g. Monitor changes in applicable regulations, policies and guidelines that relate to human research protection
   h. Complete the Tata Memorial Centre Research Training course.

2. The administrative support staff will:

   a. Organizing an effective and efficient tracking procedure for each proposal received.
   b. Preparing, maintaining and distributing study files.
   c. Organizing IEC meetings regularly
   d. Preparing the agenda and minutes of the meetings
   e. Maintaining IEC records and archives.
   f. Communicating with IEC members and PIs.
   g. Arranging training for personnel and IEC members
   h. Providing necessary administrative support for IEC related activities to the Member Secretary, IEC.
   i. Receiving IEC processing fees and issuing official receipts for the same.
   j. Corresponding with the IEC members, external experts and investigators.
   k. Making the pre and post arrangements of IEC meetings.
   l. Preparing the agenda and minutes of the IEC meetings.
   m. Answering queries of the investigators.
   n. Filing study related documents.
   o. Archiving and maintaining the study files.
   p. Preparation for accreditation, audits
   q. Complete the Tata Memorial Centre Research Training course and the IEC Administrator will also complete the designated modules of the training course of the Office for Human Research Protections (OHRP).
   r. Training for investigators, key study personnel, IEC members, and IEC staff.
   s. Participate in the development and subsequent implementation of SOPs
   t. Developing an effective and efficient tracking procedure

7.5.2 Research Staff

Who Can be the PI/Researcher:
   a. A full time employee of TMC (Tata Memorial Centre)
   b. All fulltime postdoctoral fellows & scientists
   c. All employees who conduct the research should possess appropriate educational qualification & experience in the field of oncology

Responsibilities

Interaction with Research Participants:

PI/Co-I or any study team member who are designated can interact with the research participant and access the private research data.

Principal investigators will be expected to:

a. Be appropriately credentialed for the research undertaken.
b. Complete all training requirements
c. Be responsible for the scientific conduct of the projects and the research staff involved in the projects they direct, including licensing / credentialing of all staff appropriate to their responsibilities
d. When appropriate, ensure that one of the study investigators is a qualified clinician responsible for any study-related healthcare decisions
e. When appropriate, have provisions in place for referral of subjects for any needed health care, both during a study, and for follow-up after a study
f. Submit all proposed research involving human participants, their tissue or data for review
g. Obtain informed consent
h. Submit for review all proposed changes to protocols and consents (including changes to improve subject protection), and reports of adverse events, unanticipated events involving risks to subjects, and deviations from the approved protocol or applicable policies or regulations.
i. Informs the participant's primary physician about the participant's participation in the clinical trial if the participant has a primary physician and if the participant agrees to the primary physician being informed. Although a participant is not obliged to give his or her reasons for withdrawing prematurely from a clinical trial, the researcher makes a reasonable effort to ascertain the reason, while fully respecting the participant's rights.
j. Researchers and research staff provide all disclosures and follows the requirements pertaining to consent covered by ICH-GCP

7.5.3 Research Training And Educational Program

All individuals involved in the conduct, or review of research with human subjects must complete the Tata Memorial Centre Research Training course or an equivalent course and are encouraged to attend seminars and meetings that focus on human subject research activities and current topics.

a. Training for IEC Chair, Member Secretary, and Members & Staff includes

1. HRPP Module
2. SOP Training
3. GCP Training
4. Workshops related to Ethics
5. Conflict of Interest Training

b. Training for Researcher and Research Staff includes

1. SOP Training
2. GCP Training
3. Conflict of Interest Training

Training will be held at least once in the year or whenever required. In addition to this training will be held when SOP's gets revised.

All SOP's related to HRPP are available on TMC website for investigators and other research related staff. Whenever there are revisions in the SOP's, changes are communicated to all individuals through the email/circular.

	7.5.4	**Research Application Process**
	Refer IEC SOP 3 Management of Protocol Submission	
	7.5.5	**Determination of Extent of IEC Oversight**
	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 Member Secretary, IEC or secretariat shall screen the proposals for their completeness. Depending on the risk involved in the research proposals, Member Secretary will categorise them into three types, viz., i. Initial review ii. Expedited review iii. Exemption from review An investigator may categorize his/her protocol in to the above three types, providing justification for the same, and after filling up Standard Request Forms for Expedited Review AX1-V3/SOP04b/V3 **(**SOP 04b/V3) / Exemption from review AX1-V3/SOP04c/V3 (SOP 04c/V3). However the decision to accept the request for Exemption from review / Expedited Review will be made by the Member Secretary, IEC. IEC/DSMSC 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. In case of any undue influence, IEC members and staff will report it to organization official (TRAC Administrator). The Organization official will send the response of undue influences to the IEC secretary.	
	7.5.6	**Expedited Review Procedure**
	This is described in the IEC SOP 4b Expedited Review of Submitted Protocol	
	7.5.7	**Review Procedure of IEC**
	This is described in the IEC SOP 4a Initial Review of submitted protocol	
	7.5.8	**Committee Meetings**
	This is described in the IEC SOP 5 Meeting Procedure	
	7.5.9	**Criteria for IEC Approval of Research**
	1. In order to approve research, the IEC shall determine that all of the following requirements are satisfied: a. Risks to subjects are minimized: (1) By using procedures which are consistent with sound research design, and which do not unnecessarily expose subjects to risk, and (2) Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes. b. In evaluating risks and benefits, the IEC should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits from therapies that subjects would receive even if not participating in the research). c. Selection of subjects is equitable. In making this assessment the IEC will take into account the purposes of the research and the setting in which the research will be conducted and will be particularly cognizant of the special problems of research involving special populations, such as children, pregnant women, handicapped,	

mentally disabled persons, or persons recruited or enrolled in an emergent care setting.

d. Informed consent will be sought from each prospective subject or the subject's legally authorized representative.

e. Informed consent will be appropriately documented.

f. Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

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g. Investigators' potential financial conflicts will not significantly impact the safety or outcomes of the study.

h. Ongoing review at least annually

j . Research must be conducted in accordance with the ethical principles contained in current revision of declaration of Helsinki and following principles from Indian GCP:

Principle of essentiality: whereby, the research entailing the use of human subjects is considered to be absolutely essential after a due consideration of all alternatives in the light of the existing knowledge in the proposed area of research and after the proposed research has been duly vetted and considered by an appropriate and responsible body of persons who are external to the particular research and who, after careful consideration, come to the conclusion that the said research is necessary for the advancement of knowledge and for the benefit of all members of the human species and for the ecological and environmental well being of the planet

Principle of non-exploitation whereby as a general rule, research subjects are remunerated for their involvement in the research or their experiment; and, irrespective of the social and economic condition or status, or literacy or educational levels attained by the research subjects kept fully apprised of all the dangers arising in and out of the research so that they can appreciate all the physical and psychological risks as well as moral implications of the research whether to themselves or others, including those yet to be born.

Principle of accountability and transparency whereby, the research or experiment will be conducted in a fair, honest, impartial and transparent manner, after full disclosure is made by those associated with the study of each aspect of their interest in the study, and any conflict of interest that may exist; and whereby, subject to the principle of privacy and confidentiality and the rights of the researcher, full and complete records of the research inclusive of data and notes are retrained for such reasonable period as may be prescribed or considered necessary for the purpose of post-research monitoring, evaluation of the research, conducting further research (whether by the initial researcher or otherwise) and in order to make such records available for scrutiny by the appropriate legal and administrative authority, if necessary.

Principle of maximization of the public interest and of distributive justice whereby, the research or experiment and its subsequent applicative use are conducted and used to benefit all human kind and not just those who are socially better off but also the least advantaged; and in particular, the research subject themselves.

Principle of institutional agreements whereby, there shall be a duty on all persons connected with the research to ensure that all the procedures required to be complied with and all institutional arrangements required to be made in respect of the research and its subsequent use or application are duly made in bonafide and transparent manner; and to take all appropriate steps to ensure that research reports, materials and data connected with the research are duly preserved and archived

Principle of public domain whereby, the research and any further research, experimentation or evaluation in response to, and emanating from such research is brought into the public domain so that its results are generally made known through scientific and other publications subject to such rights as are available to the researcher and those associated with the research under the law in force at that time

2. When some or all of the subjects, such as children, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence, the IEC will ensure that additional safeguards are included in the study to protect the rights and welfare of these subjects, and that they are adequate. Remuneration, monetary or otherwise, offered to research participants and/or legally authorized representatives (LAR) is an acceptable practice in so far as it fairly offsets the incidental costs and inconveniences inherent in study participation, such as travel, meals, parking, and time commitment. The IEC must review and approve the remuneration plan, including type and amount of remuneration, prior to its implementation. The IEC must determine that the remuneration is reasonable given the nature of the study and that it does not unduly influence or coerce enrollment into or continued participation in the study. The IEC will exercise heightened vigilance when reviewing proposed remuneration for studies involving vulnerable populations to ensure that the decisions of the potential participants are not influenced by the remuneration associated with the study.

7.6 Decision Making Process

This is described in the IEC SOP 05 Agenda Preparation, Meeting Procedures and Recording of Minutes

7.6.1 Investigator Notification Process

This is described in the IEC SOP 05 Agenda Preparation, Meeting Procedures and Recording of Minutes

7.7 Requirement for Investigational New Drug (IND) Application

The following definitions and references are as per the Schedule Y and CDSCO Ethical Guidelines for Biomedical Research:

Definition of New Drug

(a) a new substance of chemical, biological or biotechnological origin; in bulk or prepared dosage form; used for prevention, diagnosis, or treatment of disease in man or animal; which, except during local clinical trials, has not been used in the country to any significant extent; and which, except during local clinical trials, has not been recognized in the country as effective and safe for the proposed claim;

(b) a drug already approved by the licensing authority mentioned in Rule 21 for certain claims, which is now proposed to be marketed with modified or new claims, namely, indications, dosage forms (including sustained release dosage form) and route of administration;

(c) a fixed dose combination of two or more drugs, individually approved earlier for certain claims, which are now proposed to be combined for the first time in a fixed ratio, or if the ratio of ingredients in an already marketed combination is proposed to be changed, with certain claims, viz. indications, dosage form (including sustained release dosage form) and route of administration. [See items (b) and (c) of Appendix VI to

Schedule Y.]

Explanation: For the purpose of this rule-

(i) all vaccines shall be new drugs unless certified otherwise by the licensing authority under Rule 21;

(ii) a new drug shall continue to be considered as new drug for a period of four years from the date of its first approval or its inclusion in the Indian Pharmacopoeia, whichever is earlier.

Clinical trial on a new drug shall be initiated only after the permission has been granted by the Licensing Authority Drugs Controller General of India (DCGI) under rule 21 (b), and the approval obtained from the respective ethics committee(s).

Regulatory clearance from appropriate regulatory authorities i.e. DCGI approval is one of the essential document required to be submitted by the researcher to the Ethics Committee.

7.7.1 Clinical Trials With Surgical Procedures / Medical Devices

Definitions

Device: "An instrument, apparatus, implement, machine, contrivance, implant, in vitro agent, or other similar or related article, including a component, part or accessory,

intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease in man, or

- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease in man, or
- intended to affect the structure or any function of the body of man, and
- which does not achieve any of its primary intended purposes/ uses
- through chemical action within or on the body of man, or
- By being metabolized within the body."

Medical devices: A medical device is defined as an inert diagnostic or therapeutic article that does not achieve any of its principal intended purposes through chemical action, within or on the body.

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

Medical devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intra-ocular lenses, orthopedic pins and other orthopedic accessories. Their purpose varies from being used primarily for specific affected parts of the body to being used as adjunct to primary therapies, for eg. lithotripsy with drug therapy for kidney stone. Depending upon risks involved the devices could be classified as follows:-

a. Non critical devices - An investigational device that does not present significant risk to the patients eg. Thermometer, BP apparatus.

b. Critical devices - An investigational medical device that presents a potential serious risk to the health, safety or welfare of the participant - for example, pace markers, implants, internal catheters. A more appropriate classification and the proposed regulatory and certification procedures for Indian devices are summarized in the table

given below.

All the general principles of clinical trials described for drug trials should also be considered for trials of medical devices. As for the medicated devises, safety evaluation and pre-market efficacy of devices for 1-3 years with data on adverse reactions should be obtained before pre-market certification. The duration of the trial and extent of use may be decided in case-to-case basis by the appropriate authorities. However, the following important factors that are unique to medical devices should be taken into consideration while evaluating the related research projects:

- Safety data of the medical device in animals should be obtained and likely risks posed by the device should be considered.
- Clinical trials of medical devices are different from drug trials, as they cannot be conducted in healthy volunteers. Hence Phase I trials are not necessary for trial on medicated devices.
- Medical devices used within the body may have greater risk potential than those used on or outside the body, for example, orthopedic pins vs crutches.
- Medical devices not used regularly have less risk potential than those used regularly, for example, contact lens vs intraocular lenses.
- Safe procedures to introduce a medical device in the patient should also be followed as the procedure itself may cause harm to the patient.
- Informed consent procedures should be followed as in drug trials. The patient information sheet should contain information on follow-up procedures to be adopted if the patient decides to withdraw from the trial.
- Study design of the intra body devices like implants can be very challenging and should have adequate protective safeguards. The study should be long enough to detect if there are any late onset ADRs.
- If full assessment of safety is not complete, the Phase III could extend to Phase

Clinical trial on a device shall be initiated only after the permission has been granted by the Licensing Authority Drugs Controller General of India (DCGI) and the approval obtained from the respective ethics committee(s).

Regulatory clearance from appropriate regulatory authorities i.e. DCGI approval is one of the essential document required to be submitted by the researcher to the Ethics Committee.

7.7.2 Diagnostic Agents –Use of Radioactive Materials and X-RAYS

In human beings, for investigation and treatment, different radiations-X-ray. Gamma rays and beta rays- radiopaque contrast agents and radioactive materials are used. The relative risks benefits of research proposal utilizing radioactive materials or x-rays should be evaluated. Radiation limits for the use of such materials and X-rays should be in accordance with the limits set forth by the regulatory authority for such materials (BARC-Bhabha Atomic Research Centre, Mumbai).

Special Concerns:

- Informed Consent should be obtained before any diagnostic procedures.
- Information to be gained should be gathered using methods that do not expose participants to more radiation than exposed normally.
- In the event of death of a participant with radiological implant, due precaution as per radiation guidelines may be taken not to expose the relatives or the close co-habitants to radiation till safe.
- Research should be performed on patients undergoing the procedures for diagnostic

or therapeutic purposes.

- Safety measures should be taken to protect research participants and others who may be exposed to radiation.
- The protocol should make adequate provisions for detecting pregnancies to avoid risks of exposure to the embryo.
- Information must be given to participant about possible genetic damage to offspring.
- Non-radioactive diagnostic agents are considered as drugs and the same guidelines should be followed when using them.
- Ultrasound should be substituted whenever feasible.

7.7.3 Clinical Evaluation of Traditional AYURVEDA, SIDDHA, UNANI Remedies and Medicinal Plants :

The ASU drugs include herbal and herbo-mineral formulations. The herbal products can belong to one of the three categories given below:-

- A lot is unknown about the use of plant or its extract, metals, minerals and animal products in the ancient Ayurveda, Siddha or Unani literature or the plant may actually be regularly used by physicians of the traditional system of medicine for a number of years and the substance is to be clinically evaluated for same indication for which it is being used or as has been described in the texts.
- When an extract of a plant or compound isolated from the plant and any compound formulation having plants, metals, minerals and animal products as ingredients has to be clinically evaluated for a therapeutic effect not originally described in the texts traditional systems or, the method of preparations is different, it has to be treated as a new substance or new chemical entity(NCE) and the same type of acute, sub acute and chronic toxicity data will have to be generated as required by the regulatory authority for synthetic products before it is cleared for clinical evaluation.
- An extract or a compound isolated from a plant and any compound formulation having plants, metals, minerals and animal products as ingredients which has never been in use before and has not ever been mentioned in ancient literature, should be treated as new drug, and therefore, should undergo all regulatory requirements before being evaluated clinically.

Category I - For formulations belonging to this category, it may not be necessary to undertake phase I studies. In Phase II dose ranging should be explored to find the effective dose as also maximum tolerated dose. RCTs would be the preferable methodology to validate the claim with placebo or standard drug depending on the ethical requirement. The clinical trials would mostly fall in the non-inferiority group if literature is not available regarding the proven efficacy of the formulation. Superiority trial could be designed if the control arm is placebo or modern medicine, which is only weakly effective. Sometimes it would also be right to design pilot observational studies to explore feasibility of conducting larger trials for validation if the outcome is encouraging. It needs to be emphasized that since the substance to be tested is already in use in Indian Systems of Medicine or has been described in their texts, the need for testing its toxicity in animals has been considerably reduced. Neither would any toxicity study be needed for phase II trial. This is the unique **reverse pharmacology** approach for evaluating traditional formulations for traditional indication. If there are reports suggesting toxicity or when the herbal preparation is to be used for more than 3 months it would be necessary to undertake 4 - 6 weeks toxicity study in 2 species of animals in the circumstances described above or

when a larger multicentric phase III trial is subsequently planned based on results of phase II study. Clinical trials with ASU preparations should be carried out only after these have been standardized and markers identified to ensure that the substances being evaluated are always the same. However, Good manufacturing Practices (GMP) standards for the formulations to be tried would not be required for Phase I and II trials. But for Phase III GMP standards would be required for the formulations to be used in the trial as the number of participants would be larger and this will be followed by marketing approvals.

Category II and III: All the steps involved for regulatory approvals as in the case of synthetic drugs should be followed. However, for formulations falling under category two only limited toxicities as mentioned for category I would apply. All formulations involving herbal component should satisfy following criteria as prescribed by WHO document "Operational Guidance: Information needed to support clinical trials of herbal products (2005)":

a. For Phase I / II studies –

Herbal Substance:

• Description of the plant: genus, species (cultivar where appropriate); region(s) and country(ies) of origin; time of harvest; parts to be harvested

• Plant processing: drying, mechanical disruption, solvent extraction (aqueous or organic solvents, others)

• Analytical procedures

• Specification

• Storage conditions/shelf life.

Herbal Product:

• Amount of active ingredient

• List of excipients

• Type of product (tablet, capsule, etc.) and its method of manufacture

• Analysis of putative active ingredient(s) via chemical or biological parameters

• Analysis of a sizeable chemical constituent (analytical marker compound)

• Analysis via chemical fingerprint (analytical markers)

• Analysis for lack of contamination by pesticides, herbicides, heavy metals, synthetic drug adulterants, microbials, toxins, etc.

• Dissolution studies

• Storage conditions and stability during the length of the trial

• Specification against which a certificate of analysis can be assessed before the clinical trial material is released.

b. For Phase III studies: Performing generally the same procedures as for Phase I/II trials, but more extensively and with more stringent oversight.

Herbal Substance:

• as above for Phase I/II trials.

In addition:

• Statement that the plant is cultivated according to Good Agricultural Practices

or harvested according to Good Wild crafting Practices

• Reference batch.

Herbal Product:

• as above for Phase I/II trials

In addition:

• Environmental impact statement.

7.7.4 Vaccine Trials:

Vaccines can be prophylactic and therapeutic in nature. While prophylactic vaccines are given to normal participants, therapeutic or curative vaccines may be given to patients suffering from particular disease. Many of the prophylactic vaccines are given to pediatric group. The guidelines to conduct the clinical trial on investigational vaccines are similar to those governing a drug trial. The phases of these trials differ from drug trials as given below:

Phase I: This refers to the first introduction of a vaccine into a human population for determination of its safety and biological effects including immunogenicity. This phase includes study of dose and route of administration and should involve **low risk participants**. For example, immunogenicity to hepatitis B vaccine should not be determined in high risk participants. Pharmacokinetic studies are generally not required for injectable characteristics of the immune response to the known or presumed action of vaccine. The class, subclass, and the function of specific antibody produced and the lag time for appearance and duration of adequate antibody titer is determined. Information about the induction of cell-mediated immunity, the cross reactive antibodies and/or interaction pre-existing antibodies which might affect immune system is also obtained.

Phase II: This refers to the initial trials examining effectiveness (immunogenicity) and dose range in a limited number of volunteers forming the target groups, like, children, adults or those at risk of exposure to pathogens. Pharmacokinetics and safety of the vaccine is also studied. Early Phase II is usually an exploratory trial while the late Phase II is known as pivotal efficacy study.

Phase III: This focuses on assessment of safety and effectiveness in the prevention of disease, involving controlled study on a larger number of volunteers (in thousands) through Multicentric studies. These studies determine the protection offered by the vaccine and provide pivotal data for licensure. Efficacy in vaccine trials means reduction in incidence of the disease after vaccination compared to the incidence that prevailed before vaccination. Effectiveness on the other hand provides information of protective rate conferred on a given population. It includes measurement of direct and indirect protection to a non - vaccinated person among the defined vaccinated population determined by vaccine coverage area, and correlation of vaccine strains with circulating strains.

Phase IV Studies (Post-Licensure Evaluation): These studies are done in the entire population or a subgroup to detect the rarer or unexpected events that may not be seen in smaller Phase II/ III studies. Post-licensure studies of large populations, in a more heterogeneous group of people, over longer periods of time are necessary to provide ongoing assessment of vaccine safety and effectiveness. The Pharmacodynamics studies provide information on the vaccines when other routes of administration are claimed eg oral vaccine, or when vaccine contains novel adjuvants or excipients. These are also done to conduct

further research on age at vaccination, effect of simultaneous administration of other vaccines, efficacy and adverse events due to changes in vaccine strain, and interchangeability of vaccine. Bridging studies in vaccine trials are conducted to support clinical comparability of efficacy, safety and immunogenicity of new formulation when there is change in vaccine composition with regard to adjuvant, preservative, or a change in manufacturing process, site or scale. These are performed either before or after product licensure. The rationale of bridging clinical studies is. The goal is to demonstrate product equivalency to that used in earlier pre-clinical or clinical testing. When serologic bridging studies are to be done, only comparison of sera with historical control from an efficacy trial is warranted, and no clinical trial need be undertaken.

Combination Vaccines

Combination vaccines are being used commonly at present. The main goal in efficacy trial design of such vaccines is to evaluate the efficacy of each antigenic component. When correlates of protection are validated for each component, immunogenicity end- points should be used. When they are not validated for each component, prospective controlled trial is required. Further, non-inferiority trials should be conducted to demonstrate that the combination vaccine is not inferior in terms of immunogenicity or efficacy, to vaccines with individual components.

Vaccines Administered Simultaneously with the Combination Vaccines

Immunogenicity and safety data should be obtained in Phase III (Pre-licensure) studies to support the simultaneous administration of a new vaccine with already licensed vaccines that would be given to the same target population using the same (or overlapping) schedule. With regard to immunogenicity, assessment should be performed to show that subjects still attain an acceptable immune response to both the combination vaccine and the other simultaneously administered vaccine. The immunogenicity obtained with such simultaneous administration should be evaluated early in clinical development for all components to detect any possible immunological interference and such assessment would be valuable before proceeding to a large-scale trial of the investigational vaccine. These studies will evaluate safety and interference of the new combination vaccine with one type of simultaneously administered vaccine, *e.g*., for a new DTaP vaccine, safety and interference will be evaluated in a statistically valid manner with one type of simultaneously administered *Haemophilus influenzae* type b conjugate vaccine. If no such studies have been conducted, it should be stated in the package insert that no safety or immunogenicity data has been generated.

Special Concerns

I. Some vaccines that contain active or live - attenuated micro-organisms can possibly possess a small risk of producing that particular infection. The participant to be vaccinated should be informed of the same.

II. The participants in control groups or when subjected to ineffective vaccines run a risk of contracting the disease. In such an event free treatment for the disease should be given and if it is a disease where lifelong treatment is required then this should be insisted upon by IEC/ In dEC.

III. The risks associated with vaccines produced by recombinant DNA techniques are not completely known. However, for all the recombinant vaccines/ products the Guidelines issued by the Department of Biotechnology should be strictly followed.

IV. Post trial access to the vaccine should be available to the control group. But if the vaccine is for pediatric age group and by the time the study gets over the children in the control arm may cross the age when the vaccine is supposed to be protective. In such instances the control arm could be some other alternative vaccine for that pediatric age group although this does not restore clinical equipoise. EC may examine the feasibility and ethical aspects on a case-to-case basis.

V. Post trial access to the vaccine should be given first to the community from which the participants were drawn.

VI. When a trial of HIV preventive vaccine is being conducted, positive serology may result after the vaccination. This may not indicate infection but may create problems for employment and travel purposes. To avoid confusion, a certificate stating that the person is a trial participant in an HIV vaccine trial may be issued.

VII. Children being a vulnerable group, care should be taken to choose the particular age with regard to gender, ethnic background and health profile for testing vaccines for this age especially if they are from over-researched community.

VIII. In RCTs if no effective vaccine exists as comparator then placebo can be used. The community should be involved to decide on the choice of comparator.

7.7.5 Clinical Trials on Contraceptives

I. All procedures for clinical trials are applicable. Participants should be clearly informed about the alternatives available.

II. In women where implant has been used as a contraceptive for trial, a proper follow up for removal of the implant should be done, after the trial is over or the participant has withdrawn from the trial.

III. Children born due to failure of contraceptives under study should be followed up for any abnormalities if the woman does not opt for medical termination of pregnancy.

7.8 Review of Amendments

This is described in the IEC SOP 06 Review of Amended Protocol Related Documents

7.9 Adverse Event Reports

This is described in the IEC SOP 09 SAE Review

7.10 Progress Reports

This is described in the **IEC SOP 7 Continuing Review**

7.11 Monitoring of the Projects

This is described in the IEC SOP 15 Site Monitoring

7.12 Approval Withdrawal

The committee has the authority to suspend or terminate previously approved research that is not being conducted in accordance with the committee's requirements.

7.13 Reporting Responsibilities

Upon receiving knowledge of any of the following, the IEC will forward a written report to the chairman, who may determine the action to be taken if the incident is minor, or will present it to the full committee for consideration, Chairperson, IEC may temporarily suspend the study, pending review in IEC.

IEC will forward the notification of any kind, SAE or AE to the Head, institute / TRAC chairman.

1. Injuries or any other unanticipated problems involving risks to subjects or others.
2. Serious or continuing non-compliance with state or federal regulations or decisions of the committee.
3. IEC will communicate with the TRAC in following cases
    a. In case of AE, SAE, Undue influences
    b. In case of non- compliance
    c. Changes in the regulations
    d. Changes in the SOP's of IEC
4. To discuss the above issues or changes, TRAC will hold a meeting at least twice a year or earlier if required.

7.14 Appeal Process

- If an investigator disagrees with the IEC decision to disapprove or terminate a study, the Investigator may submit a written appeal to the decision to "disapprove of the IEC decision" within 15-20 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 to disapprove 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.
- Director of TMC/TMH/ACTREC and other Officials cannot approve research that has not been approved by the IEC.

7.15 Communications

All official communications of the IEC to the investigators as well as to all other authorities will be in writing.

7.16 Records

This is described in IEC SOP 10 Maintenance of Active Project Files, Archival / Disposal of closed files and Retrieval of documents

8. Mandate

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

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

The terms of reference for the IEC are as follows:

1. Ensure the highest scientific and ethical standards of research at TMC.
2. Review and approve proposals for clinical, basic or translational research projects (Intra and Extra mural) for scientific and ethical content.
3. Improve ethical standards and issue guidelines on ethical dilemmas related to patient care services.
4. To function as a forum to advise the administration in case of any ethical issues that may arise from patients, families or public.
5. To maintain our leadership as a national standard of reference in all fields.
6. To issue and periodically, update and revise SOPs and guidelines for effective functioning of IEC as and when necessary
7. Continuing education in clinical research bioethics and ethical aspects of clinical practice by seminars, workshops and interactive discussions for all categories of staff members including nursing and paramedical staff
8. To initiate and commission research studies on ethical aspects of practice in TMC
   - ✓ The IEC endeavors to provide guidance on a broad range of topics such as disclosures of diagnosis, diagnosis of brain death, indications for stopping resuscitation, true informed consent, etc.
   - ✓ The committee does not address or interfere in matters of administration, nor does the committee function as a grievance cell for staff members.

9. Institutional Authority (Chairs – Job Description – HRD)

	As Director of the Tata Memorial Centre, the primary focus is to ensure continued provision of highest standards of patient care and treatment. To provide leadership and co-ordinate guidance to Directors and other medical doctors specialized in multi-discipline facets of Oncology, and scientists pursuing basic and clinical research are yet another area of primary responsibility. As Head of the institute, he is responsible for supervising various basic and clinical research programmes, coordination with pharmaceuticals industries in clinical trials in human subjects, ensuring compliance by the Project Investigators, with recommendations of Institutional Review Boards, applicable legislations and regulatory directions, and protecting the interests of patients and institutions in clinical trials agreements executed with external research organizations. To give thrust to continuous development of in-house research programmes, including the foray into translational research programmes in new areas like genome re-sequencing and stem cell biology. The translational research process has seeded many other thoughts to kick start novel projects in cancers. A visionary responsibility lies on the Director of the Centre, to gear cancer research and treatment programmes in the context of ever dynamic and newer evolving dimensions in cancer biology and human genetics. The Tata Memorial Centre has been recognized nationally and internationally as one of the pioneering institutions in the field of diagnosis, treatment and research in cancer. The Director has the responsibility to take the Institute to further heights in this pursuit, playing a vital role in enlisting the continued cooperation and medical inputs from national and international organizations.
10.	**Ethical and Regulatory Compliance (ICMR / DCGI)**
	➢ Ethical principles expressed in the Declaration of Helsinki (Adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964, and amended by the 29th World Medical Assembly, Tokyo, Japan, October 1975; 35th World Medical Assembly, Venice, Italy, October 1983; 41st World Medical Assembly, Hong Kong, September 1989; 48th World Medical Assembly, Somerset West, Republic of South Africa, October 1996; and the 52nd World Medical Assembly, Edinburgh, Scotland, October 2000; Note of Clarification on Paragraph 29 added by the World Medical Assembly, Washington 2002; Note of Clarification on Paragraph 30 added by the World Medical Assembly, Tokyo 2004, 59th WMA general Assembly, Seoul, October 2008) ➢ It makes further reference to the International Ethical Guidelines for e.g. The Nuremburg Code (1945), the Council of International Organizations of Medical Sciences (CIOMS), the Belmont Report 1979, the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Geneva 2002), and the European Convention on Human Rights and Biomedicine 1977 ➢ The IEC establishes its own Standard Operating Procedures based on the ICMR guidelines (2006), Schedule Y (Drugs and Cosmetics Act 1940., amendment 20th Jan 2005), Operational Guidelines for Ethics Committees that Review Biomedical Research (WHO 2000), and ICH-GCP, 1996 and the local regulations ➢ IEC–seeks to fulfill the requirements for international assurances and is established and

	functions in accordance with the national law and regulations
11.	**Research under HRPP**
	11.1 Retrospective Data Collection Studies
	What makes a study retrospective? A retrospective study only involves data or specimens that are in existence prior to the research application's submission **Is Institutional Ethics Committee (IEC) review required?** Research activities involving the use of human data or specimens are subject to IEC review. Not all retrospective research studies require IEC oversight and approval, but member secretary, IEC makes the determination whether the activity is research and the IEC determines what type of oversight is required. Often these types of studies qualify for expedited IEC review or an exemption. **What information is needed to decide whether IEC review is required?** It is important that the research application explain: • Why the data are being collected • What data are being collected • Whether the data include individual identifiers • The type of informed consent requested The IEC cannot process an application until these specifics are known. Incomplete information about study specifics is the most common reason for review process delays. **What forms must be submitted to IEC?** A Tata Memorial Centre Research Application is required to review the activity and determine whether it is research and if IEC review is required. The Human Studies Form is included in the application and provides the HRPP and IEC with important study-specific information.
	11.2 Prospective Data Collection Studies
	What makes a study prospective? A prospective study involves data or specimens that will be created after the research application's submission. **Is Institutional Ethics Committee (IEC) review required?** Research activities involving the use of human data or specimens are subject to IEC review. Research Administration makes the determination whether the activity is research and the IEC determines what type of oversight is required. **What information is needed to decide whether IEC review is required?** It is important that the research application explain: • Why the data are being collected • What data are being collected • Whether the data includes individual identifiers • The type of informed consent requested The HRPP and IEC cannot process an application until these specifics are known. Incomplete information about study specifics is the most common reason for review process delays. **What forms must be submitted to IEC?**

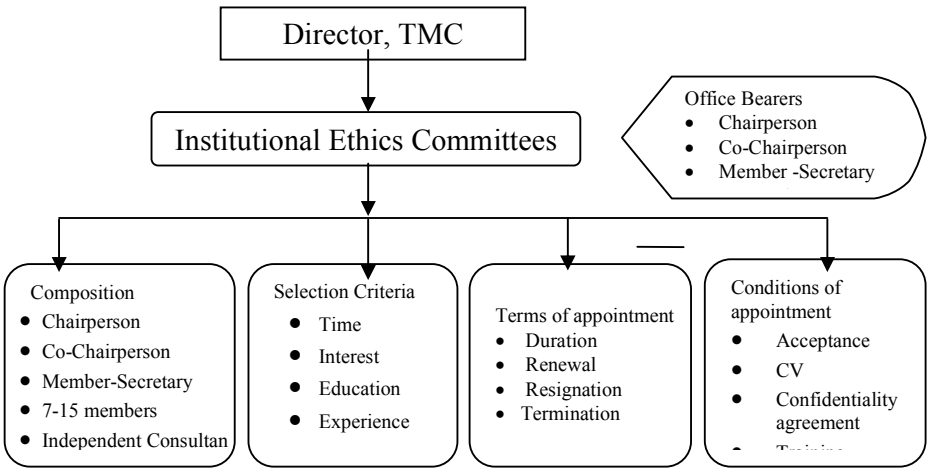
	A Tata Memorial Centre Research Application is required to review the activity and determine whether it is research and if IEC review is required. The Human Studies Form is included in the application and provides the HRPP and IEC with important study-specific information.
	11.3 Prospective Research Intervention Studies
	What makes a study an intervention study? A research intervention study involves interaction with human subjects that would not take place without the research study. Some study components may involve standard treatment interventions or quality of life surveys, but at least one study procedure is planned only for the study itself. **Is Institutional Ethics Committee (IEC) review required?** All prospective intervention studies that involve living human subjects, including staff members, require IEC review. Research Administration makes the determination whether the activity is research and the IEC determines what type of oversight is required. Often these types of studies require full board IEC review, but they may qualify for expedited review. The IEC meets once per month to review activities that require full board review. **What information is needed to decide whether IEC review is required?** It is important that the research application explain: • Why the study is being conducted • What procedures are investigational • How the risks have been minimized • How the data will be used and stored The HRPP and IEC cannot process an application until these specifics are known. Incomplete information about study specifics is the most common reason for review process delays. **What forms must be submitted to IEC?** A Tata Memorial Centre Research Application is required to review the activity and determine whether it is research and if IEC review is required.
12.	**Research activities not under HRPP**
	Research undertaken without the intention of involving human subjects does not fall under the scrutiny of the HRPP. In the event research is undertaken without the intention of involving human subjects, but it is later proposed to involve human subjects in the research, the research shall first be reviewed and approved by the IEC.
13.	**HRPP Organizational Structure**
	

13.1.1 Organizational Officials (TRAC)

Director TMC (Chairman)
Director, ACTREC (Secretary)
Director, TMH (Member)
Director, Academics (Member)
Director, CCE (Member)
Dy Director, ACTREC (Member)
Medical Superintend, TMH
Officer-In-Charge, CRS
Secretary, TMC-IEC I , II & III (Member)
Secretary, DSMSC
Coordinator, TRAC

13.1.2 IEC

Flow Chart



13.1.3 IEC Chair

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

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

13.1.4 IEC Member Secretary

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

13.1.5 IEC Secretariat

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

The secretariat shall have the following functions:

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

The IEC Administrative Staff: Working Rules

1. There will be administrative officer/s and attendant/s /helper/s who will help the IEC Chairperson and Member Secretary in executing functions of the IEC. Additional staff may be appointed and duties assigned as and when deemed necessary by the IEC. The eligibility criteria for new staff to be appointed will be laid down depending on the required job profile. The need for appointment of administrative staff, job profile and qualifications may be recommended by IEC members during regular IEC meeting and will be recorded in minutes. These will be forwarded to the Director, TMC.
2. The administrative staff will be appointed by conducting formal interviews as per TMC policy.

Duties of the administrative officer/s/staff:

a. Organizing an effective and efficient tracking procedure for each proposal received.
b. Preparing, maintaining and distributing study files.
c. Organizing IEC meetings regularly
d. Remind IEC members to report disclosures to the IEC on at least an annual basis and as needed to reflect changes that add or delete conflicts of interest.
e. Preparing the agenda and minutes of the meetings
f. Maintaining IEC records and archives.
g. Communicating with IEC members and PIs.
h. Arranging training for personnel and IEC members
i. Providing necessary administrative support for IEC related activities to the Member Secretary, IEC.
j. Receiving IEC processing fees and issuing official receipts for the same.
k. Corresponding with the IEC members, external experts and investigators.

l. Making the pre and post arrangements of IEC meetings.
m. Preparing the agenda and minutes of the IEC meetings.
n. Answering queries of the investigators.
o. Filing study related documents.
p. Archiving and maintaining the study files.

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

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

4. The administrative staff will report to the Chairperson and/or Member Secretary.
5. The office timings for the administrative staff will be as per TMC rules and regulations.

The administrative staff will avail leave as per TMC norms.

13.1.6 Investigators

A **clinical investigator** involved in a clinical trial is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation. The qualifications must be outlined in a current resume and readily available for auditors

13.1.7 Research Staff

- Trial Coordinator - The Clinical Research Coordinator (CRC) or Trial Coordinator (TC) is responsible for conducting clinical trials using good clinical practice (GCP) under the auspices of the Principal Investigator (PI)

- Research Nurse - Research nurses play a vital role in ensuring clinical research studies run smoothly and that participant are safe and fully informed.

- Research Fellow - A research fellow may act either as an independent investigator or under the supervision of a principal investigator.

- Data Manager – Data Manager is responsible for the creation, updating, maintenance and validation of clinical study databases and for the provision of computerized reports of these data. He or she is a key member of the clinical project team and should be able to prioritize work in line with project management decisions.

- Data Entry Operator - Data entry operator enters data into a machine using a alpha-numeric keyboard with speed and accuracy.

- Office Assistant - Employees in this job perform and oversee a variety of general office support assignments where the processing of documents and recording, retrieving, and distribution of data or information is an essential and/or substantial part of the work

14	**HRPP Resources (IM / DAECTC / WCI / TF)**
	14.1. Intramural – TMC Supports innovative research projects initiated by investigator. **14.2 DAECTC –** Department of atomic energy supports randomized controlled trials in Cancer, Education, infrastructure, human resources and meeting. **14.3 WCI –** Women Cancer Initiative gives grants for research in female cancer (Breast/Cervix/Ovary). 20% of total budget is reserved for research projects. **14.4 TF –** Terry Fox supports research projects in basic and clinical cancer. **14.5 TMC –** Apart from other funding agencies TMC also helps HRPP in its operations by providing • Administrative resources – TMC provide administrative support for the HRPP • HRPP educational program – TMC IEC helps to conduct educational programs to enhance knowledge of HRPP • Personnel – TMC also appoints the person for HRPP • IEC's – TMC IEC's helps HRPP to carry out its activity. • Legal Counsel - In TMC organization counselor work for HRPP also. • Conflict of Interest – HRPP follows same plan of conflict of interest as IEC. TMC is equipped with all necessary office space, meeting space, storage space and equipment to perform the functions required for the HRPP. The adequacy of personnel and non-personnel resources of the HRPP program is assessed regularly by the TMC Research Administrative Council (TRAC). The additional resources required for the HRPP are forwarded to the institute's administrative cell, which are discussed in meetings of governing body of the institutions.
15.	**Sponsored Research**
	All Pharmacy Companies sponsor research initiated by Principle Investigators
16.	**Monitoring, Evaluation, Quality Improvement**
	16.1 Monitoring of the projects **Refer IEC SOP 15 Site Monitoring** **16.2 Evaluation of IEC Chair, Member secretary, members & Staff:** • Annual Self Evaluation of Chairperson will be done. • Annual Evaluation of IEC members will be done by Chairperson. The individual feedback will be provided by email to the members. • Annual Evaluation of IEC staff will be done by Member Secretary. The individual feedback will be provided to the staff. **16.3 Quality Improvement plan:** Aim: The aim of the Quality program is to measure the level of compliance with the SOPs, regulations and the level of effectiveness of the Human Research Protection Program, and to plan improvements to the program, which are, in turn, monitored to see how effective they have been. Quality improvement is a continuous process, and can involve changes to policies, procedures, systems, and training.

Element of Quality Program:

1. Periodic monitoring of studies, including monitoring of informed consent and other research activities by DSMSC members.
2. Internal audits of IECs/ CRS & DSMSC
3. Decrease the turnaround time for review of the projects
4. Continuing review application

Process: The Record of IEC (Minutes, Protocol files etc.) will be audited by the Quality Person. Findings in the summary reports and issues that are identified during the audit process will be intimated to the TRAC/ HRPP office. These findings will be intimated to the respective bodies. Corrective action will be undertaken and intimated to the TRAC/ HRPP office. Appropriate modifications to IEC procedures, improvement initiatives and additional training if needed to be introduced shall be discussed and approved by the IEC.

17. Feedback for HRPP

If any researcher, research staff have queries, concerns or suggestions regarding HRPP. They can submit their queries in the following format to the TRAC office. These queries will be analysed and forwarded to respective departments (e.g. If query or suggestion is related to EC then it will be forwarded to IEC for further action).In case of general suggestion or query discussion will be held in TRAC meeting. Necessary action if any will be implemented thereafter.

HRPP Feedback Form

To,
TRAC Office,
3rd Floor Main building,

1. Comments:_____
_____
_____

2.Suggestions:_____
_____
_____

18. Record Retention (SOP IEC)

This is described in IEC SOP 10 Maintenance of Active Project Files, Archival / Disposal of closed files and Retrieval of documents

19. Conflict of Interest Management:

19.1 Definitions / Abbreviations

1. **Actual conflict of interest:** when an individual's judgment is compromised by financial or business relationships or interests

2. **Business entity:** A business entity is that group of people organized for some profitable or charitable purpose. Business entities include organizations such as corporations, partnerships, charities, trusts, and other forms of organization.

3. **Clinical research:** Clinical research is a branch of medical science that determines the safety and effectiveness of medications, devices, diagnostic products and treatment regimens intended for human use. These may be used for prevention, treatment,

diagnosis or for relieving symptoms of a disease. Clinical Research is different than clinical practice. In clinical practice, one used established treatments while in clinical research evidence is collected to establish a treatment.

4. **Code of Ethics:** A written set of guidelines issued by an organization to its workers and management to help them conduct their actions in accordance with its primary values and ethical standards.

5. **Compensation :** something, typically money, awarded to someone in recognition of loss, suffering, or injury

6. **Compliance (in relation to trials):** Adherence to all the trial-related requirements, Good Clinical Practice (GCP) requirements, and the applicable regulatory requirements.

7. **Conflict of commitment:** Conflicts of commitment arise from situations that place competing demands on researchers' time and loyalties. At any time, a researcher might be:

    - working on one or more funded projects;
    - preparing to submit a request for a new project;
    - teaching and advising students;
    - attending professional meetings and giving lectures;
    - serving as a peer reviewer;
    - sitting on advisory boards; or
    - Working as a paid consultant, officer, or employee in a private company.

    Each of these activities requires time and makes demands on a researcher's institutional commitments. Care needs to be taken to assure that these commitments do not inappropriately interfere with one another.

8. **Conflict of interest (COI)** has been defined as "a set of conditions in which professional judgment concerning a primary interest (such as patients' welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain)".

9. **Consulting:** Consulting is providing opinion, advice, and counsel.

10. **Existing conflict of interest:** when a perceived or actual conflict of interest develops into a situation that must be managed

11. **Family member:** spouse, domestic partner, significant other, or dependent children

12. **Financial conflict of interest:** Financial conflict of interest means a Significant Financial Interest of an Investigator or researcher that could directly and significantly affect the design, conduct, or reporting of Research or adversely affects a Technology Transfer Transaction.

13. **Financial interest:** Financial interest generally refers to any pecuniary interests gained like salary or other payments for services or equity interests like stocks, stock options, intellectual property rights and the like.

14. **Hire:** effective date of an individual's employment, contractual, or business relationship with Tata Memorial Centre.

15. **Investigator:** the project director or principal investigator and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of funded research, or proposed for such funding, which may include collaborators or consultants

16. **Intellectual property rights**: Intellectual property (IP) is a legal concept which refers to creations of the mind for which exclusive rights are recognized. Under intellectual property law, owners are granted certain exclusive rights to a variety of intangible assets, such as discoveries and inventions; and words, phrases, symbols, and designs. Common types of intellectual property rights include copyright, trademarks, patents, industrial design rights and in some jurisdictions trade secrets

17. **Organizational responsibilities:** an individual's professional responsibilities on behalf of Tata Memorial Centre, which may include, but are not limited to activities such as research, research consultation, teaching, professional practice, organization committee memberships, and service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards

18. **Perceived conflict of interest:** when a reasonable person would think an individual's judgment is likely to be compromised by financial, social, or business relationships or interests

19. **Potential conflict of interest:** a situation that may develop into an actual conflict of interest

20. **Significant financial interest:**

An SFI is an external financial interest that would reasonably appear to be related to the individual's, including:

- Any equity interest, including stock options in a non-publicly-traded entity held by an individual or Members of the Immediate Family;
- Any equity interest, including stock options in a publicly-traded entity held by an individual or in the aggregate with Members of the Immediate Family, that exceeds 5% ownership interest or a current value of Rs.100000/- as determined through reference to market prices, recent financing events, or other reasonable measures of fair market value;
- Salary, consulting fees, honoraria, royalties, and other licensing proceeds received directly from a single outside entity that, when aggregated for the individual and Members of the Immediate Family, are expected to exceed Rs. 100000 in a 12-month period;
- Being the inventor of a technology on which research is continuing that has been patented, optioned, or licensed to an external entity;

- Being the author of copyrighted technology on which research is continuing that has been optioned or licensed to an external entity;
- Holding a management or operating position in any outside entity.

The term SFI does not include

- Salary or supplementary payments from TMC;
- income from seminars, lectures, or non-promotional engagements sponsored by governmental or non-profit entities;
- income from service on advisory committees or review panels for governmental or non-profit entities;

Abbreviations:

a. TMC : Tata Memorial Centre
b. COI : Conflict Of Interest

19.2 Policy

Conflicts of interest and commitment in research can adversely impact the integrity of research results and the confidence of prospective volunteers in the research enterprise. The Tata Memorial Centre seeks to identify, disclose, and avoid or manage conflicts to avoid these negative repercussions.
The mission of Tata Memorial Centre (TMC) is to promote, restore and maintain the health of all the people we serve. This is to be accomplished through excellence in patient care, education, and research. TMC is committed to

- Promote quality in clinical research
- Facilitate partnership between hospital, academia and industry
- Education and training of investigators in clinical research methodology, and good clinical research practice
- Facilitate partnerships between research networks.

The academic researchers may have entered into a variety of relationships with industry, such as sponsored research agreements, cooperative research activities, speaking on behalf of commercial enterprises ; consultancies for companies and may have a financial stake.

The opportunity for TMC personnel to receive financial or other personal rewards from such endeavors creates a potential for conflicts of interest that must be addressed to ensure that they do not threaten the integrity of the professional commitment of investigators.

19.3 Scope

This policy and the associated procedures and forms apply to all Research stake holders.

19.4 Purpose

The purpose of this policy is to support Tata Memorial Centre Research activities including grants and contracts, regardless of funding source, by enabling Tata Memorial Centre Research to avoid, identify, and manage financial conflicts of interest. This policy is also

intended to ensure the design, conduct, and reporting of research is not biased by financial conflicts of interest, and the rights and welfare of human research subjects are not adversely affected by potential or existing, perceived or actual, financial conflicts of interest.

19.5 Procedure

TMC has put in place this Conflict of Interest (CoI) Policy, which requires disclosure from investigators, research staff, and ethics committee members.

TMC has CoI form which will be submitted by

- Principal Investigator (PI): Employee who is responsible for the design, conduct, and reporting of research.

  With each new research proposal, PI will submit COI form duly filled to IEC

- Member of ethics committee (IECs)

  The member of IEC will submit COI form duly filled at beginning of their term and will update during their tenure

Investigators and administrators must declare conflict of interest in any research proposal that fulfils the above criteria and will not participate in discussions or decision regarding such research proposals in IECs in which they or Members of their Immediate Families have a financial interest.

Steps to be followed during the conduct of such a research study in the Hospital: Issues with administration of the ICF, etc. will be as suggested below.

Responsibilities of IECs

Review

In case, the PI or research staff has SFI declared, the chairperson, in convened IEC meeting, will review the COI disclosures for existing or potential conflicts of interest, and request and document additional details, including precise amount (in Rs) or percentages for ownership interests or remuneration, if such details appear necessary to determine whether there is an impermissible conflict of interest. The IEC will recommend the appropriate actions to resolve COI such as

a. Public disclosure of SFIs in abstracts, publications, presentations, press releases, and applications or proposals for research funding

b. Monitoring of research by independent reviewers or an oversight committee;

c. Selection of a non-conflicted PI or the PI may identify possible subjects for the protocol but will not participate in enrollment.

d. The PI will not be involved in subjective assessments of eligibility criteria

and intervention outcomes.

e. The PI will not administer the informed consent.

f. The informed consent document should include a disclosure of the existence of the PI's financial interest, in a form approved by the IEC

g. Disqualification from participation in all or a portion of the funded research;

h. Divestiture of SFIs;

i. Severance of relationships that create actual or potential conflicts;

j. Participation of one or more non-conflicted persons in the evaluation of research data and/or preparation of manuscripts;

k. Forward to TRAC the reasons/ grounds that may have the potential/ or may to conflict with, or appear to conflict with, commitments to the institute

19.6 Record Keeping

Tata Memorial Centre will maintain records of all disclosures and actions taken by the organization to identify, disclose, and manage financial conflicts of interest in disclosure form included in protocol.

19.7 Organizational Financial Conflicts of Interest

As an organization that conducts research involving human subjects, The TMC has an obligation to protect the rights and welfare of research participants and to ensure the integrity of the research. The TMCs' key leaders may have a financial interest in or relationship with an external entity that has the potential to conflict with these obligations. For example, the TMC or one of its key leaders may have a financial interest in a company sponsoring human subjects research being conducted by the institute or own proprietary technology that is being utilized in the research. Such financial or proprietary interests must be disclosed and managed in a way that meets the above obligations.

The purpose of this policy is to describe the process to identify, evaluate, manage, and minimize or eliminate the organization's proprietary interests, financial investments or holdings, and the personal financial interests of key organizational leaders when such interests could conflict with the organization's obligations to protect research participants, maintain the integrity of research, and ensure the credibility of the human research protection program.

Organizational Conflict of Interest is defined as "A situation in which the financial investments or holdings of an organization (including licenses, royalties, intellectual property rights, patents, certain gifts) or the personal financial interests or holdings of a key leader might affect or reasonably appear to affect organizational processes for the design, conduct, reporting, review, or oversight of human subjects research".

For purposes of HRPP policy, key organizational leader is a faculty member or administrator who has direct authority over personnel appointments, salaries, promotions,

and/or allocation of organizational resources (e.g., funding, space, assignment of graduate students or other trainees) for individuals involved in the design, conduct, reporting, review, or oversight of human subjects research.

Procedures for the Review and Management of Potential Organizational Conflicts

The organization official(s) will submit COI form duly filled to HRPP coordinator annually. The HRPP coordinator in consultation as necessary will determine if an identified organizational conflict of interest or holding is "significant as mentioned below

Project or internally-funded human subjects' research, and the key organizational leader's financial interest or holding meets the definition of "significant" under the current COI policy

a. Any financial interest in a non-publicly-traded company
b. Any financial interest in an approved start-up company that is commercializing institute approved licensed technology
c. Current or pending ownership interest (including shares, partnership stakes, or derivative interests such as stock options) in a publically-traded company of Rs. 1,000,000 or more
d. A gift of Rs. 1,000,000 or more by an individual or third-party company that may reasonably be seen as directly benefitting from a specific human subjects research project

Significant organizational conflicts will be reviewed by legal advisor of the institute and provides recommended actions to the reviewing IEC.

19.8 Conflict of Interest Form

Tata Memorial Centre
Disclosure of Conflict of Interest

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**

20.	**References**
	1. Schedule Y (Drugs and Cosmetic Act 1940) amendment 2013 2. Central Drugs Standard Control Organization (CDSCO) http://cdsco.nic.in 3. ICMR Ethical Guidelines for Biomedical research on Human Participants, ICMR (2006)