KIMS DENTAL COLLEGE & HOSPITAL
for a healthy smile
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STANDARD OPERATING

PROCEDURES

For

INSTITUTIONAL HUMAN

ETHICS COMMITTEE

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INTRODUCTION

A centre of excellence for learning, teaching, research, healthcare, and community involvement on a global scale is KIMS Dental College and Hospital. It provides both undergraduate and graduate dental surgery programmes. DR.NTR University of Health Sciences, Vijayawada-affiliated and approved by Dental Council of India.

The KIMS Dental College and Hospital strives to provide students with an education of the highest calibre while upholding high moral standards, preparing them to meet the demands of the workforce of the future. It fosters clinical and ethical dental research in areas of regional and local health issues and offers inter- and transdisciplinary high-quality innovative programmes in the broad domains of Dental Sciences and related technologies.

The understanding that affirming human rights as a fundamental entitlement to all members of society led to the need for institutional human ethics committees in medical/dental and research organisations. There are several ethical concerns involved here that must be resolved.
The Institutional Human Ethics Committee (IHEC) is crucial in assisting researchers with the moral questions raised by their research. The National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, released by the Director-General of the Indian Council of Medical Research in 2017*, served as the basis for the previously mentioned guidelines.

Do no harm was the overarching universal concept underlying the old Indian systems of medicine, in addition to other principles that were relevant to the prevailing culture and the social class structures of the time. The Policy Statement on Ethical Considerations Involved in Research on Human Subjects was published by the Indian Council of Medical Research (ICMR) in 1980. New ethical considerations arose as a result of the quick advancements in biological science and technology, necessitating further updating of these recommendations. Following that, the Ethical Guidelines for Biomedical Research on Human Subjects were published in 2000, and the updated version was then made available in 2006.

The Nuremberg Code of 1947 was the first worldwide treatise on the morality of human subjects research, and it emphasised the significance of gaining informed consent. The Declaration of Helsinki, which the World Medical Association created in 1996, contains recommendations for doing human research. The most recent revision was released in October 2013 in Fortaleza, Brazil, after seven modifications.

The three fundamental ethical principles for research involving human subjects—respect for persons, beneficence, and justice—were first stated in I979, the Belmont Report published by the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research in the United States of America (USA). The Federal Policy for the Protection of Human Subjects was published as the "Common Rule" by the Department of Health and Human Services (DHHS) of the United States in I991. (revised in 20I7). The Good Clinical Practice Guidelines (ECPG) E6 (R1) were published by the International Conference on Harmonization (ICH) in 199611 and were updated as E6 (R2) in 2016. The Council for International Organizations of Medical Sciences (CIOMS), Geneva (2002 updated in 2016), the National Bioethics Advisory Commission, USA (200I), and the Nuffield Council of Bioethics, UK (2002) 16 published recommendations/guidelines pertinent to research in developing countries. The universal codes of ethics that the member nations are required to embrace were further defined by UNESCO's Universal Declaration on Bioethics and Human Rights (2005) and other international agreements on human rights. The updated ICMR ethical guidelines highlighted the following crucial advice: Taking into account the unique sociocultural environment of our nation, our country receives 1 point under these worldwide standards.

The socio-cultural ethos of India and its disparate healthcare norms present special difficulties for the application of overarching ethical standards to biomedical and health research.
The National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017, were created in response to recent ethical developments that forced further revision of the preceding standards.

These guidelines have expanded on a few specialised areas, such as the informed consent process, biological materials, biobanking and datasets, and vulnerability, while covering some newer topics, such as public health research, social and behavioural sciences research for health, responsible conduct of research, and research during humanitarian emergencies and disasters.

Application:

These rules apply to any health-related biomedical, dental, social, and behavioural scientific research projects carried out in the facility that involve human participants, their biological materials, or their data.

Such research should aim to:

1. Advance understanding of the human condition while preserving sensitivity to the Indian cultural, social, and environmental contexts;
2. carried out in a way that ensures no person or persons become merely tools for the benefit of others and that people taking part in biomedical and/or health research or scientific experiments are treated with respect for their dignity and well-being under conditions of professionalism, fairness, and openness; and

3.subjected to a regime of evaluation at all stages of the research, such as design and execution.

STATEMENT OF GENERAL PRINCIPLES

1.0 A wide variety of scientific inquiry, including research involving human subjects, aims to produce generalizable knowledge that enhances health, deepens our understanding of disease, and is morally justifiable by its social worth. Each study carries certain inherent risks and risks to participants or communities of injury or annoyance hence, safeguarding. The study's design should take participants into consideration. Observe do no harm (non-maleficence) been the guiding idea for health care in all systems of medicine worldwide the globe. The four fundamental ethical tenets should be followed when doing scientific and health research. Specifically, fairness, beneficence, non-maleficence, and respect for

people's (autonomy) been established to safeguard the safety, wellbeing, and rights of study participants. All biomedical, social, and behavioural science research for health involving human participants, their biological material, or their data must adhere to the twelve general principles that have been enlarged from the original four fundamental ones. These 12 general principles are outlined below.

1.1 General Principles

1.1.1 The essentiality principle states that the use of human subjects for the proposed research is required after carefully weighing all alternatives in the context of the available knowledge. An Ethics Committee (EC) that is unaffiliated with the proposed research should properly review this.

1.1.2 The principle of voluntariness states that it is essential to respect a participant's right to decide whether or not to participate in research and their right to leave at any moment. The procedure for informed consent makes sure that participants' rights are protected.

1.1.3 The non-exploitation principle requires that research subjects be properly chosen, distributing the advantages and disadvantages of the study without bias or arbitrary selection. There should be adequate measures in place to protect vulnerable groups.

1.1.4 The principle of social responsibility states that research should be designed and carried out in a way that doesn't create or widen social and historical gaps or otherwise upset interpersonal peace.

1.1.5 The principle of protecting privacy and confidentiality states that in order to protect the privacy of a possible participant, access to her/his identity and information is restricted to those who have been given permission. The right to life of an individual supersedes the right to privacy of the research participant, but under some circumstances (suicidal ideation, homicidal tendency, HIV positive status, when required by law, etc.) privacy of the information can be breached in consultation with the EC for valid scientific or legal reasons.

1.1.6 The principle of risk minimization states that at every stage of the research, all parties involved (including but not limited to researchers, ECs, sponsors, and regulators) must take reasonable precautions to ensure that risks are minimised and that the proper care and compensation are provided in the event that harm occurs.

1.1.7 The professional competence principle states that the study must be designed, carried out, reviewed, and continuously supervised by individuals who are competent and possess the necessary and pertinent education, training, and/or experience.

1.1.8 The maximisation of benefit principle states that all reasonable efforts should be made to plan and carry out the research in a manner that directly or indirectly maximises the benefits to the research participants and/or to society.

1.1.9 The institutional arrangements principle states that institutions where research is being done must have policies for proper research governance and must assume responsibility for facilitating research by offering the necessary resources, including funding, people, and training opportunities.

1.1.10 The principle of openness and accountability requires that the study strategy and results be made public through registries, reports, and academic and other publications while protecting the participants' right to privacy. Participants in the research should disclose and adequately manage any conflicts of interest that

may occur. To ensure accountability, the research should be carried out in a fair, honest, objective, and open manner. Records, information, and notes related to the subject matter should be kept for the necessary time frame in case of an external audit.

1.1.11 The totality of responsibility principle, according to which each research stakeholder is solely accountable for their own acts. All stakeholders, whether directly or indirectly, are subject to the professional, social, and moral obligations in accordance with relevant laws and ethical standards.

1.1.12 The idea behind environmental protection is that it is the responsibility of the researcher to ensure that the environment and resources are protected throughout the study process in accordance with all laws and regulations currently in effect.

GENERAL ETHICAL ISSUES

2.0 Basic and general ethical norms should be followed in all research with human subjects. Protecting the rights, safety, dignity, and general well-being of the study participants is under the purview of the researcher and the team. They must be proficient in research methods and hold the necessary credentials and must be knowledgeable of, and adhere to, all applicable scientific, medical, dental, ethical, and legal the proposal's societal criteria. It is up to the ECs to make sure that the According to the aforementioned guiding principles, research is carried out.

2.1 Benefit-risk evaluation

Any positive result of the research, whether direct or indirect, that is beneficial to the individual, the community, or society is referred to as a benefit. The risk, defined as the likelihood of producing discomfort or suffering expected as physical, psychological, social, economic, or legal, should be justified by the societal and scientific value of the research.

2.1.1 In order to balance risks and provide potential benefits at the individual, societal, and/or community levels, the researcher, sponsor, and EC should make an effort to maximise benefits and reduce risks to participants.
2.1.2 Prior to authorising a research project, the EC should review the inherent benefits and dangers, assure a favourable balance of benefits and risks, assess plans for reducing risk and discomfort, and determine the merit of the research.
2.1.3 When conducting the ongoing evaluation, the EC should additionally evaluate any changed hazards in the research.
2.1.4 Table 2.1 categorises the different types of EC reviews based on the level of risk associated with the research.

2.2 Process of informed consent
The freedom of the individual to decide whether or not to engage in the research is safeguarded by informed consent. Three steps make up the process: informing potential participants about pertinent information, ensuring that they understand it, and ensuring that participation is voluntary. The language used in informed consent should be clear enough for the subject to understand and should explain any medical or dental terminology.

Table 2.1 Types of risk

Type of Risk	Definition/Description
Less than minimal risk	The likelihood of injury or discomfort is zero or not expected, according to the research. Research on unidentified or anonymous subjects, data from the public domain, meta-analysis, etc. are a few examples of this type of study.
Minimal risk	The likelihood of discomfort or harm anticipated by the research is not greater than the likelihood of such events occurring during routine tests, where it is unlikely that serious harm or an adverse event (AE) will occur, or during the course of an average, healthy person's daily activities or those of the general population. Examples include studies that involve routine history-taking or asking, observation, physical examination, chest X-rays,

	dental IOPA, and collection of bodily fluids without invasive procedures, such as hair, saliva, gingival crevicular fluid, urine samples, etc.
Minor increase over minimal risk or Low risk	Only a small amount of the Minimal risk threshold is exceeded by the increase in the likelihood of harm or discomfort. This may occur in situations like routine research on children and adolescents, research on people who are incapable of giving consent, delaying or withholding a proven intervention or standard of care in a control or placebo group during randomised trials, use of minimally invasive procedures that might only result in brief pain or tenderness, small bruises or scars, or very slight, temporary distress, like drawing a small sample of blood for testing, trying a new treatment, or trying a new treatment. Such research ought to be worthwhile for society. Indirect dangers are also associated with the use of personally identifiable information in research. This includes social dangers, psychological harm, and discomfort.
More than minimal risk or High risk	The likelihood of harm or discomfort predicted by the study is high and poses a bigger risk than is necessary. Examples include studies that use drugs, devices, or invasive techniques including lumbar punctures, liver or lung biopsies, endoscopic procedures, or intravenous sedation for diagnostic procedures.

2.2. Before enrolling participants, the informed consent document (ICD), which contains the patient/participant information sheet (PIS) and informed consent form (ICF), should have the necessary components and be evaluated and approved by the EC. The basic duty of the researcher in any biomedical or health research involving human subjects is to secure the participant's written, informed consent or that of a legally acceptable/authorized representative (LAR). The LAR's approval should be sought in cases where the subject is unable to give informed consent. A literate impartial witness should be present during the informed consent process if a participant or LAR is illiterate.

2.2.2 In some instances, such as in some clinical trials as advised by COSCO, audio/audiovisual recording of the informed consent process may be necessary.

2.2.3 After careful consideration and EC approval, verbal or oral consent, a waiver of consent, or re-consent may be acquired in specific circumstances. For additional information, see section 5.

2.3.3 **Confidentiality and privacy**

The right to privacy is the ability of a person to decide how, by whom, and with whom information may be collected, held, disclosed, or exchanged. In order to protect the participant's information, the researcher, study team, or organisation has a responsibility to maintain confidentiality. It also entails having to safeguard data against loss, theft, and unauthorised access, use, disclosure, and alteration.

2.3.I The researcher is responsible for maintaining the confidentiality of participant and community research-related data.

2.3.2 The participant must be informed of any potential restrictions to preserve strict secrecy.
Researchers must disclose to potential participants that although every attempt would be made to maintain confidentiality and protect privacy, it might not always be practicable to do so.

2.3.3 Any publication resulting from research should respect the privacy of the subjects by making sure that any images or other information that could identify a person's identity is removed aren't released. If a specific re-consent had not previously acquired, it would be needed for publication.

2.3.4 To prevent stigmatisation and/or discrimination, some information may be sensitive and should be protected. the treatment of people based on their sexual orientation, such as lesbian, gay, bisexual, and genetic data, transgender (LGBT), or any other sensitive information.

2.3.5 Coding or anonymization of personal information is important when doing research with stored biological samples or medical records/data, and access to both samples and records should be restricted.

2.3.6 With the consent of the EC, data on specific participants or communities may be disclosed in certain situations, such as when a person's or a community's life is in danger, when there is a public health risk that outweighs an individual's right to privacy, when there are serious adverse events (SAEs) that must be reported to the proper regulatory authority, etc.

2.4 Fairness in distribution

2.4.1 Efforts must be made to guarantee that those who are invited to participate in the research are chosen in a way that equally distributes the costs and rewards of the study.
2.4.2 Vulnerable people or groups shouldn't be involved in studies that only help others who are more fortunate than they are.
2.4.3 No socioeconomic, racial, or ethnic disparities should be the result of research.
2.4.4 The study should contain plans for direct or indirect benefit sharing with participants, donors of biological resources, or data donors in all forms of research, particularly if there is a chance for commercialization. The EC should reconsider the decision that was made in advance after consulting with the stakeholders.

2.5 Participant compensation

2.5.1 If appropriate, participants may receive reimbursement for costs associated with their study involvement, such as travel-related costs. Participants may also get compensation for annoyance experienced, time spent, and other incidental costs in cash, kind, or both, depending on what is thought essential (for example, loss of wages and food supplies).

2.5.2 Participants should not be required to pay for any out-of-pocket costs linked with research, such as examinations, patient work-ups, interventions, or related medical care. All participants, including those in comparison and control groups, are covered by this.

2.5.3 Participants may also be eligible for free supplementary medical care, if there are any provisions.

2.5.4 When the LAR gives consent on behalf of a participant, the EC should carefully assess the payment to ensure that it does not represent an undue inducement. Payment for travel and other incidental costs incurred as a result of the child's or ward's involvement in the study may be made available.

2.5.5 ECs must assess, authorise, and determine that there are no undue inducements in the payments (in cash or kind or both) and free services, as well as the procedures involved.

2.6 Reimbursement for damage caused by research

After a thorough assessment, research volunteers who sustain direct physical, psychological, social, legal, or economic harm as a result of their involvement are entitled to financial or other aid to fairly compensate them for any impairment or disability, whether temporary or permanent. Dependents of PM1 participants are eligible for financial support in the event of death. The research proposal should include a clause for minimising harm from the research.

2.6.1 All SAEs must be reported to the EC by the researcher to the EC within 24 hours of discovery. The reporting of SAE may be done via email or fax, even on non-working days. Within 14 days, a report detailing how the SAE linked to the research is also required.

2.6.2 The EC is in charge of evaluating the SAE's relation to the study, as reported by the researcher, and deciding how much and what kind of support should be given to the participants. periodically could be observed.

- Appropriate medical care, psychosocial support, referrals, clinical facilities, etc. should be made available to all study participants who experience damage, whether or not it is connected. If the harm is a result of the research, medical care should be provided without charge.
- Any participant who has an injury as a result of the research should be compensated. This holds true for participants in all research arms, including intervention, control, and standard of care.
- When deciding how much compensation to give injured participants, the EC should take into account a number of factors, including as the type of research (interventional, observational, etc.), the severity of the injury (temporary/permanent, short/long term), lost wages, etc.
- For other sponsored research, it is the sponsor's responsibility to include insurance coverage or a provision for potential compensation for research-related injury or harm within the budget, whether the sponsor is a pharmaceutical company, the government, an NGO, or a national or international/bilateral/multilateral donor agency/institution.

2.6.3 Depending on the level of risk and as advised by the EC, all AEs should be documented and reported to the EC in accordance with a predetermined timeline.

2.6.4 In research initiated by investigators or students, the investigator or institution where the conducts research and becomes the sponsor.

• The host institution is responsible for providing compensation and/or insurance coverage for any loss or injury resulting from research, as determined by the EC.
The organisation should develop a built-in system to be able to offer compensation, such as a corpus fund within the organisation.

• When submitting applications for national or international financing bodies,the researcher should maintain a budgetary allowance for any government or non-government organisations depending on the sort of research, for insurance coverage and/or pay dangers and the suggested participant count.

2.7 Associated care

2.7.1 If incidental conditions or findings unrelated to the research arise during a participant's involvement in the study, they may be treated for free, providing the EC determines that this does not amount to an undue incentive.

2.8 Competing interests
A conflict of interest (COi) is a set of circumstances in which a secondary interest, whether financial or not, has a tendency to improperly affect professional judgement on a primary interest, such as the welfare of participants or the validity of research (personal, academic or political). Researchers, EC members, institutions, or sponsors can all be COi. If COi is a built-in component of the research, it is critical to acknowledge this from the outset and put up the necessary controls.

2.8.1 Research institutions must create and execute policies and procedures to recognise, manage, and inform their personnel of any conflicts of interest.

2.8.2 Researchers are required to make sure that any conflicts of interest are disclosed in the documentation they submit to the EC.

2.8.3 ECs are required to assess each study in light of any reported conflicts of interest and make sure that the proper mitigation measures are taken.

2.8.4 According to the EC's standard operating procedures (SOPs), COi should be reported and controlled inside the EC.

2.9 Choosing special and vulnerable populations as research participants due to their potential lack of ability to defend their own interests, vulnerable individuals and groups may be more likely to suffer additional harm.

2.9.1 Children's legal status, clinical conditions like cognitive impairment or unconsciousness, or situational conditions like being economically or socially disadvantaged (for example, members of certain racial or religious groups, people who live in hierarchical communities, institutionalized persons, language barriers and cultural differences etc.) are all traits that make people more vulnerable.

2.9.2 In general, such volunteers should only be involved in studies when those studies directly address the needs or demands of the population in question in terms of health. On the other hand, vulnerable groups have an equal right to be involved in research so that the advantages that result from it equally benefit them. The EC and researchers alike must give this significant thought.

2.9.3 The EC should identify areas of vulnerability and make sure that new safeguards and monitoring systems are put in place. It need to provide the researcher with guidance in this area.

2.10 Participation in community

A community is any size social group of individuals who share similar characteristics, such as age, gender, occupation, lifestyle, disease, and geographic location. Before, during, and after the research, the community should be actively included in order to reduce culturally sensitive issues and provide more sensitivity to their health needs and requirements.

2.10.1 The public can participate in a variety of ways and offer insightful ideas. The level of community involvement should be determined by the kind of research being done.

2.10.2 The community (from which participants are to be selected), the researchers, and the relevant EC can all communicate with one another through the Community Advisory Board/Group (CAB/CAG).
Members of the CAB should be such that they respect the rights of the group and do not compel community members to engage in the study while also protecting those rights.

2.10.3 Community members may participate in the EC as regular members or special invitees.

2.10.4 Participation in the community does not supplant freely given consent. It guarantees that research that is conceived and carried out in the best interests of science and the community takes into account the requirements and expectations of the community with regard to health, that informed consent is appropriate, and that access to research benefits is made available.

2.10.5 In order to aid in the dissemination of the findings to the broader community, the researcher may get in touch with the community representative, local institution, or government department where the data was collected after the study is finished.

2.11 Post-research benefit sharing and access

Every time it makes sense, the advantages of research should be made available to individuals, groups, and populations. Improvements in living conditions, the establishment of counselling centres, clinics, or schools, and the dissemination of information on good health habits may sometimes have indirect benefits for the community that outweigh those to the individual participant.

2.11.1 Whenever possible, efforts should be made to inform people/communities of the research study's findings.

2.11.2 Where appropriate, the research team should create arrangements for participants, including those in the control group, to have access to research results after completion of the study and to benefit from educational or interventional benefits.

2.11.3 Post-research access plans or other forms of care must be specified in the study protocol so that the ethics committee can take them into account while reviewing the protocol.

2.11.4 Appropriate regulatory approvals must be in place before administering an experimental medicine to a participant after the trial.

2.11.5 The EC must consider the necessity of an upfront agreement between sponsors and researchers with relation to all of the aforementioned concerns (from 2.11.1 to 2.11.3).

2.11.6 Although it may not be practical to provide post-study advantages to participants in studies with a small scope, such as student projects, the institution should make an effort to improve participant support and care.

RESPONSIBLE CONDUCT OF RESEARCH

3.0 Research's worth and advantages depend on how honest the researchers are. The prevention of research misconduct and the exploitation of research results is a major social duty for scientists. The standards set by their professions, specialties, and institutions, as well as the applicable laws, are observed by responsible researchers. High standards and adherence to the core principles of research are expected of each member of a research team. The following are the key elements of responsible conduct of research (RCR): values, policies, planning, conducting, evaluating, reporting, and responsible authorship and publication.

Institutions undertaking research must establish a research office inside their institution to facilitate research, manage funds, and oversee all elements of RCR. The research office must work closely with the EC and with other stakeholders, including undergraduate and postgraduate students. All of the primary RCR components, which are mentioned in the following sections, should have SOPs in place to address them.

3.1 Research's values

The regulations pertaining to RCR should be consistent with the common principles that underpin RCR, including honesty, accuracy, efficiency, fairness, objectivity, reliability, responsibility, transparency, personal integrity, and knowledge of current best practices.

3.1.1 The scientist as an accountable citizen

Improving our knowledge of many health-related issues and their remedies requires scientific research. Cooperation and common expectations as pai1 of inter-professional ethics are prerequisites for all study components. Scientific research unethical behaviour can undermine public confidence in science and harm the study team. Meaningful research is endangered by a lack of trust among research teams, in the public, or between scientists and the public. The resources utilised in biomedical research are limited and should be handled carefully, therefore researchers should be conscious of this. They should look for ways to translate research findings into improvements in public health wherever they can.

3.1.2 Current challenges with ethics in scientific and health research

New ethical dilemmas arise as a result of developing new study fields. The utilisation of poor and vulnerable populations as research participants, post-trial access to research benefits for participants and their communities, research on developing technologies, etc. are some of the modern topics that have lately come up for discussion. To stay current on issues, academics must pursue continuing education.

3.1.3 Sensitivity to the effects of biomedical and health research on society and culture analyzing how the health industry and general public interact with the outcomes of biomedical and health research is necessary to comprehend the social and cultural influence of research. This must be kept in mind by researchers while designing, carrying out, and analysing their studies because doing so will increase advocacy on the part of the public, private, and political sectors and promote public accountability.

3.1.4 Coaching

One of the main ways for one generation of scientists to impart their understanding, ideals, and values to succeeding generations is through mentoring. Researchers can learn from mentors in ways that go beyond

what can be learned from reading textbooks because of their experience. Trainees should be able to develop into responsible researchers thanks to their contact with mentors. Mentors should watch out for their mentees' integrity in research, avoid interfering with other researchers' work, and use resources wisely. A good mentor will be knowledgeable, teach by example, and recognise that each trainee has a different set of skills. She or he should set aside enough time and be ready to discuss, argue, and competently mentor trainees. A mentor should support the trainees' ability to make decisions, and the learner should take an active role in communicating his/her needs.

3.2 Guidelines

3.2.1 The safety of human participants

Institutions must set up rules and safeguards to safeguard human research participants. Such regulations should establish obligations on the institution, the EC, and the researchers. Additionally, protocols and procedures for monitoring research should be in place. the collection and management of data, conflicts of interest, and the disclosure of scientific misconduct, providing suitable initial and ongoing training for researchers and EC participants. Regulations can made accessible on the institutions' or organisations' websites. Academics should also adhere to their separate codes of behaviour.

3.2.2 Animal Experimentation

Animal experimenters are required to abide by all current laws and regulations, such as the Prevention of Cruelty to Animals Act, 1960, as amended in 1982, the Breeding and Experimentation Rules, 1998, as amended in 2001 and 2006, the Guidelines for Care and Use of Animals in Scientific Research (Indian National Science Academy, 1982, as amended in 2000), the ICMR Guidelines on Humane Care and Use of Laboratory Animals, 2006, and the Committee for the Purpose of Control and supervision of Experiments of Animals (CPSCSEA) Guidelines for Laboratory Animal Facilities, 200318 and Guidelines for Rehabilitation of Animals used in Research, 2010.

3.3 Research design and execution - Particular Concerns

3.3.1 Problems with conflicts of interest (COI)

The term "COI" refers to a set of circumstances in which a secondary interest is believed to have an undue influence on professional judgement involving a main interest, such as the wellbeing of participants or the validity of research. The secondary interest may be personal, scholarly, political, financial, or non-financial. Although this is not intrinsically bad, COI may affect the selection of research questions and methodologies, participant recruitment and retention, data interpretation and publication, and study ethics review. The development and implementation of rules and procedures to recognise, reduce, and manage such COI, whether at the level of the researcher, the ethics committee or at the level of institution. Research institutions, researchers and research ECs must follow the steps given in Box 3.1.

Box 3.1 IDENTIFYING AND MANAGING COI

The following list outlines the general duties of persons engaged in COI research:

1. Research institutions must:
    - create dynamic, transparent, and actively communicated policies and SOPs to address COI

issues;
• put these policies and procedures into practise;
• educate their staff about these policies;
• monitor the research or check the research results for objectivity; and
• refrain from interfering with the EC's operation or decision-making.

2. Scholars should:
• guard against commitment conflicts that may arise from circumstances that place competing demands on researchers' time and allegiances;
• guard against conflicts of interest (COI) that may arise from financial or nonfinancial interests that may affect their research; and
• prevent intellectual and personal conflicts by making sure they do not serve as reviewers for grants and publications submitted by close colleagues, relatives, and/or students.

3. ECs must:
• evaluate each study in light of any disclosed COI and ensure that appropriate measures are taken to mitigate this;
• require their members to disclose their own COI and take the necessary steps to recuse themselves from reviewing or making decisions on protocols related to their COI; and
• make the proper management recommendations if COI is discovered at the institutional or researcher level.

3.3.2 Data collection, management, ownership, and sharing

• There is no one optimum method for gathering data. For different sorts of research, different collection methods are required. When collecting data, researchers should follow best practises and show consideration for the participants.

• Data collection is the process of physically recording data on permanent media, such as hard copy, soft copy, or electronic copy. The physical formats used to store data might range greatly, from measurements or observations to photos or audio recordings of interviews. Research data must be accurately recorded in order to be useful.

• Institutions receiving research funding are accountable for managing budgets, complying with regulations, and managing data gathered for funded research. This means that if researchers transfer to another university, they must get the necessary permissions/approvals in order to take their funds and data with them.

• Prior to data collection, ownership concerns and obligations must be carefully sorted out, and researchers must guarantee that there is no confusion over data ownership, publication rights, and obligations after data collection. The institution's and/or the EC's MoUs should be in place.

• In the case of biological samples, participants (donors) retain ownership of the sample. Unless the latter is necessary for outcome measurement and is specifically stated as such in the first informed consent statement, she/he may withdraw both the biological sample and the associated data.

The data/samples are the property of the institutions hosting/conducting the research, and the research must be carried out using appropriate and reliable techniques to provide reliable data.
The integrity of study data is compromised by the use of improper methodologies, which is why it should be avoided.

• Careful consideration of every detail is necessary for thorough study. It is necessary to create appropriate methods and to accurately record, interpret, and publish the results. Poorly designed research should not be implemented because it wastes resources. In some circumstances, consent is required before data gathering. It is the responsibility of researchers to understand when permission is required in order to gather or use particular data for their studies.
Box 3.2 contains more information.

Box 3.2 Without first obtaining permission, the following categories of research cannot have data collected:
1.Human subjects and lab animals used in research;
2. Information published on some websites;
3. Dangerous substances and biological agents;
4. Storage and future testing of biological samples;
5. Information from some libraries, databases, and archives;
6. Publicly available images and other information; and
7. Other copyrighted or patented processes or materials.

Once acquired, data must be adequately preserved and stored since they may be required later to corroborate research findings, establish priority, or be re-analyzed by other researchers. The first step in responsible data handling is proper data storage and security against unauthorised access, loss, or theft. It is important to take precautions to lessen the chance of fire, flood, and other catastrophes.

Computer files ought to be backed up, and the backup data should be kept in a safe location at a distinct location from the original data storage site.

• Research data should be shared because it is essential and necessary, but choosing when and with whom to share may present challenging issues. All the material related to an experiment, including the final data, should typically be openly accessible for other researchers to review and utilise once the results of the experiment have been published. If necessary, data should be shared or made available to the public in a de-identified or anonymous form; otherwise, the appropriate permissions or re-consent should be requested.

3.4 Analyzing and summarising research

A key element of ethical and responsible research is the public's confidence in published findings.

3.4.1 The fundamental tenet of all reviewers and editors is that the work has been carried out honestly, that its reporting is open and truthful, and that the researchers' integrity is unquestionable.

3.4.2 Transparency includes the researcher as well as the research site (s). This would necessitate the publication of the research's location, its cooperating sites/institutions, and its authors.

3.4.3 No matter the outcome of the research, it must be publicised since it would be unethical to subject another group of volunteers, patients, or participants to the same risks in order to acquire the same outcomes.

3.4.4 Researchers should post study findings in the Clinical Trial Registry-public India's database (CTRI).

3.5 **Responsible authorship and publication**

3.51. Authorship

Box 3.3 Criteria for authorship

The following 4 criteria should be used to determine authorship, according to the ICMJE: 1.contributions of a significant kind to the idea or design of the work, or to the collection, analysis, or interpretation of data for the work; AND 2.writing the piece or critically editing it for significant intellectual value; AND 3.final approval of the published version; AND 4.Consent to take responsibility for all aspects of the work in order to guarantee that any concerns about the accuracy or integrity of any portion of the work are duly investigated and addressed.

An author should be able to specify which co-authors are accountable for particular other elements of the work in addition to being accountable for the portions of the work that they have done. Additionally, authors should have faith in the honesty of their co-authors' contributions.
All persons recognised as writers should satisfy all four authorship requirements, and those individuals who do should be acknowledged as such. Those who don't fit all four requirements ought to be recognised; see Section II.A.3 below. These authorship requirements are meant to reserve authorship for people who merit it and are capable of taking ownership of the work. The requirements are not meant to be applied as a means of barring coworkers from authorship.

The criteria should not be used to deprive colleagues who otherwise meet the requirements for authorship the chance to satisfy criteria #2 or #3, disqualifying them from authorship. The review, preparation, and final approval of the manuscript should therefore be open to everyone who fulfils the first requirement.

3.5.2 Peer review

The sole person who assumes main responsibility for communication with the journal during the manuscript submission, peer-review, and publication processes is the corresponding author. Although these responsibilities may be delegated to one or more co-authors, the corresponding author typically makes sure that all the journal's administrative requirements, such as providing details of authorship, ethics committee approval, clinical trial registration documentation, and disclosures of relationships and activities, are properly completed and reported. The corresponding author should be available to respond promptly to editorial questions throughout the submission and peer-review processes. The corresponding author should also be accessible following publication to address any criticisms of the work and assist with any requests from the journal for data or additional information, should those requests come up.

The ICMJE advises editors to provide copies of all correspondence to all listed authors, even though the corresponding author is primarily responsible for communication with the journal. It is best for a large

multi-author group to decide who will be an author before the work begins and to confirm that person before submitting the book for publication. All group members who are listed as authors must satisfy all four requirements for authorship, including approval of the final manuscript, be able to publicly accept responsibility for their contributions, and have complete faith in the veracity and integrity of the work of their fellow group members. They will also be required to fill out disclosure papers on their own.

Peer review is the process through which professionals who are often not on the editorial staff evaluate manuscripts that have been submitted to journals. Peer review is a crucial addition to the scientific method since objective, independent criticism is a fundamental component of any scholarly work, including scientific inquiry.

Peer review's true worth is hotly contested, although it does help ensure that an article receives a fair hearing from the scientific community. Practically speaking, it aids editors in selecting the papers that are appropriate for their publications. Peer review frequently assists writers and editors in raising the calibre of reporting.

The journal is in charge of making sure that processes are in place for choosing qualified reviewers. The editor must make sure that reviewers have access to all information that might be important for evaluating the manuscript, including any supplemental materials intended for publication online only, and that reviewer comments are appropriately evaluated and interpreted in light of their disclosed affiliations and activities. A peer-reviewed journal is not required to send submitted manuscripts for consideration or to abide by positive or unfavourable reviewer recommendations. A journal's editor is ultimately in charge of choosing all of its articles, and editorial choices may be influenced by factors unrelated to a manuscript's quality.
Any time before publication, including after approval if doubts are raised about the objectivity of the work, an editor has the right to reject any article. Journals should recognise the value of peer reviewers and inform reviewers of their journal's final decision to approve or reject a paper. Editors are urged to share reviewers' feedback with other reviewers of the same paper so that everyone involved in the review process can benefit.
Editors are invited to assess research protocols, statistical analysis plans (if distinct from the protocol), and/or contracts related to project-specific investigations as part of peer review. Before approving such research for publication, editors should advise authors to make such documents publicly accessible at the time of or after publication.
These papers may need to be publicly posted in order for your submission to be accepted by some journals.

Each journal should decide on and publicise its unique standards for data analysis and publishing in a location that is accessible to prospective contributors.
Some individuals think that a paper's publication marks the start of the real scientific peer review process. In that regard, medical journals ought to provide a way for readers to submit comments, inquiries, or criticisms about articles that have already been published. Authors should take this idea to heart and comply with any requests from the journal for data or additional information that might come up after the article has already been published

ICMJE is of the opinion that researchers have a responsibility to keep the primary data and analytical techniques supporting the published results for at least ten years. To ensure these data are available for a longer period of time, the ICMJE supports their storage in a data repository.

3.6 Policies for managing misbehaviour in research

Data fabrication, falsification, and plagiarism are important challenges on a national and international level and constitute research misconduct. Box 3.4 contains more information.

3.6.1 Institutions should create policies to deal with misbehaviour in science and research.

3.6.2 Research misconduct must be looked into if it is believed to exist. If facts are not presented honestly, the lives of current or future participants may be in danger, hence an institution must look into any complaints of misbehaviour. Such investigations must be carried out promptly, fairly, and transparently, and the findings must be made public.

3.6.3 Establishing institutional protections for the researcher accused of research misconduct as well as the whistle blower is crucial. Until the investigation is over, this material must be kept private.

Box 3.4 Types of research misconduct

Misconduct in research includes the following:
Fabricating data or findings with the goal to record or report them is known as fabrication.

Falsification is the modifying, omitting, or suppressing of data or results without a valid reason based on science or statistics, resulting in an inaccurate representation of the research in the research record.

• Plagiarism is the "wrongful appropriation" and "theft and publication" of another paper or another author's "language, thoughts, ideas, or phrases," and the presenting of them as one's own original work.

The college utilises the online programme "Urkund" (To verify a student's research paper for plagiarism, go to https://secure.urkund.com/account/account/ereate.) Students can upload their research papers to check the degree of content similarity with outside sources by logging in with their username and password.

3.6.4 It is not permissible to submit the same grant proposal to multiple funding agencies at the same time, nor is it appropriate to submit papers or publications to journals simultaneously, as this could result in needless repetition during the review process or in meta-analysis.

3.7 Enrollment in the Indian Clinical Trials Registry

On July 20, 2007, the ICMR introduced the Clinical Trials Registry-India, a free and online public record system for registering clinical trials, PG theses, and other biomedical research being carried out in the nation. It is linked to the WHO registry. On June 15, 2009, COSCO mandated that all clinical trials registered under the Drugs and Cosmetics Act and its Rules must be registered in the CTRI. It is optional for other biological and health studies to register with CTRI. In addition, editors of India's top biomedical journals announced that only studies from any public database will be taken into consideration for journal publishing. The Declaration of Helsinki clearly specifies that "Every research study involving human beings must be registered in a publicly accessible database before recruitment of the first subject," according to the 64th WMA General Assembly,

held in Fortaleza, Brazil, in October 2013. In May 2017, the ICMR and other parties signed a joint statement on the public sharing of findings from all international trials under the auspices of WHO.

3.7.1 All clinical research involving human subjects, including any intervention (drugs, surgeries, devices), biomedical, educational, or behavioural research, public health intervention studies, observational studies, implementation research, preclinical studies of experimental therapeutics and preventives, or AYUSH studies, may be prospectively registered with the CTRI.

3.7.2 When registering a trial, information about the investigators, sites, sponsors, ethics committees, regulatory approvals, diseases and conditions, research kinds, procedures, results, etc. must be provided.

3.7.3 By registering research in CTR!, one can guarantee that more thorough, trustworthy, and easily accessible facts about research are made available to the public. Transparency, accountability, and accessibility are all enhanced by this.

3.8 Group research

Researchers are working more frequently with peers who have the knowledge and/or resources necessary to complete a certain project. This could involve governmental, commercial, or interdepartmental research centres and organisations as well as interinstitutional, international, and multicenter collaborations. The main moral concerns with collaborations have to do with sharing methods, material and data ownership, IPRs, collaborative publications, managing research findings, controlling COi, and commercialising research results. Researchers should become familiar with all local, national, and international requirements for research collaboration, including required approvals, memorandums of understanding (MoUs), and material transfer agreements (MTAs), as well as European Commission (EC) approval of collaborating institutes.

3.8.1 Considerations for ethical collaboration in research

Studies conducted in collaboration should consider the values/benefits anticipated from the research in comparison to the dangers concerning the individuals/population being examined.

• In terms of sample and data ownership, analysis, dissemination, publication, and IPR if necessary, the participating centres shall work as partners with the collaborator(s) and sponsor(s). At the bilateral and multilateral levels, knowledge and skills must be freely exchanged.

• Protecting the participants' dignity, rights, safety, and well-being should be carefully considered in situations where the social circumstances of the planned research can make it more likely that they would be exploited or put them at risk of harm.

• The kind, scope, and likelihood of any harm that could reasonably be expected to come from involvement. In a collaborative research programme, the research protocol should be clear and detailed.

• Participants chosen by all parties should get the same advantages and burdens.

• If there is an exchange of biological material between collaborating sites, the EC may require an appropriate MoU and/or MT A to safeguard the interests of participants and ensure compliance while addressing issues related to confidentiality, data sharing, joint publications, benefit sharing, etc.

All participants in collaborative research should have access to the best nationally available standard of care.

3.8.2 Responsibilities of institutions, researchers, and ethics committees

Collaborative research should be reviewed, conducted, and monitored, and stakeholders need to be informed of the needs of various regulatory and funding bodies.

• A communication channel between the ECs of the many participating centres should be established. • An EC should assess the protocols in the local social and cultural context and ensure respect for the sensibilities and values of participants and communities at collaborating sites. In the event of a dispute, the local EC's judgement based on pertinent facts, regulations, and local law shall take precedence.

• An EC should determine if the researcher possesses the necessary skills and education for teamwork.

• An EC should ensure that the collaborating researcher(s) are not considered as merely sample or data collectors and should safeguard their interests and rights.

• When creating the study proposal, participating researchers from partnering sites should be fairly represented.

• To protect the interests of participants, researchers, and institutions, institutions are responsible for negotiating fair contracts in collaborative research partnerships (including benefit sharing and avoiding unlawful use of their knowledge, biological samples, and data).

• In order to develop capability and engage in research that is mutually beneficial, institutions should offer possibilities for collaboration.

3.8.3 Worldwide cooperation

In recent years, the extent of international cooperation in scientific and health research has grown to the point that it may have exploitative human and business implications. While working together in medical research on the one hand, it could give the impression that a country is experimenting on the people of a poorer country while on the other it could be perceived as a humanistic interest in the health of civil society. An ethical framework based on equality and equity is needed to direct these collaborations due to the varied levels of development in terms of infrastructure, knowledge, social and cultural perspectives, laws relating to IPR, ethical review procedures, etc. The same holds true for research projects supported by or involving cooperation from international organisations (public or private). The partnership could entail carrying out several study components at once or just one, such laboratory testing. The applicable legislative regulations and our nation's ethical standards should be met in order to conduct collaborative research in India.

• In terms of ownership of samples and data, analysis, dissemination, and publishing, Indian participating centres shall act as partners with the collaborator(s) and sponsor(s). & IPR associated with research conducted in India, as deemed suitable.

• Effective communication should exist between international participating centres and In the event of a dispute, the EC of the Indian participating center(s) will decide. The pertinent facts, rules, and laws of the land shall apply.

• The institution ought to provide protection against the imposition of the moral or ethical sponsoring nation (ethical imperialism), who may not share India's ethical and legal specifications.

• Researchers and EC members should be trained to comprehend and recognise ethical viewpoints that reflect India's best interests.

• The institution/EC should not accept international proposals which cannot be conducted in the place of origin. International partnership types are listed in Box 3.5.

Box 3.5 Types of international collaboration

1.All or any of the following elements can be a part of an international collaboration:
2.Funding from international organisations like the World Bank, NIH, WHO, Wellcome Trust, and others; academic partnerships with foreign institutions, universities, organisations, and foundations with or without outside funding; and
3.Official government agreements between Indian research organizations/institutions and organizations/institutions of other nations with comparable missions.

• Before beginning, the Health Ministry's Screening Committee (HMSC) should receive all biomedical and health research proposals including international assistance and/or partnership. The ICMR Headquarters in New Delhi is home to the HMSC secretariat. All research requiring international collaboration, whether technical, financial, laboratory, or data management, must be reported to HMSC in accordance with HMSC's guidelines.

• The exchange of information envisioned as part of a proposal for joint research must go through the proper channels. International cooperation are subject to appropriate considerations of universal ethical principles, while ethical evaluation and permissions are subject to the national regulatory framework. When compared to other nations and organisations, the finer details advised in the Indian context could be different due to socio-cultural conventions and local needs.

• The current Government of India (GOI) regulations for the transfer of human biological materials will apply to the export of all biological materials. The EC may, on a case-by-case basis, consider research proposals involving the transfer of biological material.

The Environmental Protection Act of 198620, the Biological Diversity Act of 200221 of the Ministry of Environment and Forests, the Drugs and Cosmetics Act of 1940 and Rules of 1945, and the pertinent revisions all require that collaborators get the necessary regulatory clearances. It may not be necessary to obtain approval for this type of material exchange between WHO Collaborating Centers and Reference Centers for specific reasons, individual cases of therapeutic intervention, or diagnostic purposes.

• Any research involving the exchange of biological material or specimens with partnering institutions requires that the Indian participating center(s) have the necessary regulatory permission and registration.

Institutions outside of India must agree to an MTA that justifies the scope and amount of the while a sample is being gathered, concerns about data sharing, confidentiality, and joint publication guidelines, benefit sharing and IPR, and post-analysis management of biological waste standards for safety, etc.

• Research in India and the sponsor nation should respect the rules, laws, and cultural sensitivities of all nations taking part in collaborative research initiatives. To protect shared interests and guarantee compliance, a suitable MoU should be in place.

ETHICAL REVIEW PROCEDURES

4.0 To protect the dignity, rights, safety, and general wellbeing of all research participants, it is essential that all research proposals on biomedical, social, and behavioural science research for health involving human participants, their biological material, and data be reviewed and approved by an appropriately constituted EC. Prior to the start of research projects, ECs are tasked with reviewing the applications. They also have a continuous duty to periodically check on approved projects to make sure ethical standards are being met. The EC should operate competently and independently.

4.0.1 Establishing an EC to ensure a suitable and long-lasting system for high-quality ethical review and monitoring is the institution's responsibility

4.0.2 The institution is accountable for providing logistical support, including infrastructure. providing the Member Secretary with the necessary personnel, resources, support, and time off to carry out EC duties

4.0.3 The EC is in charge of evaluating research proposals on a scientific and ethical level. ECs may use a preceding scientific review's evidence as proof, but they must also conclude that the use of technically sound research techniques and an examination of the moral implications of selection of a study plan or approach.

4.0.4 An EC must approve all biomedical and health research projects before they are carried out, regardless of whether they fall within the categories of clinical, basic science, policy, implementation, epidemiological, behavioural, or public health research.

4.1 The ECs' Terms of Reference

4.1.1 The institution's EC SOPs should clearly state the EC's mandate and that of its members (Annex 1 for the List of SOPs).

4.1.2 Each EC ought to have established SOPs outlining how the committee ought to operate. The EC can use CDSCO recommendations for drug and device trials that fall under the purview of the licencing body as well as ICMR standards for creating the SOPs for all biomedical and health research. Periodically updating the SOPs is necessary to reflect evolving requirements. Each member should have access to the most recent version of the SOPs and get training on them.

4.1.3 It is important to specify the EC's scope, term, and renewal policy.

4.1.4 EC members should not have a history of misbehaviour.

4.1.5 The EC must be registered with the appropriate regulatory bodies. For instance, ECs that approve clinical studies that fall within the purview of the Drugs and Cosmetics Act must be registered with COSCO.

4.2 Unique circumstances

4.2.1 Institutions may have a single EC or multiple ECs. For the purpose of reviewing numerous research ideas, the ECs can be multiplied. Each EC has the ability to operate independently and must adhere to the SOPs and TO Rs of that institution.

4.2.2 An institution (user institution) without its own EC may make use of the EC of another institution (host institution), particularly in the neighbouring or surrounding area.

Before they do, pertinent requirements must be satisfied. For more information, see Box 4.1.

Box 4.1 Utilizing the services of an EC of other Institution

Institutions that use the services of an EC from another institution must comply with the following requirements:

- The two institutions (host and user) should enter into an MoU for using the EC of the host institution's services, or the user institution should provide a "No Objection Certificate" and agree to be supervised by the EC of the host institution.

- For ongoing project assessment, including site inspections, the EC of the host institution shall have access to

all research records, including the source papers and research participants.

• The host institution's EC can conduct site monitoring and will be in charge of all duties associated with conducting an ethical evaluation of projects submitted by the user institutions.

4.2.3 For the purpose of primary review, all participating sites in multicentric biomedical and health research may choose to use the services of one common EC from a participating site designated as the main EC. This EC must be registered with the appropriate government and be located in India. However, the local EC may carry out the site-specific requirements, such as the informed consent procedure, research implementation and its monitoring, etc. Between the researchers and the EC secretariats of the participating locations, this would necessitate effective coordination and communication. The COSCO regulations must be followed for clinical trials covered by the Drugs and Cosmetics Act. For additional information, see section 4.10.

4.2.4 In accordance with the National Guidelines for Stem Cell Research, stem cell proposals must be examined and approved by the institutional committee for stem cell research (IC-SCR) before being presented to the EC for consideration (2017).

4.2.5 Researchers without institutional ties can use Independent ECs (Ind EC), which operate outside of institutions. The following prerequisites must be fulfilled in order for these committees to function:

• It should operate in accordance with SOPs that adhere to the national criteria for operating ECs.

• The Ind EC must be established as a registered legal entity, overseen by individuals who are not members of the proposed EC and who will oversee and monitor its working.

• Unless an MoU is in place, it shouldn't accept research requests from researchers connected to organisations with their own ECs.

• Its obligations and rights in relation to the projects that are presented to it shall be defined.

• It ought to have access to every piece of research documentation, including the participants' records and the original sources.

• It should familiarise oneself with local socio-cultural norms that may help to assure protection of rights and well-being of study participants.

• It should familiarise oneself with local socio-cultural norms that may help to assure the protection of rights and well-being of study participants.

• It should conduct ongoing reviews of the executed project, including site visits.

4.2.6 Subcommittees like the SAE subcommittee or the expedited review committee may exist within institutions. These should be a part of the main committee and consist of the chairperson, member secretary, and one to two main EC members who have been designated in a suitable manner in accordance with the SOPs. The concerned main EC may receive reports from these subcommittees.

4.2.7 Institutions may set up a separate committee for SAE, with one or two EC members present to ensure the continuity of EC work, and the main EC should examine the committee's report.

4.3 An EC's composition

4.3.1 ECs must span across disciplines and industries.

4.3.2 Both age and gender should be well represented.

4.3.3 At least half of the members should be outside the institution or unaffiliated.

4.3.4 An EC should ideally have between seven and fifteen members, and in order to achieve the quorum requirements, there must be at least five members present.

4.3.5 Depending on the requirements of the institution, the EC should have a balance of medical and non-medical members as well as technical and non-technical members.

Table 4.1 lists the membership, affiliations, credentials, and member-specific functions and duties.

Table 4.1 Composition, affiliations, qualifications, member specific roles and responsibilities of an EC

S.NO.	Members of EC	Definition/Description
	Vice Chairperson/Chairperson (optional) Non-affiliated Qualifications: A reputable individual from any background who has past experience serving in or currently serving in an EC	· Organize EC meetings and be responsible for the independent and effective operation of the committee. • Ensure that all members actively participate in all debates and deliberations, including unaffiliated, non-medical, and non-technical members. • Approve the minutes from earlier meetings. • The Chairperson shall propose a committee member as Acting Chairperson in the event that both the Chairperson and Vice Chairperson are expected to miss a scheduled meeting, or the members in attendance may elect an Acting Chairperson on the day of the meeting. The meeting's acting chairperson, who will have all the chair's privileges, should be an independent party. • Request members' COI declarations, guarantee a quorum, and promote impartial decision-making. • Deal with grievances against researchers, EC members, conflicts of interest, and requests to access EC data, among other things.
	Member Secretary/ Alternate Member Secretary (optional) Affiliated	• Plan EC meetings, create the agenda and minutes; • Organize EC documentation, communication, and archiving; • Create an effective and efficient process for receiving, preparing, circulating, and preserving each proposal for evaluation.
	Qualifications- should be a member of the institution's staff, possess understanding of clinical research and ethics, be driven and outgoing, and be able to spend enough time to this activity that should be	Ensure that the EC secretariat and EC members are trained; Ensure that SOPs are updated as needed; Ensure that EC operation complies with the SOPs; and prepare for and respond to audits and inspections. Make sure all paperwork is complete when it is received

	safeguarded by the institution.	and that it is added on the agenda for the EC review in a timely manner. -Determine if an accelerated review, exemption from review, or full review is necessary. -Examine if a prior scientific review is necessary; invite an impartial consultant, patients, or community representatives. -Make sure there is a quorum present during the meeting, and note discussions and conclusions.
	Basic medical researcher (s) Affliated/non-affliated Qualifications: A non-physician or physician who is qualified in the fundamental medical sciences -The basic medical scientist should preferably be a pharmacologist in cases where the EC is assessing clinical trials involving pharmaceuticals.	-Review of the science and ethics with a focus on the intervention and benefits -risk assessment, study technique, data, ongoing review process, SAE, protocol deviation, progress and completion report -Pharmacologists should assess the drug safety and pharmacodynamics for clinical studies.
	Clinician(s) Affiliatated/non-affiliated Should possess recognised medical training, expertise, and qualifications, according to qualifications	-Scientific assessment of protocols, which includes an examination of the intervention, benefit-risk analysis, research design, methodology, sample size, location of the study, and statistics. -Continuous evaluation of the protocol (SAE, protocol deviation or violation, progress and completion report) -Examine the provision for medical care, the facility and the lead investigator's suitability, management, and compensation. -Extensive evaluation of the protocol, the investigators brochure (if applicable), and all other supplied documentation pertaining to the procedure.

	Legal specialist Affiliated/non-affiliated A minimum law degree from an accredited institution is required, along with experience. Training in medical law is desirable.	-Ethical review of the proposal, translations of the ICD, a Memorandum of Understanding (MoU), a Clinical Trial Agreement (CTA), regulatory approval, insurance documentation, additional site approvals, researcher commitments, protocol-specific other permissions, such as stem cell committee approval for stem cell research, HMSC approval for international collaboration, compliance with guidelines, etc. -Interpret new regulations and update EC members as necessary.
	-sociologist, philosopher, ethicist, and theologian Affiliated/non-affiliated Qualifications: The applicant should possess social/behavioral science, philosophy, or religion training or competence, as well as	-Ethical evaluation of the translations, ICD, and proposal. - Evaluate the effect on participation in the community, the socio-cultural framework, and any religious or philosophical context.

	sensitivity to local culture and moral norms. Possibly from an NGO engaged in health-related endeavours.	-Act as a patient, participant, community, or representative of society's concerns by bringing up moral and societal issues.
	A layperson (s) Non-affiliated requirements: - Literate member of the public or community - Has not pursued a career in medicine or a health-related field in the previous five years. • Could be a member of the community where the participants will be chosen. • Has knowledge of the community's moral standards, language, and culture • Participating in social and community welfare initiatives is desirable.	-Ethical assessment of the proposal, translation, and ICD (s). -Determine whether the risks and rewards are balanced from the standpoint of the participants. -Act as an advocate for the patient, participant, or community, bringing up moral and societal issues. -Check for any societal implications.

4.3.6 The quorum should be as specified in box 4.2

Box 4.2 Quorum requirements for EC Meetings

1. There must be a minimum of five participants in the meeting.
2. Both medical, dental, non-medical/non-dental, technical, and non-technical members must be present for the meeting to be quorate*
3. There should be at least one non-affiliated member in the quorum.
4. The layperson should ideally make up the quorum.
5. The present COSCO rules should be followed when determining the quorum for assessing regulatory clinical trials.
6. Quorum requirements must be met for any decision to be valid.

*Medical/Dental members are practitioners with the necessary medical credentials. Technical members are people who have credentials in a certain field in which the research is being done, like the social sciences.

4.3.7 The institution's head should serve as an appellate authority to choose the committee and resolve conflicts rather than being a member of the EC to maintain independence.

4.3.8 The chair and member secretary may serve in separate capacities on the ethics committee. In addition to acting as chairperson or member secretary, they could fulfil a position based on their qualifications (such as that of a clinician, legal expert, basic scientist, layperson, etc.).

4.3.9 The EC may also have a group of substitute members with the ability to make decisions in order to maintain a quorum. These members can attend meetings in the absence of regular members and have the same TORs as regular members.

4.3.10 The EC may keep a roster of subject matter experts who are called upon as needed; for example, a paediatrician for research involving children, a cardiologist for research involving heart conditions, etc. They might be asked to the meeting to share their professional insight on a particular proposal, but they won't have any voting or decision-making authority.

4.3.11 For advice on a particular proposal, such as one involving HIV, genetic disorders, or cancer, the EC may invite subject specialists as independent consultants or include a representative from a particular patient group as a member of the EC or special invitee.

4.3.12 Before a proposal is forwarded to the EC, it should, to the extent practicable, also be reviewed by a separate scientific committee. In order to assure the quality of research and participant protection, EC might also raise scientific concerns in addition to ethical ones.

4.4 Members of the EC's terms of reference

4.4.1 All EC members, including the Chairperson, should be appointed by the institution's leader.
4.4.2 The TORs should be mentioned in the appointment letter sent to each member. The following information should be included in the letter sent by the institution's leader at the very least:

- The member's position on the committee;
- The length of the appointment; and
- The terms of the appointment

4.4.3 The average membership term is two to three years. The SOPs allow for the extension of the time frame. The composition of the EC could fluctuate on a regular basis by a specified proportion.

4.4.4 Members of the EC may receive a fair honorarium for attending the meeting.

4.4.5 Applicants for EC membership should be prepared to meet the criteria outlined in Box 4.3.

Box 4.3 Requirements of EC Members

Each EC member is required to:
l. submit a most recent CV that has been duly signed, as well as training certificates for good clinical practise (GCP) standards and human research protection, if applicable.
2. either receive human research protection and/or good clinical practises (GCP) training at the time of induction into the EC, or must complete training and submit training certificates within six months of appointment (or in accordance with institutional policy);
3. be willing to participate in training or continue to learn new things while serving as an EC member;
4. be knowledgeable about pertinent rules and regulations;
5. read, comprehend, accept, and abide by the EC's COi policy; if applicable, declare it at the proper time;
6. agree to sign a confidentiality and conflict of interest agreement;
7. be willing to make public their full identity, occupation, and affiliation with the EC; and
8. be committed to and understand the value of doing research and providing study participants with protection.

4.5 Selection criteria for members of an EC

4.5.1 Members should be chosen based on their qualifications, expertise, interests, dedication, and readiness to give the necessary time and effort for the EC, all in their individual capacities. For more information, go to Table 4.1.

4.5.2 Each member of the EC is chosen for a specific position. They are not permitted to fill in for any absent members during a meeting. Based on their qualifications, the position of Chairperson/Member Secretary is an extra task to their main duty. Therefore, if the Chairperson is an attorney, they can act as both the attorney and the Chair.

4.5.3 SOPs ought to include these requirements.

4.6 Education

4.6.1 Members should receive training on human research protection, EC duties, and SOPs, as well as knowledge of ethical standards, GCP standards (where applicable), and pertinent national laws.

4.6.2 EC members ought to receive initial and ongoing instruction in human research protection, relevant EC SOPs, and associated legal obligations. Every training should be recorded.

4.6.3 All EC members shall be made aware of any changes to the pertinent regulations or recommendations.

4.6.4 EC members should be aware of regional, cultural, and societal standards as well as new ethical developments.

4.7 Functions and obligations of the EC

4.7.1 Protecting the rights, safety, dignity, and general well-being of study participants is an EC's first duty.

4.7.2 The EC shall ensure that the investigator team conducts their research in an ethical manner.

4.7.3 The EC is in charge of making any necessary declarations of conflicts of interest to the Chairperson at every meeting and seeing to it that they are noted in the minutes.

4.7.4 The EC should carry out its duties by attending meetings, participating in discussions, and deliberating competently in the initial and ongoing reviews of all scientific, ethical, medical, and social elements of research proposals that it receives.

4.7.5 The EC must make sure that local community values and customs are upheld in accordance with global ethical principles and international scientific standards.

4.7.6 In accordance with local healthcare needs, the EC should support the growth and education of the research community at the particular institute (including researchers, clinicians, students, and others).

4.7.7 Members' responsibilities must to be made explicit (details in Table 4.1). At the time of their appointment, EC members should receive the SOPs.

4.7.8 The Secretariat should assist the Member Secretary and Alternate Member Secretary (if necessary) in all aspects of their duties and receive training in documentation and filing protocols under a confidentiality agreement.

4.7.9 The EC shall make sure that personal information is kept private and that material, including minutes of EC meetings, is kept confidential.

4.7.10 The EC reviews the AE/SAE, the final reports, and the progress reports, and if necessary, makes recommendations about how to take care of the participants and minimise risks.

4.7.11 Where necessary, the EC should advise appropriate compensation for harm attributable to research.

4.7.12 As and when necessary, the EC should conduct monitoring visits at study locations.

4.7.13 The EC should take part in ongoing training in research ethics and be current on pertinent laws and regulations.

4.7.14 The EC might observe that other researchers from the same institution are conducting the same or comparable research in a coordinated manner. Research that is "me too" (replicative) should not be promoted, and submissions of the same research to several funding agencies should be rejected.

4.8 Submission of review procedures

4.8.1 In accordance with EC SOPs, researchers should submit their research ideas to the Secretariat in either hard copy or electronic form for review. The EC is obliged to create a checklist for the paperwork listed in Boxes 4.4(a) and 4.4. (b). Depending on the nature of study, EC SOPs, and institutional regulations, this list may be modified

Box 4.4 (a) Information on the documents that must be submitted for EC review

The following are the requested review types: 1. Cover letter to the Member Secretary 2. Type of review requested 3. Initial application review form 4. The correct translation of the informed consent document (ICD) into the local tongue and English (s). certification for back-translation and translation (if applicable) 5. Case record questionnaire or form 6. Methods of hiring: notifications and advertisements (if applicable) 7. If necessary, patient instruction cards, diaries, etc.	14. A list of the lead investigator's active research projects, if applicable 15. A commitment with investigators' signatures 16. Permissions from authorities (as applicable) 17. Important administrative endorsements (such as HMSC certification for international trials) 18. Approval from the Institutional Committee for Stem Cell Research (IC-SCR) (if applicable) 19. Memorandum of Understanding (if applicable) for studies involving partnership with other institutions 20. Clinical study agreement between the investigator, the institution's leader, and the

8. The investigator's brochure (whether it applies to studies of biologicals, devices, or drugs) 9. Information about the sponsor and fund allocation (if applicable) 10. A list of each study researcher's short bios 11. A disclosure of any COI 12. A GCP training certificate for investigators (clinical trials), ideally issued within the last five years. 13. Any other research ethics or training documentation that complies with EC SOP.	sponsors (if applicable) 21. Registration documentation for clinical trials (preferable) 22. Insurance policy for research participants stating the terms of coverage, the start and end dates of the risk coverage (it is better to have the policy rather than only the insurance certificate) (if applicable) 23. An indemnity policy that expressly states the terms of insurance, the start and end dates of the risk coverage (if applicable) 24. Any further documents that the EC may request (such as supplementary EC clearances for multicentric research). 25. Protocol

Box 4.4(b) Details of documents to be included in the protocol

Followings ought to be part of the protocol: 1. the front page, which has the investigators' signatures and the proposal's title; 2. a succinct summary or lay summary; 3. background information explaining why a human study is necessary to address the research question; 4. explanation for including or excluding vulnerable populations; 5. specific research aims and outcomes (if applicable); 6. eligibility requirements and processes for participant recruitment; 7. A thorough explanation of the proposed research's methodology, including sample size (justified), study design (observational, experimental, pilot, randomised, blinded, etc.), types of data collection, intended intervention, drug dosages, administration methods, treatment duration, and information on any invasive procedures; 8. Duration of the study; 9.Benefit-risk assessment, placebo justification, plans to withdraw. To withheld standard therapies if any, should justify the same;	10. Informed consent with a sample of the patient/participant information sheet and informed consent forms in English and local languages should be followed according to the procedure. Informed consent for stored samples and AV recording if applicable; 11. statistical analysis of the study should be planned; 12.Privacy and confidentiality of the study participants should be maintained; 13. Manage the risk or injury, if research involves more than minimal risk; 14. a proposal for pay, reimbursement of ancillary costs, and management of injury or illness associated to research both during and after the research period; 15. The provision of supplemental medical care for unrelated illnesses throughout the research period; 16. A description of the storage and upkeep of all data gathered during the trial; and 17. Plans for the publication of results, whether positive or negative, while protecting the privacy of individual data/identity. 18. Moral considerations and safety measures for participant protection.

Table 4.2 Types of review

1	Exemption from review	-Research on publicly available data for systematic reviews or meta-analyses; -observation of public behaviour when information is recorded without any linked identifiers and disclosure would not jeopardise the interests of the person being observed; -quality control and quality assurance audits in the institution; -Consumer acceptance studies related to taste and food quality; quality control and assurance audits in the institution; -comparisons of teaching methods, curricula, or classroom management techniques; -public health programmes by government agencies; programme evaluation where the sole goal of the exercise is refining and improving the programme or monitoring (where there are no individual identifiers). -comparison of instructional methods, are examples of proposals with less than minimal risk where there are no linked identifiers.
2	Expedited review	-Research using non-identifiable human tissue and specimens obtained from blood banks, tissue banks, and discarded clinical samples; -Research using non-identifiable clinical documentation materials (data, documents, records); -Revisions to proposals that have already been approved through expedited review, full review, or continuing review are all acceptable. -Minor deviations from originally approved research that pose no risk or very little risk are acceptable. - Progress/annual reports where there is no additional risk, such as activity limited to data analysis, are acceptable. -The SAE Subcommittee will expedite the review of SAEs and unanticipated AEs; and • In the case of multicenter studies, if one designated main EC from among the participating sites has already examined and authorised the trial, a local EC may only carry out an expedited evaluation for site-specific needs in addition to the full committee common review. • Doing research during crises and natural catastrophes (More information is provided in Section 12)
3	Full Committee review	-Research involving vulnerable populations, even if the risk is minimal; research with a minor increase over minimal risk (see Table 2.1 for more information); -studies involving deception of participants (see section 5.11 for more information); and - research proposals that have more than minimal risk should all be subjected to full review committee review if they are not covered under exempt or expedited review. • Research proposals that have been exempted from review, expedited, or subcommittee reviewed should be approved by the entire committee, which has the authority to overturn or change any decision made by the subcommittee or accelerated committee; • modifications to proposals or related papers (such as but not limited to informed consent forms, investigator's brochures, ads, recruitment techniques, etc.) that result in an altered risk; -Any new information that becomes available during the research process may be used to modify the benefit-risk analysis and determine whether or

		not to terminate the study. -Research during emergencies and disasters may be conducted through an expedited review process or through scheduled or unscheduled full committee meetings. • Advance authorisation of research on predictable catastrophes or disasters before the actual crisis occurs for implementation later when the actual emergency or disaster occurs. This may be chosen by Member Secretary depending on the urgency and need.

4.8.2 The Member Secretary/Secretariat will examine the proposals for completeness and classify them into one of three categories—exemption from review, accelerated review, or full committee review—depending on the level of risk they pose. For more information on reviewing categories and risk categorization, see Tables 2.1 and 4.2, respectively.

4.8.3 A researcher cannot choose whether their proposal should be given an accelerated, full, or exemption review. To the EC must be submitted any research ideas. The EC will decide on a case-by-case basis what kind of review is necessary and who would conduct it. Researchers can apply for an exemption, an expedited review, or a waiver of consent by approaching the EC with the necessary justification.

4.8.4 The Chairperson, Member Secretary, one or two chosen members, or as indicated in SOPs, may undertake an expedited review.

4.8.5 At the following full committee meeting, the conclusions of the SAE subcommittee and the approval given through expedited review must be affirmed.

4.8.6 Except in cases of expedited review, EC members should be given adequate time (at least one week) to examine the proposal and any supporting papers.

4.8.7 Every proposal should be examined by every EC member. However, in accordance with their SOPs, the EC may choose to use different review processes for proposals.

4.8.8 In order to save time and increase the effectiveness of the review during the full committee meeting, the EC may adopt a system for pre-meeting peer review by subject experts and request clarifications from the researchers beforehand. This is especially true in institutions where there are no separate scientific review committees.

4.8.9 The EC might have a procedure in place for choosing primary and secondary reviewers. Depending on each reviewer's area of expertise, the Member Secretary should designate the lead and secondary reviewers for the proposal's scientific and ethical components as well as the informed consent document.

4.8.10 The Member Secretary is free to choose topic specialists as needed to assess the proposal. These experts may be invited to the EC meeting or allowed to participate via video or teleconference, but they will not be involved in determining the ultimate choice.

4.8.11 To prevent research from being held up, the EC should have regular meetings, follow best practises, work to shorten turnaround times, or set up early decision-making processes.

4.8.12 The study protocol and other associated documentation should be initially reviewed by the designated (primary and secondary) reviewers and topic experts in accordance with the specified study evaluation form and for the parameters listed in Table 4.3.

Table 4.3 Ethical concerns related to protocol review

Social values	• Health research must have predicted social value in order to meet the basic criteria for ethical approval. The study's findings ought to be applicable to societal health issues. The intended research must have a social purpose, which must be ensured by all stakeholders, including sponsors, researchers, and ECs.
Scientific design and conduct of the study	• The research must use reliable scientific procedures in order to be ethically feasible, as subpar science might put communities or research participants at risk with little chance of recovery. -The ethical considerations of the chosen study design or strategy should be considered, even though ECs may get documentation from a prior scientific assessment. They should also determine that the research procedures are solid scientifically. -Even if a scientific body has already approved the study, the EC may nonetheless raise concerns about the study's validity or the safety of its participants.
Benefit-risk assessment	• The benefits of the intended research, whether they be for the participants, the community, or society as a whole, must outweigh the dangers involved. • Risks can be either physical, psychological, economic, social, or legal, and harm can happen to an individual, their family, their community, or the entire society. Prior to evaluating the study's overall harm and benefits, it is required to examine the intervention under research and determine its potential advantages and risks. • The EC should examine risk management plans, including withdrawal criteria with rescue drugs or procedures. • The EC should, if necessary, offer recommendations for reducing risk or discomfort. • Appropriate arrangements must be developed for monitoring and auditing the research's progress, including, if necessary, the creation of a Data and Safety Monitoring Board (DSMB) (for example in clinical trials)
Selection of the study population and recruitment of research participants	• Recruitment ought to take place voluntarily and without coercion. The inclusion and exclusion criteria should be equitably applied when choosing participants. -A particular population, tribe, or economic group should not be forced to participate or reap the benefits, therefore participant selection should be equitable. -No person or group of people should be forced to participate in research without receiving any direct or indirect advantages. -Vulnerable groups may be recruited once adequate reason is given. -Participants should have the option to withdraw at any time without having their usual treatment impacted.
Payment for participation	• It is important to assess the plans for payment for participation, compensation of incurred expenses (such as travel or lost wages), incidental fees, and other inconveniences.

	• It is important to make sure that rewards are not so high as to persuade potential volunteers to take part in the study against their better judgement or without giving the risks proper consideration. No unauthorised incentives may be provided.
Protection of Research participants' privacy and confidentiality	• The procedures put in place to protect participant confidentiality and privacy should be reviewed by ECs. • Research records should be kept in a different location from ordinary clinical records, such as those kept in a hospital.
Community consideratons	• The EC should make sure that the community is treated with respect, its interests are safeguarded, and its requirements are taken into consideration in the research. • No stigma or discrimination should result from the planned research. Less harm should be done, if any. • It's crucial to consider how the results of the study will be shared with the community, and plans for doing so should be carefully reviewed after the study is complete. -Plans for distributing study findings to the public after completion should be carefully considered.
Qualification of researchers and adequacy assessment of study sites	• The EC should consider the PI's credentials and expertise as well as the suitability of the research site's facilities for participants before approving the planned study.
Disclosure and declaration of potential COI	• The EC should manage COi within the EC and members with COI should leave the room at the time of decision-making in a specific study. • The EC should assess any declaration of COi by a researcher and offer solutions to manage them.
Plans for medical management and compensation for study related injury	• It is important to examine the suggested strategy for handling any medical emergency or injuries. • The source and method of compensation for injury resulting from study should be determined.
Review of the informed consent process	It is necessary to study the informed consent procedure bearing in mind the following: • the method for gaining informed consent, including who is in charge of getting consent and the precautions taken for vulnerable populations; -The sufficiency, completeness, and understandability of the information to be provided to study participants, and when applicable, their LARs; • back translations of the informed consent document in English, where necessary; • provision for audio-visual recording of the consent process, if applicable, in accordance with applicable regulations; • contents of the patient/participant information sheet, including the local language translations (See section 5 for further details); • if consent waiver or verbal/oral consent request has been made, this should be reviewed by determining whether the protocol meets the criteria. For additional information, see Section 5.

4.9 Full committee meeting

4.9.1 At a full committee meeting, all ideas that are chosen to go through full committee assessment must be discussed and a decision made.

4.9.2 As outlined in the SOPs, ECs shall hold frequent full committee meetings to discuss proposals in accordance with a predetermined timetable.

4.9.3 Only if the quorum is met will a meeting be regarded as legitimate. When making decisions, this should be upheld throughout the meeting.

4.9.4 Before the meeting starts, the chairperson should be notified in writing if a member has declared a conflict of interest for a proposal.

4.9.5 During the discussion of the research proposal, the member who has declared COi should leave the room and leave the EC meeting. Both the quorum and this should be recorded in the minutes.

4.9.6 It is important to keep track of any attendees who aren't there as well as any attendees who arrive or leave throughout the meeting.

4.9.7 Proposals shall be discussed item by item in accordance with the agenda.

4.9.8 The number of ideas reviewed in a meeting should support the claim that each proposal is given enough time to be reviewed. If there are more ideas to be discussed at each meeting, either meetings may be held more frequently, or more ECs may be formed in accordance with the institution's needs.

4.9.9 The meeting's scheduled time needs to be adequate to allow for adequate discussion of each item on the agenda.

4.9.10 The previous meeting's minutes and a list of the procedures that were given an expedited review or were exempt from review should be approved.

4.9.11 The researcher may be contacted to offer suggestions or clarify the study protocol that has been submitted for review, but they shouldn't be present while decisions are made.

4.9.12 The members can get an update from the primary and secondary reviewers regarding the study proposal and review process as per EC SOPs.

4.9.13 The Member Secretary may submit the feedback of an independent consultant (if appropriate), or subject matter experts may be asked for their opinions, but they shouldn't take part in the decision-making process. However, it is necessary to note her/his viewpoint.

4.9.14 Representatives from the study group population may be asked to speak up during discussions but should not take part in decision-making.

4. 9.15 The EC may interact with other topic experts or independent consultants throughout the meeting via electronic means, such as video or conference calls.

4.9.16 All members of the EC present in the room, including the Chairperson and Member Secretary, are entitled to vote and should use this privilege.

4.9.17 The decision must be made and documented by either a majority vote or a decision reached by broad agreement (in accordance with SOP). Any disapproval should be documented along with the reasons.

4.9.18 The choices could be as shown in Box 4.5.

Box 4.5 Types of decisions by EC

An EC may decide one of the following:
-approved - with or without suggestions or comments;
-revision with minor modifications/amendments - after examination by the Member Secretary or expedited review, as appropriate;
-revision with major modifications for resubmission - this will be presented to the full committee for reconsideration for approval; or
- not approved (or termination/revocation of permission if applicable) - clearly stated reasons for not approving/terming out must be given.

4.9.19 Depending on the type of study, approval might be given for the entire projected research period or might be subject to annual review. The annual report (counted from the day of approval or date of the study's real commencement) should be evaluated by the EC for continuation in accordance with SOP.

4.9.20 The progress of the plan may be monitored annually or at shorter periods (quarterly, half-yearly), depending on the risk involved, in accordance with an EC directive. Continuing approval is possible if the development is satisfactory.

4.9.21 If an EC learns of material that could have a negative impact on the benefit-risk analysis, it may opt to overturn its previous positive decision on a research.

4.9.22 Before final approval by the Chairperson/Vice-Chairperson/designated member of the committee, the Member Secretary (with assistance from the Secretariat) should circulate the minutes for comments from all members.

4.9.23 The researcher should be informed of the EC's decision and any comments, if any, as well.

4.9.24 The researcher should have the chance to respond to or explain EC criticisms, as well as to talk about or convey her or his position.

4.9.25 The institute's director, who serves as an appellate body for EC issues, is another option open to the researcher.

4.9.26 The EC may be dissolved or reappointed by the head of the institute acting as appellate.

4.10 Evaluation of multicentric studies

Multicenter research is carried out at more than one centre by various researchers, typically adhering to a standard methodology. Numerous research facilities around the nation or in foreign locations conduct a vast number of clinical trials, clinical studies, and public health research, including surveys. Multicentric research studies are conducted with the main goal of giving a solid foundation for the later generalisation of its findings. All sites are expected to receive approval from their respective ECs, which would take into account the regional needs and requirements of the populations under study and protect the participants'

rights to safety, dignity, and well-being. However, there are issues with time wastage, communication breakdowns between the committees, and duplication of work in the simultaneous review by the involved ECs. Therefore, the considerations indicated in sections 4.10.1 and 4.10.2 may be made in multicentric studies using a single protocol.

4.10.1 Each participating site will be individually reviewed by ECs.

• If any EC denies clearance for a study at a site, the reasons must be communicated to other ECs, who must then consider them.

• The ECs/Secretariats of all participating sites should establish communication with one another.

-The EC can recommend site-specific methods and changes to informed consent in accordance with regional needs.

-For studies with a higher level of risk, clinical trials, intervention studies where conduct may differ depending on the site, or for any other reason requiring additional evaluation and attention, a separate review may be sought.

4.10.2 Common review for all participating sites in multicentric research

• The ECs may choose to have one main EC, whose conclusions may be accepted by other ECs, in order to save time, avoid duplication of effort, and expedite the review process. This is crucial for research that has been assessed to have little or minimal risk, survey or multicentric studies that use anonymized samples or data, as well as public health research investigations.

• Nominated members of the designated main EC of the participating centres are welcome to attend meetings of the main EC in order to discuss any ethical or human rights issues they may have, look for solutions, and inform their respective ECs of the main EC's decision.

• This EC must be registered with the appropriate government and be situated in India (if applicable).

• To ensure uniform practises at all centres, meetings should be conducted at the beginning and, if necessary, intermediate stages of the study.

-However, the site ECs retain the authority to assess any extra site-specific requirements, assure need-based participant protection, or alter the informed consent document (!CD), translations, and research monitoring in accordance with local standards.

• Once the protocol has been properly approved by the EC of the host institutes/decision of the main EC is accepted, it may be amended to meet local conditions and should be implemented.

• Protocol adherence, including steps to have the offending local centres' involvement terminated, should be watched.

• Only ECs in India are subject to the same review. The local participating sites would need to get local ethical approval in the event of an international partnership for research and approval by a foreign institution, etc. For more information, go to section 3.8.3.

• Any site-specific modifications should be disclosed to sponsor/funding organisations, and the affected site should be the only one to use the updated version.

• Prior to the start of the study, plans for the publication of the article and the creation of a shared final report with authors from the participating sites should be made.

-Site-specific data cannot be published until the combined report has been approved by the relevant authorities and the necessary permits have been secured.

4.11 Ongoing evaluation

4.11.1 Ongoing research should be evaluated on a regular basis, ideally once a year (or more frequently, depending on the amount of risk), or as may be specified in the SOP of the EC, at the time of granting approval, and as stated in the communication letter.

4.11.2 The EC should regularly analyse the progress of active proposals, review SAE reports from all locations, check for protocol deviations/violations and non-compliance, study any fresh research-related information, and evaluate the final reports of all research activities.

4.11.3 All rules governing SAEs must be followed by clinical studies that fall under the purview of a licencing authority. The EC should make sure the researcher complies as well. There should be a set institutional policy for trials conducted for academic and other purposes.

4.11.4 The EC needs to look at the actions taken to manage SAEs medically. Whether they are in the intervention arm or the control arm, participants shouldn't be responsible for the expenditures associated with the management of a study-related injury.

4.11.5 If applicable, compensation for research-related injuries must be provided, as decided by the EC and in accordance with regulatory requirements (if applicable).

4.11.6 The EC should review the corrective measures for protocol deviations/violations. The EC may halt the study if the infractions are substantial. Where there is persistent non-compliance with ethical standards, the EC may report the situation to the institutional leader or government authorities.

4.11.7 The DSMB may also request reports on the sponsor's monitoring activities.

4.12 Site surveillance

4.12.1 It is advised that ECs adhere to the procedures outlined in a SOP to monitor the authorised study site until the study is finished in order to ensure compliance or enhance the function.

4.12.2 Monitoring decisions must be made at a full committee meeting and may be routine or "with cause." The EC can recommend that routine monitoring be carried out at more frequent intervals for

research that involves participants who are more at risk or who are vulnerable, or if there is any other cause for concern, at the time of first evaluation or continuing review.
In Box 4.6, a few reasons for monitoring are listed.

Box 4.6 Examples of "for cause" monitoring

The following circumstances may warrant surveillance "for cause":
-A high rate of protocol violations or deviations;
-numerous proposals conducted at the study site or by the same researcher;
-numerous SAE reports;
-a high rate of participant recruitment;
-participant complaints; any negative media reports;
-negative information obtained from any other source;
-non-compliance with EC directives;
-misconduct by the researcher; and
-any other factor determined by the EC.

4.13 Archiving and maintaining records

4.13.1 All EC-related paperwork and correspondence needs to be date-stamped, filed, and kept on file in accordance with specified rules.

4.13.2 Designated individuals should ensure confidentiality throughout access and retrieval operations.

4.13.3 Each active and inactive (closed) file needs to have the proper labelling and be archived separately in the right locations.

4.13.4 Both hard copies and digital versions of records can be kept.

4.13.5 After the study is finished or terminated, all records must be archived for at least three years.

4.13.6 Documents pertaining to regulatory clinical trials must be kept on file for five years after the study's conclusion or as required by law.

4.13.7 Records may be kept on file for a longer time if the sponsors or regulatory agencies demand it.

4.13.8 In SOPs, EC should discuss archival and retrieval procedures.

4.13.9 Authorized representatives of regulating bodies shall be able to access and inspect EC records.

4.13.10 Wherever possible, ECs may employ techniques for electronic record storage.

4.14 Management and administration

4.14.1 The EC should have a presence in every institution.

4.14.2 The institution shall give the EC access to space, resources, and personnel for sustaining

4.14.3 Each institution should set aside a suitable amount of money to ensure the smooth operation of the EC.

4.14.4 The EC may additionally impose a fair review fee to cover costs associated with ensuring institutional policies are followed and to cover operating expenditures.

4.15 ECs must be registered and accredited.

4.15.1 ECs are required to make sure that procedures are in place to protect the standard of ethical review as well as adherence to relevant national/international and local laws.

4.15.2 ECs must register with the appropriate authority in accordance with legal requirements.

4.15.3 Efforts should be made to obtain recognition, certification, or accreditation from reputable national and international organisations, such as the Quality Council of India through the National Accreditation Board for Hospitals and Healthcare Providers (NABH), COSCO, Association for the Accreditation of Human Research Protection Programmes (AAHRPP), and Strategic Initiative for Developing Capacity in Ethical Review (SIDCER). Such accreditation/certification should be continuously updated.

4.15.4 The voluntary processes of certification and accreditation support quality assurance and improvement by ensuring that ECs adhere to the highest standards for safeguarding the participants' safety, security, and well-being.

PROCESS FOR INFORMED CONSENT

5.0 Any biomedical and health research involving human participants must first receive the prospective participant's free, written informed consent. This condition is founded on the idea that competent individuals have the freedom to decide whether or not to engage in the research. Three key steps make up the ongoing process of informed consent: presenting pertinent information to potential participants, confirming the person's competency, ensuring the information is understandable by the participants, and confirming the voluntariness of the participation. Individual liberty and choice are respected and protected by informed voluntary consent.

5.1 Requisites

5.1.1 The participant must have the capacity to understand the proposed research, be able to make an informed decision on whether or not to be enrolled and convey her/his decision to the researcher in order to give consent.

5.1.2 The consent should be given voluntarily and not be obtained under duress or coercion of any sort or by offering any undue inducements.

5.1.3 The LAR's consent must be obtained in cases where the subject is unable to give willing, informed consent. For additional information, see section 6.

5.1.4 Before beginning any participant-involved study-related operations, a researcher must obtain consent.

5.1.5 It's important to protect the anonymity and secrecy of participants in the stage.

5.2 Important details for potential research participants

5.2.1 Before asking someone to consent to engage in research, the researcher must provide them all the facts they need to know and answer any questions they may have in a language they can comprehend. In addition to being straightforward and scientifically accurate, the language should also be considerate of the participant's social and cultural environment.

5.2.2 The informed consent form (ICF) and the patient/participant information sheet (PIS) are the two components of the ICD. The PIS contains information on known research facts that are pertinent to participation. The ICF, which the participant completes after acknowledging understanding of the PIS's material and agreeing to participate in the study, comes next.

5.2.3 Before deciding to participate in the research, the participant should be given enough time to read the permission form, if necessary, discuss it with family and friends, and ask the researchers or research team to clarify any questions.

5.2.4 The key components of a permission form are listed in Box 5.1.

Box 5.1 Essential and additional elements of an informed consent document

An informed consent form must include the following:	Depending on the sort of study, the following components may also be necessary:
1. Indication that the work is research 2. A clear explanation of the study's goals and procedures 3. The anticipated duration of the participation, the frequency of interaction with the anticipated enrollment of participants, and the types and methods of data collection. 4. Benefits that could reasonably be anticipated as a result of the research for the participant, the community, or other parties 5. Any anticipated dangers, discomfort, or difficulties the participant may have as a result of taking part in the study. 6. The degree to which records' confidentiality could be upheld, including the extent to which the researcher would be able to protect it and the likely repercussions of a breach. 7. Depending on the type of study, payment or reimbursement for participation and incidental costs 8. Participants who suffer harm or injury as a result of study are given free care or compensation. 9. Individuals are free to participate in research and/or to withdraw at any time without penalty or loss of benefits to which they would otherwise be eligible. 10. The names of the research team members and their contact information, including phone	1. Any alternate methods of therapy or procedures that might be equally beneficial to the participant as those that she or he will be subjected to. 2. If there is a chance that the research could result in a disease that is stigmatising, like HIV or genetic illnesses, provision should be made for pre- and post-test counselling. 3. Any insurance coverage for accidents or other unfavourable outcomes associated to research. 4. The amount of information about potential uses of the biological material and the data that will be produced from the research that may be foreseen. The following additional details: i. The amount of time the sample or data will be stored, and the likelihood that the material will be put to other uses. ii. It should be made very clear whether or not the material is to be shared with others. iii. The ability to refuse use of any biological sample, such as DNA or a cell line, as well as any associated data, at any point during or following the completion of the research. iv. The chance that biologically sensitive information will be uncovered and the safeguards in place to protect confidentiality. v. If research on biological material or data results in commercialization, there will be a post-research strategy and benefit sharing.

numbers and addresses (for example, the principal investigator or co-principal investigator for questions about the research and the chairperson, member secretary, or helpline for appeals against violations of ethical principles and human rights).	vi. If there is a publication plan, it should include pedigree charts and images.

5.3 Researchers' accountability

5.3.1 The consent form, including any local translations, should only be used by the researcher if it has been approved by the EC.

5.3.2 Prospective participants should be given access to sufficient information required for informed consent in a language and style that is simple for them to understand.

5.3.3 When dealing with participants who are differently abled, such as those who have physical, neurological, or mental impairments, appropriate techniques should be employed to improve the participants' understanding, such as braille for the visually impaired.

5.3.4 There shouldn't be any limitations on the participant's ability to inquire about the study, talk to family and friends, or take their time before making a decision.

5.3.5 The researcher shouldn't coerce or threaten a potential participant into participating in the study, nor should they offer any implausible assurances.

5.3.6 The participant must be competent, have a thorough understanding of the study, and grant consent voluntarily, according to the researcher. An impartial literate witness who is unrelated to the research should be present during the consent process if the participant and/or the LAR are illiterate.

5.3.7 For sensitive investigations, the researcher should whenever possible conduct an understanding test. The test may be given again if necessary to ensure that the individual has understood the material completely.

5.3.8 Verbal or oral consent may be obtained upon approval by the EC, in the presence of an unbiased witness who should sign and date the consent document, when a participant is willing to participate but not willing to sign or provide a thumbprint or is unable to do so. The participant, the principal investigator (PI), and the unbiased witness can all be heard or seen in the frame as part of an audio or video recording that documents the process. However, oral or verbal permission should only be obtained under extraordinary conditions and for clear, acceptable reasons with the EC's consent. This shouldn't happen.

5.3.9 Each participant must give their consent again or provide new, informed consent under the conditions outlined in section 5.8.

5.3.10 The researcher shall guarantee potential subjects that their choice to participate in the study will not affect their rights, the patient-physician relationship, or any other advantages to which they are entitled.

5.3.11 After receiving EC clearance, reimbursement for travel, incidental costs, and research participation may be offered.

5.3.12 The researcher is required to ensure free treatment for injuries resulting from research (disability, chronic life-threatening disease, congenital anomaly or birth defect), as well as the payment of compensation above and beyond medical management by the investigator and/or institution and sponsor(s), as applicable.
5.3.13 The researcher must make sure that even in the event of participant withdrawal, the individual can still get routine care.

5.4 Informed consent procedure documentation
This exercise must include documentation of the informed consent procedure.

5.4.1 Each potential participant must complete the informed consent process, which entails obtaining information, comprehending it, and voluntarily deciding to participate in the study. Then they must sign the informed consent form.

5.4.2 If the participant is unable to provide consent due to illness or incapacitation, the LAR's consent must be recorded.

5.4.3 An impartial literate witness who is not a participant's relative or otherwise involved in the research's conduct should be present when an illiterate participant or LAR is giving consent. Examples of such witnesses include other patients on the ward who are not participating in the study, staff from the social services department, and counsellors. The witness needs to be literate, able to read the permission form and participant information sheet, and conversant in the participant's language.

5.4.4 A thumb impression must be taken if the participant is unable to sign.

5.4.5 The consent form must be signed and stamped by the researcher who is granting consent.

5.4.6 In the event of institutionalised individuals, authorization for conducting the research should be sought from the institution's head in addition to individual/LAR consent.

5. 4. 7 In certain forms of study, the spouse or partner may be required to give their consent.

5.4.8 Other family members may participate in genetic studies as secondary participants if their information is included in the family history. It will also be necessary to obtain the secondary participants' informed consent if information about them can be identified
5.4.9 Online permission may be gained, for instance, in studies containing sensitive information like unsafe sex, risky behaviour, the use of contraceptives (condoms, oral pills), or emergency contraceptive tablets among unmarried Indian women, among other topics. Investigators are required to respect participant confidentiality and participant privacy.

5.5 Online authorization
The written informed consent document can be administered and documented utilising electronic informed consent systems. Electronic media can be utilised to provide information as in the written informed consent document. These are electronic methods that explain study-related material and document informed assent/consent from participants or LARs using a variety of electronic formats, including text, graphics, audio, video, podcasts, or interactive websites.

5 .5 .1 The EC must initially examine and approve the procedure, electronic materials, method of documentation (including electronic/digital signatures), procedures used to safeguard participant privacy, confidentiality, and security of the information, as well as data use policies at the study site.

5.5.2 The electronic consent must include all components of informed consent and be written in a language that the participant can comprehend. See Box 5.1 for more information.
5.5.3 The process must be under the PI's or her/his designee's control.

5.5.4 If paper or digital copies are needed for archiving purposes in addition to the electronic version, they are provided to the participant as well.

5.5.5 If interactive formats are employed, they should be easy to use.

5.5.6 If participants, for any reason, demonstrate a lack of comfort with electronic media, no electronic methods should be employed.

5.5.7 Before being used, these instruments may be examined and approved by EC.

5.6 Particular problems with clinical trials
According to COSCO's guidelines, there can be additional requirements for informed consent for clinical research.

5. 7 Consent is waived
If the research involves less than minimal risk to participants and the waiver will not negatively impact their rights and wellbeing, the researcher may submit an application to the EC for a waiver of consent.

Box 5.2 Conditions for granting waiver of consent

The European Commission (EC) may grant consent waiver in the following circumstances: - when the research cannot practically be conducted without the waiver and when the waiver is supported by scientific evidence; - when conducting retrospective studies in which the participants' identities have been removed or they cannot be located; - when using de-identified or unreachable biological samples or data; - when using certain public health studies, surveillance programmes, or programme evaluation studies; - when using publicly available data; or when conducting research. - At the earliest opportunity, make an effort to get the participant's permission.

5.8 New or renewed consent

Re-consent is required in the following circumstances:

• a research participant who is unconscious regains consciousness or who had lost insight regains mental competence and is able to understand the implications of the research;

• new information pertaining to the study that has implications for the participant or that alters the benefit to risk ratio becomes available;
• there is a change in the treatment modality, procedures, site visits, data collection methods, or tenure of participation that may affect the participant's decision to continue in the research;
• there is a possibility of identity disclosure through data presentation or photographs (this should be adequately camouflaged in an upcoming publication);
• the research requires a long-term follow-up or requires extension;
5.9 Steps to take following the permission process
5.9.1 Unless the participant is unwilling to accept these documents, a copy of the PIS and the signed ICF should be delivered to them after consent has been acquired. Such resistance ought to be noted.

5.9.2 The researcher owes it to the participant to explain in detail how confidentiality will be upheld.

5.9.3 The original PIS and ICF should be archived in accordance with the specifications stated in the rules and recommendations.

VULNERABILITY

6.0 The Latin term vulnarere, which meaning "to wound," is the root of the English word vulnerability. People who are vulnerable lack the power, knowledge, or communication necessary to protect their own interests because of a personal disability, environmental constraints, social injustice, a lack of power or understanding, or because they are in a circumstance that makes it impossible for them to do so. These vulnerable individuals have some of the traits that are outlined in Box 6.1.

Box 6.1 Characteristics of vulnerable individuals/populations/group

People may fall under the category of "vulnerable" if they are: • socially, economically, or politically underprivileged and therefore vulnerable to exploitation; • unable to make an informed decision for themselves or whose autonomy is temporarily or permanently compromised, such as those who are unconscious or differently abled; • able to give consent but whose voluntariness or understanding is compromised due to their situational circumstances; or • unduly dependent on others refusal to take part, which might induce them to consent.

The main rule to follow when planning research on people who are vulnerable is that others will be responsible for defending their interests because they are unable to do it or are not in a position to do so on their own. The communities or populations described in Box 6.2 may be at risk occasionally or constantly. Note that this is not a complete list.
6.1 Guidelines for conducting research with vulnerable groups

6.1.1 Vulnerable groups have the same right to participate in research so that the findings apply to them as well.

6.1.2 The research should address the group's health requirements if it is intended to recruit only members of a vulnerable group.

6.1.3 Participants must have as much power as possible to make their own decisions about whether to consent to participation or not.

Box 6.2 Vulnerable group

Here are some instances of vulnerable groups or populations:
-Economically and socially disadvantaged people (such as the unemployed, orphans, abandoned people, people living in poverty, members of ethnic minorities, lesbian, gay, bisexual, and transgender (LGBT) people, etc.);
-people who have been unduly swayed by the expectation of benefits or the fear of retaliation in the event that they refuse to participate, which may have led them to give consent;
-children (under 18 years old); and women in special circumstances.
-have limited autonomy as a result of reliance or being subject to a hierarchical system (students, employ yees, subordinates, defence services personnel, healthcare professionals, institutionalised individuals, under trial, and prisoners); or suffer from stigmatising or rare diseases.

6.1.4 A LAR should be included in decision-making when potential participants in vulnerable communities lack the capacity to consent.

6.1.5 Participant privacy and confidentiality must be ensured with particular care, in part because a violation of either could increase vulnerability.

6.1.6 All parties involved in the study process must make sure that additional safeguards are in place to preserve the dignity, rights, safety, and wellbeing of vulnerable people.

6.2 Additional precautions and safety measures

When vulnerable people are being sought out to participate in research, extra care should be taken to prevent exploitation, retaliation, rewards, credits, etc. since they might feel frightened and unable to argue with their caregivers, or they might feel a desire to please them.They can be subjected to excessive pressure in the first situation, whilst they might be readily exploited in the second. The prospective voluntariness of the consent to participate will be compromised if the dependent feels that their caregivers are pressuring them to take part in the study or if the caregiver stands to gain from the dependent's participation.

6.2.1 Researchers must explain why they chose to study a vulnerable demographic.

6.2.2 ECs are required to verify the offered justification for themselves and include it in the minutes of the EC meeting.

6.2.3 The ECs should rigorously assess and approve any additional safety measures.

6.2.4 A thorough record of the informed consent procedure is required. When necessary, additional precautions such recording assent and reconsent should be taken.

6.2.5 ECs should also carefully weigh the study's advantages and disadvantages and look into risk-reduction techniques.

6.2.6 Due to the dependence of potential participants on others, there should be no coercion, force, pressure, undue influence, threat, deception, or incentives for participation throughout the whole research period.

6.2.7 Vulnerable people might need to be reminded about the research's advantages, hazards, and potential alternatives.

6.2.8 Participants in sensitive studies on topics like mental health, sexual habits or preferences, HIV/AIDS, drug misuse, etc. may be particularly at risk.

6.2.9 Researchers need to be more cautious and aware of potential conflicts of interest between potential participants and LAR.

6.2.10 Participants in some forms of research may be subject to stigma or discrimination, particularly if they are enrolled as normal controls or are chosen from the general community.

6.2.11 Initiatives should be taken to create support networks to address related medical and social issues.
6.2.12 It is necessary to protect participants' rights, privacy, and secrecy at all times, including after the research has been completed.

6.2.13 Whenever possible, auxiliary care may be offered, such as the establishment of a facility, a school for the members' unsupervised children, a hospital, or a counselling centre.

6.3 Stakeholder duties and obligations

Various stakeholders have different obligations to safeguard participants who are vulnerable. See Box 6.2

6.4 Women in unique circumstances.

Women have the same rights to engage in research that men do, and they shouldn't be arbitrarily denied the chance to gain from it. For some women, the informed consent procedure can be difficult due to cultural considerations. Therefore, if necessary, the women may think about speaking with their husbands or other family members. Even if a woman's liberty is crucial, the researcher must adhere to regional cultural norms in order to avoid upsetting the peace in the home, family, or community.

6.4.1 Box 6.3 goes into more detail on a woman's participation in clinical trials or intervention studies that could put her at danger. For more information, see to section 7.18.

Box 6.3 Risks for women participants in clinical trials

I. Researchers must properly justify to the EC why pregnant and nursing women should be included in clinical trials intended to address the health needs of these women, their foetuses, or nursing babies. Trials of a device for identifying foetal anomalies, trials of medicines for illnesses connected with or aggravated by pregnancy, such as nausea and vomiting, hypertension, or diabetes, are a few examples of what constitutes a justified inclusion.
2. When recruiting women of reproductive age, they should be made aware of the potential risk pregnancy poses to the developing foetus. They should be prompted to adopt an efficient method of contraception and informed of their options in contraception failure.
3. A woman who falls pregnant shouldn't be automatically withdrawn from the study if there isn't any proof that the foetus would be harmed. She should be given the chance to withdraw or continue after a comprehensive analysis of the situation. If the lady decides to continue participating, researchers and sponsors must properly monitor her and provide her with assistance for as long as is required

6.4.2 According to the Pre-Conception and Pre-Natal Diagnostic Techniques (Regulation and Prevention of Misuse) Act, 1994, as amended in 2003, research on prenatal diagnostic techniques in pregnant women should be restricted to detecting foetal abnormalities or genetic disorders and not for foetus sex determination.

6.4.3 Study on sensitive themes - Confidentiality should be scrupulously upheld and privacy safeguarded when research is planned on sensitive topics, such as domestic abuse, genetic abnormalities, rape, etc. Appropriate support systems are used in risk mitigation techniques. It is necessary to develop services like

counselling facilities and police protection. Information gleaned from a female participant must never be pointless, hurtful, or appear voyeuristic.
The EC should use extra caution when handling these delicate matters.

6.5 Youngsters

Children are people who have not reached the legal consent age (up to 18 years). Children are vulnerable when they are younger because their autonomy is undermined because they lack the cognitive capacity to properly comprehend the intricacies of the study and make decisions. Even though older people may develop the cognitive capability to understand the research, they nevertheless lack the legal capacity to provide their agreement. Therefore, in order to act in their child's or ward's best interests, parents or LAR must decide whether to allow a youngster to participate in research or to withdraw from it. The ICMR's "NationalEthical Guidelines for Bio-Medical Research with Children, 2017" has more information. Children's research can be conducted in any circumstance, condition, ailment, or "illness" as listed in Box 6.4.

6.5.1 The EC should perform a benefit-risk analysis to evaluate whether extra precautions or protections are required for the conduct of research on children.
For instance, kid-friendly environments, parent(s) present, and locations where child participants can receive proper medical and psychological assistance are all ideal for doing research.

6.5.2 The EC should evaluate the circumstances of the kids who will be participating in the study, such as their age, health status, and other things, as well as any potential advantages for other kids who have the same illness or condition, or for society as a whole.

6.5.3 When conducting research on minors, the parent's or legal guardian's consent is necessary. See Box 6.5 for further details.

6.5.4 Approval

Children aged 7 to 18 shall give their verbal, oral, or written consent, as approved by the EC, in addition to their parents' or LARs' consent. As kids get older, their mental faculties improve, enabling them to comprehend and react. Respecting the kid's response, the researcher involves the child in the consent process by explaining the intended research in a straightforward manner and using language that makes it clear that the child is being asked to participate in the study. Assent refers to a child's consent to participate in research. If the child opposes, then this request must be honoured.
However, a simple lack of opposition should not be seen as approval. But if the test intervention has the potential to save lives and is readily available the child's opposition may be disregarded only if they consent to participate in the study, with parental permission and prior EC approval. Assent requirements are listed in Box 6.6.

Box 6.4 Conditions for research on children

If a scenario, condition, ailment, or disease meets one of the following criteria, children may be included in research:
1. Children are the only ones who experience it.
2. There are both adults and children involved, but the problems are probably very different in these two groups.
3. Studies on adults have shown the necessary level of safety and efficacy, and both adults and children are involved in a similar way and are of a similar type in terms of morbidity, severity, and/or death, whenever relevant.
4. Test interventions are probably at least as beneficial to the specific child participant as any alternate intervention that may be used.

5. The knowledge that is anticipated to be gained outweighs the risk of test interventions that are not intended to benefit the specific child participant (minorincrease over minimal risk).
6. If safety has been established in the adult population or if the data that will likely be generated cannot be gathered through other means, research on children is typically allowed.
7. Based on the maturity of the drug metabolic pathways, the pharmacokinetics of many medications is age-dependent in children as opposed to adults. For instance, children metabolise many medications far more quickly than adults, hence the amount of the drug needed per kilogramme of body weight is substantially larger in children than in adults, how medications are absorbed varies with age.
From infancy to adulthood, the pharmacokinetics and toxicity profile change with growth and maturation.
8. Many medications' side effects may differ in their severity in youngsters from adults. For instance, aspirin use is linked to Reye's syndrome in infants, and tetracyclines can darken young children's teeth.
9. For precise, safe, and palatable medication administration to infants and children, age-appropriate delivery vehicles and formulations (such as syrups) are required.
10. A child's growth, development, and adaptive flexibility all influence the pathophysiology of numerous illnesses. Examples include the motor system's ability to adjust after a perinatal stroke.

Box 6.5 Consent of parent/LAR

1. The EC should decide whether or not parental permission would be necessary before a child may be enrolled.
2. In general, agreement from one parent or LAR is adequate for research that carries only a low risk and/or directly benefits the child. When the research entails greater than minimal danger and/or provides no benefit to the child, parental consent may be required.
3. Regardless of the risk involved, only one parent's consent is acceptable if the other parent is undetected, incapacitated, not reasonably available, or if only one parent is legally responsible for the child's care and custody.
4. In addition to all the components described in the participant information sheet, the protocol should, whenever applicable, include a parent/LAR information sheet that contains information about specific aspects relevant to the child, such as effects on growth and development, psychological well-being, and school attendance.
5. The EC may waive the necessity of obtaining parental/LAR approval and prescribe an adequate procedure to safeguard the interests of the child where the research concerns delicate topics relating to child neglect and abuse.
6. Children with developmental disorders or cognitive impairment are among the most vulnerable groups. In fact, there is a high risk of therapeutic misperception and their parents are also vulnerable. To ensure that parents are aware of the intended research, the benefits and hazards must be carefully discussed.
7. Permission from the necessary institutional authorities would be required for research involving institutionalised children. For instance, in a school environment, the kid, parents, teacher, principle, or management may be involved.

• The assent form's content must take into account the developmental stage and maturity of the enrolling youngsters, as well as the variations in individual comprehension. The consent form's language needs to be appropriate for the child's cognitive, social, and emotional development. It must be easy to understand and age-appropriate for the child. The following details should be provided in the assent form: m a description of the study's purpose and how the child will benefit from it; a thorough explanation of what will be done in the study, together with a description of any potential pain for the kid;
contact details for the person the child can speak with for clarification; and a sentence stating that if the child chooses not to participate in the study, it will not have any impact on how they are treated at the centre.
The items in the above list are not all included; individual cases may involve other items.
• Waiver of assent: The same restrictions that apply to adults who waive informed consent also apply to kids who waive assent. For additional information, see section 5.7. Waiver of assent might be permitted if the available intervention is projected to unquestionably benefit the kid but would only be accessible if the youngster participates in the study. However, one should accept this circumstance. Waiver of assent

might be permitted if the youngster takes part in the study. Only in extraordinary circumstances, though, where other forms of agreement or consent have failed, may this situation be accepted. The EC's consent should be sought in such circumstances.

Box 6.6 Considerations for approval

• Children younger than 7 years old do not require assent to be documented. • Verbal/oral assent must be gained from children aged 7 to 12 in the presence of their parents or LAR, and it should be documented. • Written consent must be acquired from minors between the ages of 12 and 18. The parents/LAR must also sign this assent form. • Teenagers might be able to consent just like adults. However, because they are not of legal age to give consent, it is considered acquiescence and parental or legal guardian consent should be sought. Waiver of consent from the appropriate adult should be obtained and recorded with the approval of the EC, for example, in behavioural research in IV, if the latter will impair the validity of the investigation.

6.6 Research on sex workers and sexual minorities

Researching sexual minorities and sex workers presents particular difficulties such as privacy, confidentiality, the potential for stigma, discrimination, and exploitation leading to greater vulnerability.

6.6.1 The study proposal should thoroughly address the protection of their dignity and the provision of high-quality healthcare in these situations, preferably in conjunction with the community before the plan is finished.

6.6.2 If there is a study proposal involving members of the lesbian, homosexual, bisexual, and transgender (LGBT) community, it would be wise to have a representative of that group attend the EC meeting as a special invitee or member.

6.6.3 To serve as a conduit between the researcher(s) and the community, the EC may propose the formation of a community advisory board.

6.6.4 Because there exist barriers between the various groups in the LGBT community, the specifics of the research should be conveyed to each group separately.

6.6.5 The LGBT community's peer educators or champions could first be sensitised and trained. The potential participants from the community would then better understand the details after they were explained to them.

6.7 Tribal population research

6.7.1 Only research with a clear medicinal, diagnostic, or preventative purpose that will benefit the tribal population should be done on tribal populations.

6.7.2 Prior to entering tribal lands, the appropriate approval from administrative authorities such as the tribal welfare commissioner or district collector should be obtained.

6.7.3 It is advisable to ask officials or local organisations for assistance wherever available or licenced NGOs who collaborate closely with indigenous groups and enjoy their trust.

6.7.4 In the absence of a panchayat system, the tribal chief, another culturally appropriate authority, or a member of the community may operate as the gatekeeper, from whom consent to enter and interact should be requested.

6.7.5 The decision to get informed consent should be made in the presence of suitable witnesses, community elders, and those who are familiar with the native language or dialect of the tribal population.

6.7.6 The participant's consent must be obtained, even with the gatekeeper's approval.

6.7.7 Additional safety measures must be made to prevent the participation of minors, expectant mothers, and senior citizens who belong to tribal groups that are especially vulnerable (PVTG).

6.7.8 Any research that uses tribal knowledge and has the potential to be commercialised should assure benefit sharing with the tribal group.

6.8 Research involving people who are intellectually challenged or affected by mental illness. The World Health Organization defines mental disorders as a wide variety of issues with a variety of symptoms. They typically exhibit a mix of deviant thoughts, feelings, behaviour, and interpersonal interactions. The Mental Healthcare Act of 2017 defines "mental illness" as a significant disorder of thinking, mood, perception, orientation, or memory that gravely impairs behaviour, capacity to recognise reality, or ability to meet the demands of daily life. Mental conditions associated with alcohol and drug abuse are not included, however, as they are a condition of an individual's mind's arrested or incomplete development, especially in children.

Being mentally ill does not automatically make one incapable of understanding or incapable of giving informed consent.

cognitively compromised or affected: Cognition is the term used to describe conscious mental processes including reasoning, comprehension, learning, and memory. Those with cognitive impairment are those in whom certain functions are not fully functional. These people or groups include those who lack full intellectual capacity (intellectually disabled, formerly known as mentally retarded), are unconscious, suffer from a variety of neuropsychological conditions like dementia or delirium, and those who are temporarily or permanently unable to fully comprehend or participate in the informed consent process. Other causes or factors for cognitive impairment that affects the capacity to give informed consent include, but are not limited to, being too young (kids do not yet develop the cognitive abilities to give informed consent), being in excruciating pain, being under the influence of drugs or alcohol, or being mentally retarded (which results in unconsciousness or cognitive impairment while conscious).

6.8.1 Some mental illnesses can make a person more likely to endanger oneself or others.

• Prospective participants must be made aware of how the researcher would handle their suicidal thoughts or other risks of damage to themselves or others during the informed consent process.

• The participant should be informed that, should they indicate such ideas of harming themselves or others, their confidentiality may be violated for reporting to relatives, the police, or other authorities, or they may need to be admitted to the hospital.

• Although some interventions, such as hospitalisation and treatment for suicidal or homicidal thoughts, may be primarily for the participants' own benefit, they themselves may not regard these as such and may opt to decline participation in a study if any such interventions are required.

• Interventions should be used only when necessary, with the least amount of restriction feasible, and in compliance with any applicable legislation.

• In order to accomplish the goals of the research for the benefit of the public, certain research designs may diminish or breach the protections/rights of human participants or particular requirements of informed consent by using deceit. In Box 9.5, many types of deception that might be applied to a study strategy are discussed. The EC should thoroughly scrutinise all such research before approving them.

6.9 People whose autonomy has been reduced as a result of reliance or being subject to a hierarchy
The EC must make sure of the following while examining protocols involving pupils, workers, subordinates, members of the armed forces, medical professionals, people confined in institutions, participants in legal proceedings, convicts, and others:
6.9.1 It is directly relevant to the study topics and not just a matter of convenience to enrol individuals as previously described.

6.9.2 Because people in hierarchical positions may be afraid of repercussions if they disagree or don't engage, extra care must be taken to preserve their liberty.

6.9.3 The participant's care won't be negatively impacted if they decline to participate in the study or do so later.

6.9.4 The protocol has to include information on how to prevent coercion brought on by membership in an organisation or hierarchy.

See Section 5 for informed consent issues.

6.10 Patients with terminal illnesses

Patients who are terminally sick or who are looking for new interventions after exhausting all available medicines are particularly vulnerable since they are willing to give their assent for any procedure that might provide them some hope. These studies have been permitted so that the academic or professional community won't deny these patients the potential advantages of any novel interventions that haven't been thoroughly tested.

6.10.1 Given the prevalence of therapeutic misunderstanding, suitable consent procedures should be in place, and the EC should carefully examine such protocols and recruitment procedures.

6.10.2 Extra monitoring is necessary to catch any negative events as soon as possible.

6.10.3 A benefit-risk analysis should be carried out taking into account how the potential participant will perceive the benefits and dangers.

6.10.4 Especially if the medicine is advantageous to the participant, the EC should carefully assess post-trial access to it.

6.11 Additional weaker groups

Other vulnerable demographics include those who are underprivileged economically and socially, those who are homeless, refugees, migrants, or those who live in conflict zones, riot zones, or catastrophe zones. When such people are to be recruited as research volunteers, more care should be taken to prevent exploitation, retaliation, reward, credits, and other inducements.

6.11.1 Because these people's autonomy has already been violated, researchers must provide evidence for their inclusion.

6.11.2 In order to include these participants, the ECs must be satisfied with the rationale given and record it in the minutes of the EC meeting.

6.11.3 The ECs should adhere rigorously to any additional safety precautions that were already recommended in the recommendations.

6.11.4 The informed consent procedure needs to be thoroughly recorded. There shouldn't be any very strong incentives or coercion to participate. If someone declines to engage, their decision should be accepted without consequences.

6.11.5 The EC should also carefully weigh the study's advantages and disadvantages and look into risk-reduction techniques.

CLINICAL TRIALS OF DRUGS AND OTHER INTERVENTIONS

7.0 A clinical trial is any investigation in which individuals or groups of individuals are prospectively assigned to one or more health-related interventions to assess the impact on health outcomes. The intervention could involve the use of medications, vaccines, biosimilars, biologics, phytopharmaceuticals, radiopharmaceuticals, diagnostic agents, socio-behavioral treatments, technology, equipment, surgical procedures, or traditional medical systems, among other things. Studies that are well controlled are typically clinical trials. In order to determine the effect of the investigational product (IP) or intervention and distinguish it from effects of other influences, such as spontaneous change, the placebo effect, concurrent treatment or intervention, or observer expectations, they use a design that allows comparison of participants treated with an investigational product (IP) or any intervention to a control population (receiving placebo or an active comparator).

A clinical trial is defined by the Drugs and Cosmetics Rules, 1945's amended Schedule Y (2005) as a systematic investigation of new drugs on humans with the goal of identifying and/or validating their clinical, pharmacological (including pharmacodynamic and pharmacokinetic) and/or adverse effects and determining the safety and/or efficacy of a new drug. The academic clinical trial in accordance with GSR 313 (E) dated 16 March 201627 is a clinical trial with regard to approved drug formulations for any new indication, new mode of administration, new dose, or new dosage form that is designed for academic reasons. After carefully weighing the advantages, dangers, and other ethical considerations, an EC must

approve such studies. The licencing authority must then be notified in accordance with the established procedures.

7.1 Overarching principles

7.1.1 All clinical trials must be organised, carried out, and reported in a way that protects the participants' dignity, rights, safety, and well-being.

7.1.2 Prior to the start of a trial, the risks and inconveniences that can be foreseen should be compared against the expected benefits (direct or indirect) for the trial participant as a whole and/or society. A trial should only be started and continued if the benefits outweigh the dangers.

7.1.3 Where applicable, all clinical trials must be carried out in accordance with the Indian Good Clinical Practices, the Declaration of Helsinki (2013 or later versions as appropriate), the National Guidelines for Biomedical and Health Research Involving Human Participants (2017), the Drugs and Cosmetics Act (1940), Rules (1945), and applicable amendments (including Schedule Y), as well as other pertinent rules and guidelines.

7.1.4 A participant's right to consent to or deny participation in a clinical trial must be honoured, and his or her decision should not have an impact on standard medical care.

7.1.5 A participant's privacy must always be protected, and any data acquired about them must be retained in strict confidence.

7.1.6 Therapeutic misperception in potential participants must be prevented (for instance, by having a co-investigator who isn't the main treating physician administer the consent).

7.1.7 At least one member of the research team needs to be qualified and have sufficient research background in the area where the trial is to be conducted.

7.1.8 An EC that is created and operates in compliance with these recommendations and all relevant laws is required to approve all clinical studies.

7.1.9 The necessary regulatory approvals need to be obtained (if required).

7.1.10 The Clinical Trial Registry - India must receive registration information for all clinical trials (CTRI).

7.1.11 Before doing any research-related procedure, each participant's written informed consent must be obtained.

7.1.12 If a trial is intended for a population at risk, it should only be carried out under proper reason and with all appropriate participant protections in place.

7.1.13 It is important to put procedures in place to guarantee the trial's overall quality.

7.1.14 SAEs must be reported for all trials, with any applicable time frames to be adhered to (within 24 hours to the sponsor, EC, and regulator, if necessary, and then a due analytical report in 14 days).

7.1.15 Free medical management of adverse events (AEs) and serious adverse events (SAEs), regardless of their connection to clinical trials, should be provided for as long as necessary or until it is determined that the harm is unrelated to clinical trials, whichever comes first.

7.1.16 Additionally, if it can be demonstrated that the SAE was connected to the study, recompense must be offered.

7.1.17 Clinical trial participants may receive ancillary care for illnesses that develop during the course of the experiment but are unrelated to the study or trial. If necessary, this could take the form of medical attention or a referral to a facility.

7.1.18 Institutional measures must be put in place to provide for reimbursement if the EC deems it essential, as well as insurance coverage for illnesses linked to or unrelated to the trial (ancillary care).

7.2 Development of clinical vaccines and drugs

7.2.1 The overarching goal of a new medication or vaccine's clinical development process, or "IP," is to determine whether there is a dose range and schedule at which the drug can be demonstrated to be both safe and efficacious to the extent that the benefit-risk relationship is acceptable. Drug development phases are listed in Box 7.1.

Box 7.1 Phases of drug development

Phase 0
A Phase O study is an exploratory study that is carried out to determine the distribution of an investigational novel drug (IND) in the body as well as its metabolism in humans, as well as to determine whether the IND can modulate its intended target in humans. Very little human exposure is involved in this study, which has no therapeutic or diagnostic purposes. It is carried out early in the drug development process and permits the use of an IND in humans with fewer preclinical evidence and at lower doses than are necessary for a traditional Phase I research. This will always be included in a regulatory study.

Phase I
Phase I begins with the first human administration of an experimental new medication or vaccination. These studies typically don't have therapeutic goals. In the case of medications with a high potential for toxicity, such as cytotoxic medications, phase I studies are carried out on healthy volunteers or patients.
Studies carried out in Phase I typically involve:
a) initial safety and tolerability estimation;
b) pharmacokinetics;
c) evaluation of pharmacodynamics (biological effects for vaccines); or early measurement of drug activity (including immunogenicity in case of vaccines).

Phase II
Phase II begins with the beginning of studies whose main goal is to investigate patients'/participants' therapeutic efficacy (immunogenicity in the case of vaccinations). Phase II studies are carried out on a set of patients or volunteers who are carefully supervised and who are chosen based on a set of pretty strict criteria. Phase II preliminary investigations aim to calculate the dosage response. Future research is planned to verify the dosage response.

Phase III
Phase III studies with a primary goal of proving or confirming a treatment benefit or protection rate are the first to be started (in case of vaccines). These studies are:
a) planned to support the findings from Phase II studies regarding the safety and efficacy of a drug or vaccine for use in the intended indication and recipient population;
b) intended to provide a sufficient basis for an impact on clinical practise or, where applicable, for

obtaining marketing approval; and
c) carried out to investigate alternative uses for an already marketed drug for a different indication, dosageform, dosage regimen, or route of administration. Such studies must have regulatory approval if they are meant to further the drug's commercial use. This kind of research focuses on off-label usage, and
d) planned as pivotal and bridging trials.

Phase IV

Phase IV starts following the approval of the product and is concerned with the usage of the intervention for the approved indications. For the product's use to be optimised, these studies are crucial.
They may consist of the following:
a) post-marketing surveillance, which involves keeping an eye on a product's safety after it has been put on the market;
b) phase IV clinical trials, which involve conducting research to evaluate a product's safety, tolerability, and effectiveness when used as directed by the marketing authorization, including its effectiveness and safety in particular populations.
c) outcomes research, which aims to investigate the effectiveness and efficiency of the intervention following its introduction for human use; and
d) registries, which propose to maintain data about patients with specific shared characteristics and who have undergone a specific intervention (for instance, a stent), collecting ongoing and supporting data over time on well-defined outcomes of interest.

Box 7.2: Prescriptions for which a placebo may be used

If an established effective therapy is not available, when withholding it would not expose participants to serious harm but might cause temporary discomfort or delay in symptom relief, when the disease is self-limited, or when using an established effective therapy as a comparator would not produce scientifically reliable results and using a placebo would not add any additional risk of serious or irreversible harm, then a placebo may be used.

If a placebo is required for scientific purposes, specific safety measures must be taken. The EC needs to examine and approve these. See Box 7.3 for further information.

Box 7.3 Precautions to be taken when a placebo is used

I. The protocol must include additional protections to keep participants safe, including but not limited to precise withdrawal criteria, close supervision, and rescue drugs.
2. Use a trial design that adds the IP or placebo to the usual course of treatment.
3. Limit the number of patients who receive placebos, for instance, by using a 2: I randomization with 2 participants receiving IP vs I receiving placebo (unbalanced randomization).
4. Such trials with randomization, for instance, 2:2: I, may also contain an active comparator as an additional arm (IP: active comparator: placebo).
5. Ensure that study participants transition to standard of care or active medication after research is finished, including making post-trial arrangements for putting any promising trial results into practise.

Table 7.1 Classification of medical/dental instruments

Class	Level of risk	Instrument examples
A	Low	Mouth mirrors/tongue depressors/impression plates/Tweezers/Cheek retractor
B	Low-moderate	Suction apparatus/Needle holder/Orthodontic braces/bands
C	Moderate-high	Periodontal probes/explorers/Suture material/
D	High	Dental implants/Curettes/surgical instruments/

PUBLIC HEALTH RESEARCH

8.0 With a precautionary mindset, public health raises a complicated link between the state, its policies, and society that involves both individuals and organisations. Both practise and research in public health, which rely on epidemiology and techniques from other fields to promote healthier lifestyles, must adhere to ethical standards. Since the advantages and risks do not just affect an individual but also affect communities, populations, and the environment, public health protects both the individual and the general population. It is crucial to understand that public health initiatives have the ability to reveal and maybe take advantage of the vulnerabilities of communities and demographic groups. Therefore, it is important to conduct public health research investigations and interventions after reflecting on their ethical implications and after putting in place the necessary safeguards, supervision processes, and governance systems.

Since the objectives of the research may overlap, it is still difficult to draw clear lines between public health practise and research. The practise of public health involves gathering data through surveillance, vital statistics, disease reporting, and registries; investigating outbreaks, including contact tracing, using preventive interventions, and promoting health; monitoring and evaluating programmes; and enforcing mandatory requirements, including screening, treatment, immunisation, notifying diseases, and, occasionally, quarantine depending on the situation. Some of these tasks might produce generalizable knowledge by utilising epidemiological designs, sampling methods, and analysis, which is the main goal of research. An EC may need to differentiate between these to more clearly define its mission in light of the challenges in drawing clear lines between practise and research, both of which require ethical oversight and regulation of public health information. However, this section emphasises the special ethical concerns related to public health research. The EC will decide whether a specific protocol relates to research or public health practise.

8.1 Principles of public health research

• Respect for autonomy, rights, and dignity - In public health research, the principle of autonomy is relational since the interests of an individual as a member of a community are relational in nature. As a result, occasionally using individual autonomy at the community level may not be acceptable. While it's important to take into account and uphold everyone's rights and dignity, the community should also be held to the same standards. The community can be involved in this by having a debate. After receiving the EC's case-by-case clearance, the usual way of obtaining informed consent from an individual may be substituted with alternative means. For more information, go to section 8.4.2.

• The principle of beneficence states that research in public health should prioritise the benefit of society as a whole over individual gain.

• The non-maleficence principle states that every effort should be made to prevent harm to individuals and other people, including the community, especially while gathering data and disclosing it later. Stigma, poverty, and discrimination may cause harm to those who are coping with illnesses like HIV, STDs, TB, mental illnesses, etc. There should be safeguards in place to ensure secrecy because there may also be indirect harm to the person, the community, the connections, and the gain.

The services and research in public health may overlap with the following principles.

The following ideas might be applied to research and services in public health.
(i) The damage principle states that when it is appropriate to restrict someone's freedom against their choice in order to protect others from harm, such as in the case of a disease outbreak, the action should be supported by a solid ethical case.
(ii) The principle of least infringement states that when restricting freedom, the least restrictive measures should be used.
(iii) The proportionality principle - According to this rule, public health officials must reduce hazards and advance public wellbeing. Privacy and autonomy violations should be weighed against potential public advantages and the need for such an intervention. The burdens endured by participants or communities ought to be justified.
• The benefits and costs of public health research should be fairly allocated among all study groups, according to the social justice principle. Research that maintains or strengthens current injustices should be avoided when vulnerable or disadvantaged communities are involved. This principle encourages investigation into the upstream elements among the social determinants of health that have an impact on health equity. It is implied as a positive duty to enhance the health of the least advantaged.
• The idea of reciprocity calls for giving something back to people or communities who have taken on an excessive amount of risk or responsibility for the benefit of others. Benefits include protection from additional exposure, access to food, healthcare, clothing, and shelter, communication, or replacement of lost revenue should be situation-specific.
• Solidarity principle - Public health research should acknowledge the inter- and intradependence among community members that fosters solidarity for a community's overall welfare or the common good.
• Transparency and accountability are key principles that must be followed when doing research. The outcomes ought to be made accessible to the general public.
An EC must carefully consider the points listed in Box 8.1 before beginning a review of public health research.

Box 8.1 Public health research proposal review

The following factors should be taken into account by ECs when evaluating research proposals in public health:
1. Are the study's goals based on good science and relevant to the advancement of objectives for public health?
2. Is a written informed permission from each individual required?
• If not, does the approval or consent of the gatekeeper suffice? Who decides who is a gatekeeper, and how?
• Does it involve a two-step process that starts with gatekeeper consent or authorization and ends with individual consent?
3. If applicable, does community engagement promote respect for the community? If so, is the approach suitable?
4. What are the anticipated benefits and which demographic groups are likely to benefit?
5. Does the potential for greater community gain outweigh any harm to the individual?
• Is it justifiable, if so?
• What kinds of possible danger are there?
• Who would suffer damage?
• What steps, if any, may be made to lessen or alleviate this?
Is the harm distributed fairly?
• How do society advantages outweigh personal disadvantages?
6. Is social justice taken into account when planning, carrying out, and evaluating the study's results?

8.2 Ethical concerns with the methods used in epidemiological and public health research studies

8.2.1 Studies on epidemiology and public health

These entail employing several study techniques and instruments on a sizable research population in a single or a variety of venues. These comprise experimental studies (such as field trials and cluster randomised controlled trials, stepped-wedge and quasi-experimental study designs involving groups, geographic areas, institutions, or systems collectively rather than individually), observational studies (such as cross-sectional studies), case control studies, cohort studies, case reports, case series, and other descriptive studies.

• The scientific merit, design, and implementation of the research raise specific ethical considerations that EC should take into account.

8.2.2 Monitoring, programme evaluation, and surveillance data

Measuring and monitoring changes in health status, risk factors, and the use and access to health services is a key public health task. Data pertaining to an outcome are continuously and systematically collected, analysed, and interpreted as part of surveillance, with prompt distribution to those in charge of preventing and controlling sickness or harm. Researchers may use these data to produce fresh evidence to enhance programme performance as well as more general applications at different sites and situations. Program evaluation is the methodical use of scientific and statistical techniques to assess the effectiveness of a program's conception, design, execution, and use; the comparison of these metrics and the utilisation of the knowledge obtained to improve programme results. Human participants in evaluation study, including healthcare professionals, patients, members of the community, and other stakeholders, may or may not be used. Additionally, screening of the documents and observation of various activities at various levels will be required.

• These studies may fall under the "exempt from review" category in certain circumstances, such as when the exercise's sole goal is to refine and improve the programme or when a large number of stakeholders, who are dispersed across a wide geographic area, are to be interviewed.

• Programme evaluation research activities must undergo proper ethical review if their purpose is clearly to generate knowledge that can be applied to other situations.

• If programme evaluation research clearly aims to advance generalizable knowledge, then appropriate ethical review must be conducted in order to ensure the validity of the research, assess the protocol's potential benefits and risks for public health, and determine whether permission from the appropriate public health authorities is required.

8.2.3 Websites and registers for demographic monitoring

A geographically defined population that is subject to ongoing demographic surveillance and regular data and report generation on all births, deaths, and migrations is referred to as a demographic surveillance site. A platform for evaluating a wide range of health-systems, social, and economic initiatives should be made available through this monitoring system. These locations can also be utilised to track environmental and developmental factors, as well as their interactions with and effects on human health.

The sites serve as testing grounds for novel health and non-health treatments and can offer insight into the efficiency of programmes. A surveillance site's objective is to offer a solid evidence base for influencing current and future health-related policy and practise in order to improve the lives of people in developing nations. A pertinent research and development agenda can also be established with their aid.

- Setting up the demographic monitoring sites, with or without the use of GIS facilities, requires prior consent from the relevant state/national authorities and from the community leadership. Such sites can be set up without needing an EC's prior review and approval.

• Procedures for conducting research studies at these locations, including data collection and storage with plans to ensure anonymity, will need to go through the proper EC review. Data collected at demographic sites must be stored in an encrypted format with primary identifiers restricted to specific specified personnel who are obligated by a confidentiality agreement in order to protect the confidentiality of personally identifiable records.

• Because spatial epidemiology, including the use of GIS technology, is a developing field, it is important to address any potential ethical concerns as expertise increases.

• Registries are organised collections of information about certain illnesses and/or medical problems at one or more locations. The previous authorisation of the EC is necessary for registers that are created as a result of research programmes or if the data that emerges from these registries is intended to be utilised for research. However, registries created by national authorities as part of public health initiatives may be exempt from the ethical review procedure if the data has been de-identified. These registries must still follow governance procedures and obtain a certificate from an EC stating that they are exempt from the ethics review process and for waiver of informed consent.

8.2.4 Research on implementation

Implementing and expanding policies, programmes, and treatments that can save lives and improve health on a large scale at local, national, and international levels is a recurring challenge. Implementation research (IR), which enables well-informed decisions on health policies, programmes, and clinical practises, is a new strategy for attaining these objectives. IR is a sort of health policy and systems research that incorporates several research traditions and disciplines. It builds on management science, quality improvement, implementation science, participatory action research, and effect assessment. In order for research to be applicable to public health, it must be co-designed and co-implemented with implementers and end users to comprehend and promote uptake of a research or programme that has been piloted or finished. This necessitates a long-term, mutually beneficial relationship between researchers, other stakeholders, and the community beginning at the project's inception stage. Issues like question framing, research design, and delivery of a strategy for influencing implementation and wider dissemination as part of its design are involved. Simple procedures or more complex research strategies may be used in IR, which frequently combines quantitative and qualitative methods. In order to have an equal population health impact, analyses are conducted with outreach rather than treatment in mind. A policy's effectiveness, the most effective way to scale an intervention, or the best way to introduce and spread an invention can all be explained using specialised studies. In many cases, it may not be possible to pre-specify treatments and outcome measures in detail in order to take into account the changing settings and interventions within the relevant period. Unlike protocols that call for precise pre-definition of interventions, mode of delivery, outcome measurement, and the involvement of research participants, IR is fundamentally adaptive in nature.

Therefore, when considering IR projects, ECs should be aware of this demand for flexibility or resilience.

• The IR process aims to, at least in part, divide roles and responsibilities between researchers and other stakeholders, such as those being investigated.

• Both formally (by taking training) and informally (by fostering discussion and debate), ECs should acknowledge these features of strong participatory practise in IR and delivery sciences.

• While allowing for and recognising the study design's distinctive flexibility and resilience, the theoretical underpinnings of a complex intervention must remain constant. The field of IR ethics is still in its infancy and will continue to expand as more expertise is gained. Due to the asymmetry of power and knowledge

linkages, governance and accountability of all stakeholders play a crucial role that must be taken into account.

Demonstration projects, 8.2.5
A demonstration project examines in-depth the impact of a new policy strategy on the healthcare system. Such projects, by their very nature, alter the status quo of current public programmes, having an impact on communities, users/beneficiaries, providers, and expenditures. They assist policymakers in learning, although in a more controlled setting and on a limited basis, about the possible impact and operational issues of a new policy/program or adjustment of the existing policy to a public health system. A district, group of districts, or state may be the target of a demonstration project. As a result, hundreds of thousands of people (users and healthcare providers) are involved, and significant resources are expended.

• When developing, putting into practise, and reviewing demonstration projects, several important factors must be taken into account. In order to support their creation and evaluation and to provide suggestions to the policy makers regarding the suggested strategy, this most frequently necessitates some amount of research for cultural and geographic suitability (formative research).

• Ethical review of all demonstration initiatives is necessary.

The European Commission should ask several important questions, including:
• Why is the demonstration project being carried out?
• How is this being planned, started, or carried out?
What effects might the project have on larger health systems?
• Are there going to be concerns with equity and disadvantaged groups?
• How diverse are the actual design and execution contexts?
-Should a case-by-case determination be made regarding the exemption from review and consent waiver?

8.2.6 Public trials
These are trials that are conducted on communities or groups, with communities receiving the treatment or intervention rather than individuals. Both of these studies could be observational or interventional. Such research may be done for conditions that are influenced by social factors, and therapies may also target group behaviour. These studies focus on the entire community, and the randomization also occurs at the community level. Typically, the strategy is helpful for researching public health interventions or disease preventive strategies.
• As with any research, EC must review and oversee the investigations.
• The details of section 8.4 can be found since informed consent concerns are complicated.

8.3 Using administrative data as well as other types of data in research

Administrative data are regularly gathered or compiled pieces of information used to support organisational and programmatic activities. These data sets are now used more for research and policy-making than for operating and monitoring programmes and executing audits. State health departments, national surveys, commercial sources, other data repositories, and other big data sources may all provide large volumes of data that are accessible. Administrative data have been used for research increasingly frequently in recent years, and the increase is linked to technological advancements that make data collection, access, and time- and cost-effectiveness possible. Data files are frequently population-based, offering details on enormous populations of people and enabling longitudinal research over several years.
• While such data can offer quick and simple access to information for secondary analysis, there is a risk of misinterpretation, violations of the terms and conditions for which data access was permitted,

compromising data security, confidentiality of information, disclosure permissions, unauthorised and inappropriate use of the data, and unethical publication.
• ECs should make sure that any research utilising administrative data complies with all applicable ethical standards for public health research.

8.4 Informed approval

8.4.1 Obtaining informed consent - Some public health research projects, such cluster randomized field trials or IR, contain participants who are unable to refuse interventions.
This suggests that the informed permission of the participant only applies to the data gathering and not the provision of an intervention. Complete participant information could occasionally be a cause of bias in the selection of participants, which creates methodological issues. Because of the methodological ramifications, participant informed consent in these sorts of research procedures should be reviewed by an EC in a different way than it is in individually randomised trials.

8.4.2 Such trials' hierarchical structures suggest that two levels of consent be taken into account.
The gatekeeper(s), who grant authorization for participation and randomise individual involvement, are at the first level. They could be the parent or other local authority typically in charge of participants' safety. The second level consists of individual participants, whose consent may be obtained in a variety of ways, including: consent for the collection of routinely held information about an individual; consent for the

addition of data; consent for active participation; and, for field trials involving novel pharmaceutical agents, individual consent for both passive and active participation.

8.4.3 Consent forms
The standard for research consent is written, informed, and voluntary. The EC may, however, take into account the following sorts of consent for particular research.

Box 8.2 Types of consent

• Verbal/oral consent: With the required EC approval and the necessary paperwork, verbal/oral consent or pseudonyms may be appropriate for research on sensitive themes. • Broad consent: If a person has the opportunity to opt out, consultations may be performed only with a small representative sample of the target population. • Group consent: Cluster randomised trials (CRT), IR, and demonstration projects are examples of situations in which ethics committees (ECs) must make decisions regarding the difficult questions of viability and the kind of participant consent to be sought.

The EC should approve the procedure for acquiring such forms of consent and the supporting paperwork.

8.4.4 Absence of consent The majority of epidemiological and public health research would adhere to accepted standards for informed consent. However, under the circumstances listed in Box 8.3, the EC may take into account consent waiver.

Box 8.3 Waiver of consent in public health research

Based on routinely collected data under programme settings, including research including connection to sizable anonymous databases of data that have been routinely acquired like administrative data and

through surveillance activities. However, the individuals concerned may have been informed that the data would be used for other purposes, such as research, at the time of collection;
• in situations where obtaining consent is impractical, such as for stored anonymous data/biological samples, surveillance and administrative data, or personal non-identifiable information
data or materials from public health initiatives;
The following studies may be exempt from the requirement for informed consent:
• studies carried out within the purview of regulatory and public health authorities, such as process and impact evaluations of national policies and programmes, including neonatal screening programmes or diabetes screening as part of national programme activities;
• studies whose main objective is the improvement of public health programmes; and
• studies using authorised health-related registries.
• When obtaining consent for cluster randomization trials and several IRs in vast geographic clusters is not feasible or useful.

Re-consent is required in longitudinal studies when the protocol is changed, new information is sought, a new intervention is implemented, or new information becomes available that may have an impact on the safety of the participants. There is no requirement for new consent if the study protocol remains unchanged. Other requirements for re-consent are outlined in section 5 and must be adhered to.

8.5 The EC's Function

8.5.1 ECs shall confirm that the researcher has taken the necessary steps to protect the security of the data, the privacy of the information, get disclosure authorization, and declare the proper use of the data obtained.

8.5.2 EC members must accord these studies' potential effects on social benefit, public good, and public health the proper weight. Consent decisions must be made by the ECs on a case-by-case basis.

8.5.3 The EC should ask or solicit input from public health experts when holding the appropriate meeting, or the EC should include public health experts in its membership.

8.5.4 When evaluating a study on public health, the following factors should be taken into account:
· the requirements for public health care.
The researcher is responsible for scaling up, advocating for, promoting uptake, or maintaining the public health intervention. Stakeholder involvement entails identifying and defining stakeholders' roles, particularly in IR, health systems, and policy research.

8.6 Guarding participants and locals

8.6.1 Special provisions should be made when planning and carrying out public health studies that could potentially take advantage of study subjects, particularly those from socioeconomically disadvantaged backgrounds.

8.6.2 People with limited access to healthcare might mistakenly believe that participating in the research entitles them to financial rewards as well as medical care and other benefits.

8.6.3 ECs must think about these problems in a proactive and thoughtful manner. To protect the welfare of members of the same community who have not engaged, specific procedures should also be put in place.

8.7 Stakeholders in public health research

8.7.1 It is important for ethical conduct of research to engage with all stakeholders, such as researchers, public health providers/professionals, sponsors, government agencies, participants, ECs, institutions, NGOs, and others who are involved in public health research in any manner.

8.7.2 The involved stakeholders must make every effort to provide post-research public health interventions, post-research use of the findings, or sustainability of the public health action.

PRINCIPAL
KIMS DENTAL COLLEGE
& HOSPITAL
AMALAPURAM, E.G.Dt.(A.P

DR V SHIVA KUMAR

(Principal, KIMS Dental College & Hospital)