Medical Research

Research is indisputably an integral part of medicine. "Research" means "systematic investigation and study in order to establish facts and reach new conclusions" (The Pocket Oxford Dictionary, 1984).

Knowledge gained through research has provided answers to the etiology of many diseases and facilitated treatment strategies that have improved the health and quality of life. Everyday scientists are constantly engaged in research to unravel the mysteries of many more. It is the need of the hour as it will impact the health of generations to come.

With so many researches being conducted today and the race to provide the right answer first, there is a risk of bypassing or side stepping some of the rules. In its guidelines on biomedical research, the Indian Council of Medical Research (ICMR) has said, "While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects". Medical research must therefore conform to ethical standards and ensure protection of the health and rights of the participants.

PRINCIPLES OF ETHICS IN MEDICAL RESEARCH

- The Nuremberg Code of 1947 was the first international treatise on the ethics of research involving human beings and highlighted the essentiality of obtaining voluntary consent.
- In 1964, the World Medical Association formulated guidelines on conducting research on humans, known as the Declaration of Helsinki. This has undergone seven revisions with the latest version being issued in October 2013 at Fortaleza, Brazil.
- In 1979, the Belmont Report released by the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research in the United States of America (USA), for the first time enunciated the three basic ethical principles for research involving human subjects: respect for persons, beneficence and justice.
- UNESCO's Universal Declaration on Bioethics and Human Rights (2005) and other international instruments on human rights further defined the Universal Codes of Ethics to be adopted by the member countries.

Research is essential for progress of medicine, yet it falls upon those striving to find answers to the mysteries of science to ensure that all research involving human participants should be conducted in accordance with the four basic principles of ethics in healthcare viz. autonomy (respect for person/s) beneficence, non-maleficence (do no harm) and justice. Ethics are as important as the quality of research.

The "Indian Council of Medical Research National Ethical Guidelines for Biomedical and health Research involving human participants 2017" guidelines have expanded these four basic principles into 12 general principles described below. These are common to all areas of biomedical research for health involving human participants, their biological material and data.

The 12 general principles of ethics in medical research are:

1. **Principle of essentiality** whereby after due consideration of all alternatives in the light of existing knowledge, the use of human participants is considered to be essential for the proposed research. This should be duly vetted by an ethics committee (EC) independent of the proposed research.
2. **Principle of voluntariness** whereby respect for the right of the participant to agree or not to agree to participate in research, or to withdraw from research at any time, is paramount. The informed consent process ensures that participants' rights are safeguarded.
3. **Principle of non-exploitation** whereby research participants are equitably selected so that the benefits and burdens of the research are distributed fairly and without arbitrariness or discrimination. Sufficient safeguards to protect vulnerable groups should be ensured.
4. **Principle of social responsibility** whereby the research is planned and conducted so as to avoid creation or deepening of social and historic divisions or in any way disturb social harmony in community relationships.
5. **Principle of ensuring privacy and confidentiality** whereby to maintain privacy of the potential participant, her/his identity and records are kept confidential and access is limited to only those authorized. However, under certain circumstances (suicidal ideation, homicidal tendency, HIV positive

status, when required by court of law etc.) privacy of the information can be breached in consultation with the EC for valid scientific or legal reasons as the right to life of an individual supersedes the right to privacy of the research participant.

6. **Principle of risk minimization** whereby due care is taken by all stakeholders (including but not limited to researchers, ECs, sponsors, regulators) at all stages of the research to ensure that the risks are minimized and appropriate care and compensation is given if any harm occurs.
7. **Principle of professional competence** whereby the research is planned, conducted, evaluated and monitored throughout by persons who are competent and have the appropriate and relevant qualification, experience and/or training.
8. **Principle of maximization of benefit** whereby due care is taken to design and conduct the research in such a way as to directly or indirectly maximize the benefits to the research participants and/or to the society.
9. **Principle of institutional arrangements** whereby institutions where the research is being conducted, have policies for appropriate research governance and take the responsibility to facilitate research by providing required infrastructure, manpower, funds, and training opportunities.
10. **Principle of transparency and accountability** whereby the research plan and outcomes emanating from the research are brought into the public domain through registries, reports and scientific and other publications while safeguarding the right to privacy of the participants. Stakeholders involved in research should disclose any existing conflict of interest and manage it appropriately. The research should be conducted in a fair, honest, impartial and transparent manner to guarantee accountability. Related records, data and notes should be retained for the required period for possible external scrutiny/audit.
11. **Principle of totality of responsibility** whereby all stakeholders involved in research are responsible for their actions. The professional, social and moral responsibilities compliant with ethical guidelines and related regulations are binding on all stakeholders directly or indirectly.
12. **Principle of environmental protection** whereby researchers are accountable for ensuring protection of the environment and resources at all stages of the research, in compliance with existing guidelines and regulations.

The National Medical Commission Registered Medical Practitioner (Professional Conduct) Regulations, 2023 also say that "*the registered medical practitioner should protect and minimize risk of patients who participate in medical research, conscious that the dual role as researcher-practitioner would require disclosure to patients and additional regulatory and ethical compliance*". Further, "*clinical drug trials or other research involving patients or volunteers must comply with ICMR guidelines and the New Drugs and Clinical Trials Rules, 2018. Consent taken from any patient or participant for the trial of drug or therapy which is not as per the guidelines shall be construed as misconduct*".

INFORMED CONSENT PROCESS

Informed consent protects the individual's autonomy to freely choose whether or not to participate in the research.

Informed consent is a continuous process involving three main components – providing relevant information to potential participants, ensuring competence of the individual, ensuring the information is easily comprehended by the participants and assuring voluntariness of participation. Informed voluntary consent protects the individual's freedom of choice and respects the individual's autonomy. Informed consent should explain medical terminology in simple terms and be in a language that the participant understands. Documentation of the informed consent process is an essential part of this exercise.

For all biomedical and health research involving human participants, it is the primary responsibility of the researcher to obtain the written, informed consent of the prospective participant or legally acceptable/authorized representative (LAR). In case of an individual who is not capable of giving informed consent, the consent of the LAR should be obtained.

The informed consent document (ICD), which includes patient/participant information sheet (PIS) and informed consent form should be reviewed and approved by the Ethics Committee before enrolment of participants.

REQUISITES FOR CONSENT

- 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.

- The consent should be given voluntarily and not be obtained under duress or coercion of any sort or by offering any undue inducements.
- In the case of an individual who is not capable of giving voluntary informed consent, the consent of LAR must be obtained.
- It is mandatory for a researcher to administer consent before initiating any study related procedures involving the participant.
- It is necessary to maintain privacy and confidentiality of participants at all stages.

An informed consent form must include the following:

- Statement mentioning that it is research.
- Purpose and methods of the research in simple language.
- Expected duration of the participation and frequency of contact with estimated number of participants to be enrolled, types of data collection and methods.
- Benefits to the participant, community or others that might reasonably be expected as an outcome of research.
- Any foreseeable risks, discomfort or inconvenience to the participant resulting from participation in the study.
- Extent to which confidentiality of records could be maintained, such as the limits to which the researcher would be able to safeguard confidentiality and the anticipated consequences of breach of confidentiality.
- Payment/reimbursement for participation and incidental expenses depending on the type of study.
- Free treatment and/or compensation of participants for research-related injury and/or harm.
- Freedom of the individual to participate and/or withdraw from research at any time without penalty or loss of benefits to which the participant would otherwise be entitled.
- The identity of the research team and contact persons with addresses and phone numbers (for example, PI/Co- PI for queries related to the research and Chairperson/Member Secretary or helpline for appeal against violations of ethical principles and human rights).

In addition, the following elements may also be required, depending on the type of study:

- Any alternative procedures or courses of treatment that might be as advantageous to the participant as the ones to which she/he is going to be subjected.
- If there is a possibility that the research could lead to any stigmatizing condition, for example.
- HIV and genetic disorders, provision for pretest- and post-test counseling.
- Insurance coverage if any, for research-related or other adverse events.
- Foreseeable extent of information on possible current and future uses of the biological material and of the data to be generated from the research.

WAIVER OF CONSENT

The researcher can apply to the EC for a waiver of consent if the research involves less than minimal risk to participants and the waiver will not adversely affect the rights and welfare of the participants. The EC may grant consent waiver in the following situations:

- Research cannot practically be carried out without the waiver and the waiver is scientifically justified.
- Retrospective studies, where the participants are de-identified or cannot be contacted.
- Research on anonymized biological samples/data.
- Certain types of public health studies/surveillance programs/program evaluation studies.
- Research on data available in the public domain.
- Research during humanitarian emergencies and disasters, when the participant may not be in a position to give consent. Attempt should be made to obtain the participant's consent at the earliest.

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