**Evolution of ICMR ethical guidelines from 1980 to 2017**

**Abstract:**

The Indian Council of Medical Research felt the need for standard national requirements of Biomedical research and issued a policy statement on ethical considerations involved in human subjects in 1980. With rapid evolution and adoption of science and technologies in the field of Biomedical research and changes in concepts of morality and philosophy, the guidelines incorporated many changes to cater to the needs of the advancing technological development and adopted International guidelines with modifications that suit to our population with varied social, cultural and religious backgrounds. The National Ethical Guidelines for biomedical and health research involving human participants, National Guidelines for Stem Cell Research, National ethical guidelines for Biomedical Research involving children released in 2017 has become the reference document both by the researchers and Ethics Committee members and the Stakeholders for all biomedical research conducted in India.

**Keywords:** Indian Council of Medical Research, Biomedical research, Institutional Ethics Committee

**Introduction:**

Though there were existence of International guidelines like “The Nuremberg Code of 1947”, Universal declaration of Human rights, Geneva (1948), Declaration of Helsinki (1964), Belmont report (1979) and National guidelines like Schedule Y of the Drugs and Cosmetic act (1940), Code of Medical ethics, MCI (1956), the need for standard national requirements was felt by the Indian Council of Medical Research (ICMR) to protect and safeguard the rights, dignity and wellbeing of the research participants and to prevent them being exploited by unethical experiments.

**Evolution of the ICMR guidelines:**

ICMR issued a policy statement on ethical considerations involved in research in human subjects in the year 1980. With rapid evolution and adoption of science and technologies in the field of Biomedical research and better insights about disease pathogenesis paving way for discovery of newer medical treatments, there is a need to modify the ethical guidelines from time to time and hence ICMR released the revised guidelines in the year 2000. Even after the release of these guidelines in 2000, violation of ethical norms were observed in many researches like John Hopkins-RCC collaboration trials, VEGF trial in New Delhi, Genetic research on tribals funded by NIH. Hence Indian Medical Council amendment in 2002 and Drugs and Cosmetics Act amendment: Schedule Y in 2005 indirectly mandated the following of the ethical guidelines.

Changes in concepts of morality and philosophy as to what is right and wrong drived the guidelines to undergo drastic revisions from time to time. What was considered wrong in ancient times is now considered right. As guidelines evolved, this document adopted guidelines from World Medical Association guidelines on conducting research (Declaration of Helsinki) (7th version 2013), Federal policy for the protection of Human Subjects as the ‘Common Rule’ in 1991(Revision 2017) released by the Department of Health and Human Services (DHHS), USA, Good Clinical Practice Guidelines E6 (R1) in 1996 [Revision E6 (R2) in 2016] by the International Conference on Harmonization (ICH), Recommendations of National Bioethics Advisory Commission, USA (2001), Council for International Organizations of Medical Sciences (CIOMS), Geneva (2002, revised in 2016), Nuffield Council of Bioethics, UK (2002) and it incorporated the same to suit our varied social, cultural and religious diverse populations.

Although ethical guidelines are undergoing repeated revisions, the basic concepts remained the same. With each revision, care was given to the finer details and was represented more elaborately. Many new topics were added, irrelevant topic removed and many concepts elaborated.

Table.1 highlights the evolution of the title and pages of the ICMR guidelines from 1980 to 2017.

**Contents of the guidelines**:

The 1980 guidelines document was only 9 pages and outlined the major rules to be followed in biomedical research. It covered the need for Institutional Ethics committee (IEC) and implementation of the ethical committee’s guidelines. Topics like support of clinical research by the council and other agencies, drug trials, clinical trials with plants and indigenous systems of medicine were covered. The importance of Informed consent was highlighted and the clinical research on vulnerable population like children, mentally deficient subjects, prisoners, medical students and laboratory personnel was dealt. It also dealt the financial reimbursements to the study subjects participating in the clinical research projects and the publication of research papers in Indian Journal of Medical Research.

**Changes incorporated in Ethical Guidelines for Biomedical Research on Human Subjects in 2000**

It included new topics like clinical evaluation of drugs/devices/diagnostics/ vaccines/herbal remedies, epidemiological studies, human genetics research, transplantation including foetal tissue transplantation and Assisted reproductive technologies.

**Changes incorporated in Ethical Guidelines for Biomedical Research on Human Participants” in 2006**

The 2006 guidelines document was much more elaborate with 120 pages. The various topics were classified into chapters with a total of 8 chapters. The topics were similar to the 2000 guidelines with following changes:

* Two new subtopics on *conflict of interest* and *post trial access* were included in the topic on *General ethical issues.*
* *Bioavailability studies* was included in drug trials in chapter on *Statement of specific principles for clinical evaluation of drugs/devices/diagnostics/vaccines/herbal remedies*.
* *Community participation* was added to the specific principles in chapter *Statement of specific principles for epidemiological studies*.
* The term *genomics research* was added to the chapter on genetic research, since an important milestone was achieved in the year 2003, the human genome project was completed. Thus, the chapter title is *Statement of specific principles for human genetics and genomics research*. Also biobanking was included in detail in this chapter.
* A sub-topic on *Stem cell* was included as a part of *Statement of specific principles for research in transplantation*.

**Changes incorporated in “National Ethical Guidelines for biomedical and health research involving human participants” in 2017**

The 2017 guidelines document has many new topics added, some deleted and some topic written in more detailed manner. It consists of 187 pages and the various topics are classified into 12 sections with sub-sections. New topics like Responsible conduct of research, Public health research, Social and Behavioral Sciences Research for Health (for first time ethical guidelines on qualitative research has been formulated in 2017 ICMR guidelines), Datasets in section on *Biological Materials, Biobanking and Datasets* were included.

The topics that were deleted from 2017 ICMR guidelines are:

* Statement of specific principles for research in transplantation including foetal tissue transplantation
* Statement of specific principles for assisted reproductive technologies

This is because separate guidelines named *ICMR -DBT Guidelines for Stem Cell Research and Therapy* was formulated for research using stem cells in the year 2006 and later revised in 2017 as *National guidelines for stem cell research* and hence title on principles for research in transplantation was removed. The title on principles for assisted reproductive technologies (ART) was also deleted in 2017 guidelines because ART is mainly therapeutic and hence it need not be included in guidelines for biomedical research. Moreover, a separate “National Guidelines for Accreditation, Supervision and Regulation of ART Clinics in India” was formulated in the year 2005.

The topics/sections like Informed consent process, Vulnerability and Biological Materials, Biobanking and Datasets, Research during Humanitarian Emergencies and Disaster were further elaborated and formulated as separate sections in 2017 ICMR guidelines.

**General statement**

The general statement in 2000 and 2006 ICMR guidelines was removed in the 2017 guidelines.

**Statements of general principles:**

The basic 12 statements of general principles formulated in 2000 guidelines remained the same till 2006. In 2017, minor alterations were made. Out of the 12 general principles in 2006 ICMR guidelines, 3 principles - the Principles of the maximization of the public interest and of distributive justice, Principles of public domain and Principles of compliance were removed and replaced by Principle of Social Responsibility, Principle of Maximization of Benefit and Principle of Environmental Protection.

**General Ethical Issues**

In “general ethical issues” section of 2017 ICMR guidelines, an additional risk category called as “minor increase over minimal risk” has been added compared to previous 2006 guidelines. Also in this section, subsections like “distributive justice”, “payment for participation” and “ancillary care” were included in 2017 guidelines. Also the subsection on “post-trial access” was modified as “post research access and benefit sharing” in 2017 guidelines.

Evolution of changes in the guidelines for Ethical review procedures in ICMR guidelines from 1980 to 2017 are shown in Table.2 .Although these changes were made in the guidelines for Institutional ethics committee, the basic motto or responsibility of the IEC remains the same and has stood the test of time. It is to safeguard the dignity, welfare and rights of potential research participants and to ensure that research on humans is conducted in an ethical manner.

With regard to submission of application to IEC formulated in 2000 guidelines, an addition of study title with signature of investigators must be present in the protocol.

Compared to the 2006 ICMR guidelines, the following subtopics have been added/modified in the section on “ethical review procedures” in the 2017 ICMR guidelines.

* Table on “Composition, affiliations, qualifications, member specific roles and responsibilities of an Ethics Committee” has been added.
* Table on “Ethical issues related to reviewing a protocol” has been added.
* A box on “Types of decisions by Ethics Committee” has been added.
* A subsection on “Review of multicentric research” has been added.
* In site monitoring – cause monitoring and a box on “examples for cause monitoring” has been added.
* “Documents to be maintained by EC for record” has been modified and classified based on “type of document” into “administrative related documents” and “proposals-related documents”.
* Registration and accreditation of Ethics committees has been added.

**Clinical trials of drugs and other interventions**

In this section in 2017 ICMR guidelines, the following topics not present in chapter on “Statement of specific principles for clinical evaluation of drugs/devices/diagnostics/vaccines/herbal remedies” in the previous 2006 guidelines were added.

* Biologicals and biosimilars
* Clinical trials with stem cells
* Surgical interventions ( including Conditions for sham surgery)
* Community trials (public health interventions)
* Clinical trials of interventions in HIV/AIDS
* Investigator initiated clinical trials
* Clinical trials on contraceptives
* Clinical trials in oncology
* Clinical trials of products using any new technology
* Synthetic biology

**Human genetics testing and research**

* In this section in 2017 ICMR guidelines, the following topics have been added and they were not present in 2006 guidelines. The Topics like Culturally sensitive issues, storage of samples for future genetic research, results of genetic testing, publication aspects, Commercialization and COI, Misuse of genetic technology, Population screening, Pre-implantation genetic screening and diagnosis, Screening for carrier status, Use of newer technologies - Chromosomal micro array, Whole exome sequencing and whole genome sequencing, Gene editing technology – Clustered, regularly interspaced, short palindromic repeat (CRISPR), Genome-wide association study (GWAS), Research on human embryos and Foetal autopsy were included in the Human genetics testing and research.

Many new issues like sexual minorities (LGBT – Lesbian Gay Bisexual and Transgender), PVTG – Particularly Vulnerable Tribal Groups were included. The topics like Biologicals and biosimilars, Community trials, Clinical trials of interventions in HIV/AIDS, Clinical trials on contraceptives, oncology and Investigator initiated clinical trials were included.

**Highlights of current ICMR guidelines 2017 :**

* Previous grey zones have been clarified.
* These guidelines can be used as a reference document both by the researchers and Ethics Committee members and the Stakeholders.
* Easy to reference or clause it. More organized as guidelines evolved. Colorful and visually appealing.
* At the end of the guidelines, separate segments like Suggested further reading, Abbreviations and acronyms and Glossary are included to guide the reader further. Annexure 1 contains list of Standard Operating procedures and Annexure 2 contains list of members of committees involved in revision of guidelines (2015-2017).
* The language of the guidelines is simple so that even the lay person in the ethics committee can understand it.
* Even Undergraduate students can understand the guidelines and especially students who do STS projects can be instructed to read it and follow it.

**Conclusion:**

Thus, with evolution, the ICMR guidelines became more organized, refined and elaborate. Also many ambiguities present in the previous guidelines were clarified. The guidelines incorporated many additions and deletions to cater to the needs of the advancing technological development and recent advances in the field of medicine. Also the guidelines was developed to suit to our population with varied social, cultural and religious backgrounds. Thus, it has become the reference document for all biomedical research conducted in India.

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