**Commentary on Revision of**

**National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017**

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Indian Council of Medical Research (ICMR) is the apex body for formulation, coordination and promotion of biomedical research in India and is well recognised globally for its landmark initiatives in formulating ethical guidelines for biomedical research. One year after release of Belmont Report in 1979, ICMR had issued a Policy Statement related to ethical aspects of human research in 1980 (1). In line with the advances in medical research, ICMR updated the ethical guidelines in 2000 (2) and then in 2006 (3). The third revision become overdue since lot of scientific and technical advances were posing ethical challenges that continued to emerge at a fast pace. A need was felt to have additional guidance in areas such as responsible conduct, research during emergency situations, public health and socio behavioural research as well as using stored biological material and data. In October, 2015, the first meeting of the Core Advisory Group decided the topics to be included in the latest revision and the approach to involve various stakeholders – bioethicists, researchers, ethics committees, institutions, sponsors and all other interested parties including the public in the process of revision. In order to have extensive participation, the core committee appointed a sub-committee for each of the 12 identified topics comprising of 48 members. They were drawn from various research organisations and included trained bioethicists and ethics committee members besides clinician and researchers. Following a series of meetings, an initial draft capturing the latest national requirements and global standards was circulated for comments.

**Core Advisory Group consisted of Dr Vasantha Muthuswamy (Chairperson), Dr SD Seth (Co-Chairperson) and members Dr Nandini K Kumar, Dr NK Arora, Dr Urmila Thatte, Dr Vijay Kumar and Dr Roli Mathur (Member Secretary)**

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**Table 1: List of sections in the National Ethical Guidelines for Biomedical and Health Research involving Human participants, 2017**

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| **SN** | **Sections** |
|  | Statement of general principles |
|  | General ethical issues |
|  | Responsible conduct of research |
|  | Ethical review procedures |
|  | Informed consent process |
|  | Vulnerability |
|  | Clinical trials of drugs and other interventions |
|  | Public health research |
|  | Social and behavioural sciences research for health |
|  | Human genetics testing and research |
|  | Biological materials, biobanking and datasets |
|  | Research during humanitarian emergencies and disasters |

Efforts were made to consult clinicians, scientists, lawyers, social scientists, civil society, patient representatives and public from across the country to ensure responsiveness to the health needs while accommodating our varied socio-cultural ethos. WHO-Country Office India partnered with ICMR Bioethics Unit and supported two consultation programs at the regional and national level (4). The regional consultation program was organised on 4th Oct 2016 at Bangalore and was attended by relevant stakeholders from all across the various regions of the country attended and provided valuable suggestions. In the National Consultation meeting held on 14th Dec 2016, at New Delhi, stakeholders from the various public as well as private institutions, various relevant Government Departments and agencies, Members of Central Ethics Committee on Human Research (CECHR), International agencies and others provided relevant feedback. Comments received from Individuals, institutions, agencies, industry, associations both national and International, through public consultation, regional and national consultations were extensively discussed for updating the draft document. In addition a number of separate expert group meetings were held to get relevant advice in specific areas such as Ethical Review Procedures, Public Health Research, Socio behavioural research, Human Genetic Testing and Research, Clinical Trials, New technologies etc.

The National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017 was released on 12th Oct 2017 by Hon’ble Union Minister of Health and Family Welfare at ICMR (5). It is a detailed document covering a wide range of topics in which the existing chapters have been updated and newer sections of current importance were added. The general principles in the present document have been simplified in language for easy understanding. The principles of social responsibility and environmental protection have been added in order to stress upon the need for protecting the social and cultural harmony and conserve our limited resources in the conduct of biomedical and health research. In the general ethical issues section, risk categorisation has been added which would help ethics committees (EC) conduct a more objective benefit risk assessment. The earlier version of Ethical Guidelines had separate chapters on transplantation and assisted reproductive technologies which were removed in this version because they are more applicable to medical practice. Some topics given in brief in the earlier version were expanded into complete sections, such as informed consent, vulnerability, biological materials and biobanking. Newer sections were created to cover areas like responsible conduct of research (including publication ethics), public health research, socio behavioural research and research during humanitarian disasters and emergencies. Another important inclusion in the revised guidelines is the introduction of research using datasets which has now been added to the section on biological materials and biobanking since the basic ethical requirements for both are common. The chapters on ethical review procedures, clinical trials, and genetics research have also been also elaborated considerably and will be helpful for researchers as well as EC in their functions.

Guidance was needed for researchers in the country regarding responsible conduct of research (RCR) since there is lack of formal education/ training on this. The newly created section on RCR will help the scientist understand the measures required for data acquisitions, management and sharing, collaboration (including both national and international), responsible authorship and publication ethics.

In the section on ethical review procedures, each EC member’s affiliation, qualification, role and responsibilities have been described to remove the existing confusion about their appointment, composition and quorum. It is hoped that the document would help, especially the non-medical members to have more clarity about their role and responsibilities and make their participation more meaningful and effective in the EC meetings than just to fulfil the quorum. In addition efforts have been made to harmonize and explain the differences between regulatory and non-regulatory/ academic clinical trials. Clear guidance has been given regarding setting up of independent ethics committee or when and how services of other ECs can be utilised. Review of multicentre research has been a challenge in view of the varied requirements put forth by the different participating ECs. For the first time, in India, the guidelines have proposed that a common EC may be identified from the participating sites to act as the main designated EC. This can have representatives from ECs of other participating sites and a common review can be carried out. At present this provision is suggested for low risk multicentre research but it is hoped that this would greatly reduce time and effort required in reviewing a common proposal at multiple sites. Also this process would help to initiate a dialogue among the concerned EC and build an EC network with communication channels. In the long run this would help to streamline and strengthening ethical review systems.

The guidelines advice EC’s to undertake regular monitoring of research and explain conditions when site monitoring may be essential. Institutions are now requested to make adequate provisions (manpower, infrastructure, funds) to run the ethics committee office smoothly. EC work should no longer be regarded as a part time voluntary activity but would require protected time of member secretary to improve EC efficiency. The guidelines have explained the need for building quality EC systems, build conflict of interest policies and stresses upon the need for registration of EC as well as its participation in national or international recognition or accreditation programs.

Guideline have not only highlighted the need for payment of compensation in case of research related injury, but also suggested mechanisms for putting a system in place to make such payments. At present only sponsored clinical trials may have the provision for paying compensation for research related injury, since that is required by law, however there a is complete lack of clarity regarding payment of compensation in academic or investigator initiated or non-funded research. The institutions where research is conducted will now be required to create corpus fund or to seek insurance coverage or to seek grants to cover for compensation if required to be paid to research participants.

There is a full section on informed consent process detailing the information required to be effectively communicated for understanding and to seek voluntary consent of the participant. High risk research may require even a test of understanding. There is a description regarding use of electronic methods for seeking consent, waiver of consent, re-consent/fresh consent, consent under special situations involving gatekeepers, community and vulnerable groups obtaining assent for children and processes involved after obtaining consent etc.

The guidelines describe the additional protections needed for conducting research involving vulnerable people. Besides women and children, others such as, sexual minorities, sexual workers, tribal populations, persons who are cognitively affected/impaired, those with reduced autonomy, terminally ill patients or those who are economically and socially disadvantaged may be vulnerable and this must be determined. The underlying principle is that since they are unable to protect themselves adequately they are prone to exploitation and need protection. The Guidelines also discuss the need to be inclusive so that no group is deprived of the probable benefits from research.

The clinical trials section has been expanded considerably and guidance has been included regarding investigator initiated trials, academic research, student research, multicentre trials or those involving communities, or traditional systems of medicine or using new technologies etc. The importance of a priori arrangements for post-trial access and benefit sharing after completion of research has been highlighted and this is to ensure that the outcomes are translated back to participants or communities and do not remain limited to publication alone. It is clarified that the clinical trials protocols for marketing approval of products need to follow the Drugs and Cosmetics Act and its Rules and the amendments from time to time (6). The need for registration of all such trials under the Clinical Trial Registry of India has also been highlighted (7).

The epidemiology chapter of the earlier guidelines has been replaced with Public Health Research section. In this subject there is an overlap between service and research and therefore ethical aspects are often not clearly understood. This section has provided specific guidance for the conduct and review of surveys, implementation research, demonstration projects, community trials, surveillance studies, program evaluation studies etc. Relevance of informed consent and EC review depending on type of research has been elaborated.

A new section on ethical aspects of social and behavioural research related to health has been included for the first time. In this arena, there was lack of clarity about the requirements such as review by EC, informed consent and others. In addition sometimes socio behavioural research involves research on sensitive topics or involves risk, which require more guidance. The guidelines discuss the need for community engagement whenever possible and to understand their requirements and health needs of the participants. It suggests the need for reaching out to leaders, community advisory boards, or community representatives or having them participate in EC discussions so that research is more responsive and customized to be health needs of the community.

In Genetics section, the distinction between testing for clinical services verses research has been addressed. The importance of genetic counselling as well as having appropriate safeguards to maintain privacy and confidentiality is explained in order to prevent stigma or discrimination. Ethical issues specific to different types of screening programs such as prenatal or new-born screening are explained. Newer technologies, especially the recent CRISPR technology and the ethical dilemmas that it poses are discussed and there is a hope that this would show a way forward for research despite the unclear challenges to human health and safety.

The section on biomaterials, biobanking and datasets makes it clear that the donor is the owner and the researcher and institutions are only custodians of the materials and the data. The different options for consent, maintenance of confidentiality, use of left over clinical samples, long term storage, return of results and benefit sharing are explained and should be considered by researchers, biobanks, forensic laboratories and ECs.

The last section on research on humanitarian emergencies and disasters, has been prepared on account of the recent domestic and international events like the Tsunami, Chennai floods, Ebola and Zika virus infection which necessitated emergency research. The requirements for emergency review by EC, prior preparedness, consent documentation, sensitivity involved in dealing with affected community and planning as well as protection from invasion into privacy are described while balancing the need for conducting research.

In order to increase the awareness and use of ICMR’s ethical guidelines by researchers, EC members and others, series of dissemination programs are being organised across the country. The first such event took place on 16th Nov 2017 at All India Institute of Medical Sciences, New Delhi and then on 14th Dec 2017 at Postgraduate Institute of Medical Education and Research, Chandigarh followed by Dissemination programs on 7th Feb 2018 at Chennai and 17th Feb, 2018 at Bhubaneswar, which were attended by researchers, EC members, clinicians, students from medical colleges, dental colleges, pharmacy, nursing colleges, research institutions, NGOs, patient representatives, sponsors, government agencies and other stakeholders. ICMR Bioethics Unit, National Centre for Disease Informatics and Research (NCDIR) and Clinical Development Services Agency (CDSA) under the Translational Health Sciences and Technology Institute (THSTI) have further collaborated and four such events were organised; on 30th Nov, 2017 at Ahmedabad, 21st Dec 2017 at Visakhapatnam, 22nd Feb, 2018 at Kochi and on 8th March 2018 at Guwahati. Many more dissemination programs are being planned across the country during this year in order to reach out to people and create awareness. The guidelines have also been made available on ICMR website [www.icmr.nic.in](http://www.icmr.nic.in) and on NCDIR website [www.ncdirindia.org](http://www.ncdirindia.org) and can be downloaded at no cost.

Clinical trials for marketing approval are regulated under Drugs and Cosmetics Act and Rules (6) and the biomedical and health research must follows the ICMR National Ethical Guidelines. There is therefore a need to harmonize and make sure that research participants whether participating in clinical trial, or basic or applied biomedical, health or socio behavioural research can be protected.

Unfortunately in our country, ethics is still not part of existing curriculum, both medical and non-medical, and for quality outputs in biomedical and health research and for ensuring protection of human participants, ethical conduct of research is essential. ICMR National Ethical Guideline document sets the standards for the ethical requirements to be followed in India. It is expected that all biomedical and health research in the country should follow the guidance which would greatly help to improve quality and outcomes of research.

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