COMMENTS

National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017: A commentary

ROLI MATHUR, SOUMYA SWAMINATHAN

Abstract

The Indian Council of Medical Research (ICMR) has been at the forefront in setting up the ethical guidance for the conduct of biomedical and health research in India. The latest version of National Guidelines for Biomedical and Health Research Involving Human Participants, 2017 was planned in order to provide a more detailed guidance to the existing topics in view of emerging ethical concerns and to add a number of newer areas in which guidance was lacking. The scope of the guidelines has been expanded to include socio-behavioural research related to health and research involving biological material and datasets. The guidelines have 12 sections which cover a wide range of topics and areas of research. The first six sections are more generic, applying to all types of biomedical and health research, while the next six sections are more subject specific. The guidelines have been revised in consultation with a large number of experts and stakeholders and went through an exhaustive process stretching over a period of two years in its drafting, review, consultation and finalisation. This commentary seeks to explain the process and key components of the Guidelines.

Introduction

The Indian Council of Medical Research (ICMR) is the apex body under the Department of Health Research (DHR), Ministry of Health and Family Welfare, Government of India 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 the release of the 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 had become overdue since a number of scientific and technical advances had been made and were posing serious challenges to ethical review and conduct of research. The need was felt to elaborate on existing guidance as well as to have additional guidance on topics such as, responsible conduct of research, public health and socio-behavioural research, conduct of research during emergency situations, use of stored biological material and data and others. In October 2015, the first meeting of the Core Advisory Group* set up by ICMR (5:Annex. 2.B) decided on the topics to be included in the latest revision and the approach to involve a variety of stakeholders in the process of revision. In order to ensure the widest possible participation, the core group appointed a sub-committee for each of the 12 identified topics, comprising of 48 members (5: Annex 2.C). They were drawn from various research organisations and included trained bioethicists and ethics committee members, clinician and researchers, sponsors and the public. Following a series of meetings, an initial draft capturing the latest national requirements and global standards was circulated for comments and was posted on the ICMR website for a period of eight weeks to obtain comments from the public.

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

SN	Sections
1	Statement of general principles
2	General ethical issues
3	Responsible conduct of research
4	Ethical review procedures
5	Informed consent process
6	Vulnerability
7	Clinical trials of drugs and other interventions
8	Public health research
9	Social and behavioural sciences research for health
10	Human genetics testing and research
11	Biological materials, biobanking and datasets
12	Research during humanitarian emergencies and disasters

Efforts were made to consult with stakeholders from across the country to ensure responsiveness to health needs while accommodating our varied socio-cultural ethos. The WHO-Country Office India partnered with the ICMR Bioethics Unit and supported two consultation programmes at the regional and national levels (4). The regional consultation programme was organised on October 4, 2016, at Bangalore and was attended by the relevant stakeholders from across various regions of the country, who provided valuable suggestions. At the National Consultation meeting held on December 14, 2016, in New Delhi, representatives of various public and private institutions, the relevant government departments and agencies, members of the Central Ethics Committee on Human Research (CECHR), international agencies, and others provided relevant feedback. Comments received from all these sources, through public consultation, both regional and national, were extensively discussed for updating of the draft document. In addition, a number of separate expert group meetings were held to get the 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, were released on October 12, 2017 by the 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 new sections of current importance have been added. The general principles in the present document have been simplified for easy understanding (5:Sec 1). The principles of social responsibility and environmental protection have been added in order to stress the need for protecting social and cultural harmony and conserving our limited resources in the conduct of biomedical and health research. In the General Ethical Issues section (5: Sec 2), the addition of the topic of risk categorisation will help ethics committees (EC) conduct a more objective benefit-risk assessment. The earlier version of the Ethical Guidelines had separate chapters on transplantation and assisted reproductive technologies, which were dropped in this version because they are more applicable to medical practice rather than to research.

Some topics dealt with in brief in the earlier version have been expanded into complete sections, such as those on informed consent, vulnerability, biological materials and biobanking. Newer sections were created to cover areas like the 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 for ethics committees (EC) in their day to day functioning.

Guidance was needed for researchers in the country regarding the responsible conduct of research (RCR) since there is a lack of formal education/ training on this. The newly created section on RCR will help the scientist understand the measures required for data acquisition, management and sharing, collaboration (both national and international), responsible authorship and publication ethics (5: Sec 3).

In the section on Ethical review procedures (5: Sec 4), each EC member's affiliation, qualifications, role and responsibilities have been described to remove the existing confusion about their appointment, composition of the committee, and quorum. It is hoped that the document will help, especially the non-medical members, to have greater clarity about their roles and responsibilities and make their participation at EC meetings more meaningful and effective beyond just fulfilling quorum requirements. In addition, efforts have been made to harmonise and explain the differences between regulatory and non-regulatory/academic clinical trials Clear guidance has been given regarding the setting up of independent ethics committees with special reference to when and how the 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 (5: Sec 4.2). This can have representatives from ECs of other participating sites and a common review can be carried out. It is hoped that this would greatly reduce the time and effort required for reviewing a common proposal at multiple sites and would help to initiate a dialogue among the concerned ECs and build an EC network with communication channels. In the long run, this would help to streamline and strengthen ethical review systems in the country.

The Guidelines advise ECs to undertake regular monitoring of research and explain conditions when site monitoring may be essential. Institutions are now requested to make adequate provision (manpower, infrastructure, funds) to run the ethics committee office smoothly. EC work should no longer be regarded as a part-time voluntary activity but as an essential function requiring protected time of the member secretary for efforts to improve EC efficiency. The Guidelines have explained the need for building quality EC systems, laying down conflict of interest policies, and stressed the need for registration of an EC as well as its participation in national or international recognition or accreditation programmes (5: Sec 4).

These Guidelines 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 is a 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 a corpus fund, or to seek insurance cover, or grants to cover compensation, if required to be paid to research participants.

There is an entire section on the informed consent process, detailing the information required to be effectively communicated for understanding and seeking voluntary consent of the participant (5:Sec 5). 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 (5: Sec 6). Besides women and children, others such as sexual minorities, sex 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 that are likely to emerge 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 (5:Sec 7). 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 into benefits and meaningful outcomes for participants or communities and do not remain limited to publication alone. It has been clarified that the clinical trials protocols for marketing approval of products need to follow the Drugs and Cosmetics Act 1940, and Rules, 1945, and the relevant 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, 5: Sec 7.1.10).

The epidemiology chapter of the earlier Guidelines has been replaced with the Public Health Research section (5:Sec 8). On 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 (5:Sec 9). In this area, 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 requires more guidance. The Guidelines discuss the need for community engagement whenever possible and to understand the requirements and health needs of the participants. They suggest the need for reaching out to leaders, community advisory boards, or community representatives or having them participate in EC discussions so that the research is more responsive to and customised for the health needs of the community.

There is a very narrow gap between routine genetic testing and research raising several ethical, legal and social issues warranting monitoring and responding to emerging ethical concerns (5: Sec 10). 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 programmes 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/ research participant owns the biological sample. For data that is collected, institutions are the custodians or trustees through their ECs and, researchers have no claim for either ownership or custodianship (5: Sec 11). The different options for consent, maintenance of confidentiality, use of left over clinical samples, transfer of biospecimens, 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 recent domestic and international events like the tsunami, the Chennai floods, and the Ebola and Zika virus infection which necessitated emergency research (5:Sec 12). The requirements for emergency review by the EC, prior preparedness, consent documentation, sensitivity involved in dealing with the affected community and planning as well as protection from invasion of privacy are described, while balancing these with the need for conducting research.

In order to increase the awareness of and use of ICMR's ethical guidelines by researchers, EC members and others, a series of dissemination programmes are being organised across the country. The first such event took place on November 16, 2017, at the All India Institute of Medical Sciences, New Delhi, on December 14, 2017, at the Postgraduate Institute of Medical Education and Research, Chandigarh, followed by dissemination programmes on February 7, 2018, at Chennai and on February 17, 2018, at Bhubaneswar. These 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 in organising four such events on November 30, 2017 at Ahmedabad, on December 21, 2017 at Visakhapatnam, on February 22, 2018, at Kochi and on March 8, 2018 at Guwahati. Many more dissemination programmes and trainings are being planned across the country during this year to reach out to people and create awareness. The Guidelines have also been made available on the ICMR website (www.icmr.nic.in) and on the NCDIR website (www.ncdirindia.org) and can be downloaded at no cost.

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

In our country, ethics is, unfortunately, still not part of the existing teaching curriculums in both the medical and non-medical streams. This influences both the quality of output in biomedical and health research and the protection of human participants for which the ethical conduct of research is essential. The ICMR National Ethical Guidelines document sets the standards for the ethical requirements to be followed in biomedical research in India. It is expected that all biomedical and health research in the country should follow this guidance which will go a long way towards improving the quality and outcomes of research.

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Note The 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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Benefit sharing in the revised Indian National Ethical Guidelines for Biomedical and Health Research Involving Human Participants

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Abstract

Though not an ethical principle per se, benefit sharing is still an important tool to achieve justice in international research. It comes back as a transversal issue through the revised Indian Ethical Guidelines for Biomedical and Health Research Involving Human Participants (hereafter referred to as "the Guidelines"). The guidelines invoke this principle with reference to the responsible conduct of research, ownership of biobanks and data repositories, informed consent process, community engagement, international collaborative research, and research in emergency or disasters, while using the phrase "maximization of benefit" instead of "benefit sharing". This approach may be seen as quite innovative, in that it sees benefit sharing (ie, maximisation of benefit) as a key ethical requirement. Unfortunately, it does not explicitly state that the principle is relevant to all research involving human participants, not only to specific situations such as biobanks,

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