AI-BADAR DENTAL COLLEGE AND HOSPITAL

ETHICAL GUIDELINES
FOR BIOMEDICAL AND HEALTH RESEARCH
INVOLVING HUMAN PARTICIPANTS

ALIGNED WITH

INDIAN COUNCIL OF MEDICAL RESEARCH-2018

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Content

The guidelines have 12 sections focusing on different areas of research and the corresponding ethical requirements. The initial 6 sections are more general and cover topics that apply to all types of biomedical and health research. The later 6 sections are more specific to the types of research carried out by researchers. The highlights of each section is provided in brief:

Section 1: Statement of General Principles

The first section presents the basic and general principles that govern biomedical and health research. The principles of "autonomy", "beneficence," "nonmaleficence" and "justice" are to be followed to protect the dignity, rights, safety, and well-being of research participants while undertaking biomedical and health research. The guidelines expand upon the basic principles and provides 12 general principles as given in [Table 1].

Table 1: General principles

Principle of essentiality
Principle of voluntariness
Principle of non-exploitation
Principle of social responsibility
Principle of ensuring privacy and confidentiality
Principle of risk minimization
Principle of professional competence
Principle of maximization of benefit
Principle of institutional arrangements
Principle of transparency and accountability
Principle of totality of responsibility
Principle of environmental protection

Principle of Social Responsibility and Principle of Environmental Protection have been added in the ethical guidelines and urge the scientists to become aware of their social responsibilities as well as to protect the limited resources available for research. The section highlights the need to review the purpose and essentiality of research objectives and justification for involving human participants in research. Selection of research participants should be done equitable to ensure that the benefits and burdens are distributed fairly. Participation has to be voluntary with an opportunity to discuss to agree or disagree to participate. Sufficient safeguards must be in place to protect vulnerable groups. Research should be carried out in a manner that there is enough trust building while ensuring adequate engagement with the involved communities and conducted in a manner that it preserves the social harmony. Researchers, institutions and ethics committees involved must be accountable for their decisions and must take due care to maximize benefits and minimize the harms or the risks involved while ensuring that the privacy and confidentiality of participants is protected. Institutions must provide required infrastructure, manpower, funds, training opportunities and research should be carried out by persons who are

competent and trained. It is also important to ensure that the results or outcomes are published and brought out in public domain after completion of research. Guidelines and regulations should be adequately followed and the researchers have the responsibility to keep themselves updated. The general principles lay the foundation to good ethical practices in biomedical and health research.

Section 2: General Ethical Issues

This section explains the general ethical issues involved in different types of research studies. An attempt has been made to explain the method of benefit-risk assessment which involves identification of both risks and probability of harm such as physical, psychological, social, economic or legal and also assessing the benefits whether direct or indirect extended to the individual, community or society for ensuring a favourable benefit-risk ratio. It is the duty of the stakeholders involved (researcher/ sponsor/organization, etc.) to safeguard identifying information of research participants in order to prevent against any unreasonable harm, stigmatization or discrimination. The participants invited for research should be selected equitably for fair distribution of benefits and burdens. Adequate safeguards must be put in place to protect vulnerable individuals/ groups and if the researcher would like to exclude vulnerable persons, it must be due to appropriate reasons and not just arbitrarily. This is important because a blanket exclusion of any particular group for unspecified reasons may also exclude them from the anticipated benefits that may be possible due to their participation in research. Due care should be taken to rule out any form of inequality due to racial, social, or ethnic reasons. Payment of compensation in case of injury was suggested even in earlier ethical guidelines (2006) but in the present

document, mechanisms to provide for compensation have been discussed to guide researchers and institutions to set up adequate systems. Institutions engaged in biomedical and health research can make provisions for an insurance cover, or create a corpus fund or seek grants from funding agencies to cover costs related to payment of compensation for research related injuries. This is applicable to all types of biomedical research including academic research. The concept of conflict of interest (COI) is generally not well understood by most of the stakeholders and at present, a lot of institutions do not have any policies to guide researchers. COI may exist at various levels, such as at the level of institutions, EC members, researchers and should be declared and managed appropriately. Institutions must not only have policies for declaration and management of COI but should also teach and sensitize their staff in this regard. Community engagement is essential for many types of research studies such as those involving particular communities. In order to efficiently answer the specific health needs, it is essential to understand the issues which are culturally sensitive and to tailor make the research to suit local needs and requirements. Post research access and benefits may also be provided to individuals, communities and populations, wherever possible and indirect benefits can be extended by establishing counselling centres, clinics, schools, etc. Prior planning is needed right at the time when the research is conceived and this needs to ascertained by the EC at the time of initial review.

Section 3: Responsible Conduct of Research

A new section on Responsible conduct of research (RCR) has been developed to describe the responsibilities of the scientist, in their pursuit for good science to also be aware about the ethical issues that are contemporary and the need to be sensitive to societal and cultural

requirements. Research institutions must invest manpower as well as resources to oversee grant management and promote responsible conduct of research. Policies for protection of research participants should be in place and roles and responsibilities assigned to EC and researchers by the institution. Applicable professional codes of conduct should be followed by the researchers. Research misconduct is not well understood though is a serious matter of concern and may involve plagiarism, falsification and fabrication of data. Researchers should be educated about this and needful monitoring should be carried out by the research institutions. In case of any allegations of research misconduct, the institution should investigate and make sure that the facts are presented accurately. Before planning publication, a number of safeguards are required. The "International Committee of Medical Journal Editors (ICMJE)" guidelines on authorship should be followed by the researchers. Prospective registration is required for clinical research involving human participants with the Clinical Trials Registry of India (CTRI) so that it improves accessibility, accountability and transparency. This section also discusses in detail about requirements for collaborative research and the need for having appropriate agreements in place. In collaborative research settings, needful measures can be taken to mask direct identifiers before sharing any confidential information. Needful permission and consent is required for placing data in public domain. Also the researchers must familiarize themselves with the local requirements, seek approvals, sign the agreements and obtain EC approvals from collaborating institutes. Local social and cultural sensitivities should be considered by the EC while reviewing protocols. In case of collaborative research including that conducted in international collaboration, the participating centres in India should function as equal partners in terms of ownership of data and samples, publications, IPR, etc., related to

research. Research involving international funding or international collaboration should be approved by the "Health Ministry's Screening Committee (HMSC)." Responsible conduct of research is very relevant to all researchers in the country and if followed, can greatly help to improve quality of research outcomes as well as safety of participants.

Section 4: Ethical Review Procedures

The section on ethical review process gives details about EC structure, composition, membership roles and responsibilities, etc., and will be useful to guide EC functioning across the country. The institution's engaged in biomedical and health research are responsible for establishing an EC and to provide necessary logistic support. For running the EC functions smoothly, the guidelines have suggested that the Member Secretary should be provided with protected time for this additional work. The EC should be capable, efficient, updated and independent in its functioning and the Chairperson and 50% members should be non-affiliated. Institutions that do not have their own EC can enter into an agreement with another institution preferably in the nearby area to utilize the services of the EC. Once a proposal is received by the EC for review, depending on the risk involved, the Member Secretary/Secretariat should screen the proposals and categorize them into full committee review, expedited review or exempt from review as given in [Table 2].

Table 2: Types of review

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health research and 5 years for regulatory clinical trials). ECs should be registered with the relevant authority and should make efforts to get accredited from national bodies such as NABH, or from international bodies such as SIDCER, AAHRPP, etc.

Section 5: Informed Consent Process

Informed consent is an important component of any research study and helps to ensure better understanding and voluntariness to participate in research. The essential information to be provided in Informed Consent Document (ICD) is stated in [Table 3].

Table 3: Essential elements of an informed consent document

The following must be included in an informed consent form
1. Statement highlighting it as research
2. Research purpose and methodology
3. Duration, data collection types
4. Benefits accrued from participating
5. Any foreseeable risks, discomfort or inconvenience
6. Maintenance of confidentiality of records
7. Reimbursement for participation
8. Compensation for injury and/or harm
9. Autonomy to take part/pull out without loss of benefits
10. Identity of research team and contact persons

The EC approved version of the informed consent documents should be used by the researchers. In research a lot of confidential information may be obtained and it is the responsibility of the researchers to maintain participant's privacy and confidentiality of related data. Informed consent should be voluntary and be signed by the participant after receiving information, understanding it and discussing with family/friends (if required).

When a participant is incompetent, there is a need to obtain consent of legally acceptable representative or in a case where participant is illiterate, there is a need for a literate impartial witness. To provide information as in the written informed consent document, many tools could be used including electronic media such as videos, graphics and podcasts but these would require prior approval from EC which would review and approve the process, electronic materials, method of documentation, privacy and confidentiality of the information, policies of data use at the site. If research involves less than minimal risk and does not adversely affects the rights of the participants, the researcher can request the EC for a waiver of consent. In certain studies, permission of the head of the group or appropriate community authority may be additionally required. EC should carefully review the consent process for studies involving deception in socio behavioural research studies.

Section 6: Vulnerability

There is an added responsibility for the researcher if a study involves vulnerable persons or groups. Safeguards should be in place since the vulnerable participants may be unable to protect their own interest and informed consent process may also be compromised. The characteristics of few vulnerable individuals/persons/groups are given below:

- Economically, politically or socially, deprived and therefore prone to exploitation
- unable to make decision on their own or those with compromised autonomy
- can consent, but due to certain circumstances, their voluntariness is compromised

- influenced by the expected benefits or fear of revenge in case of rejection to take part which might direct them to provide consent.

The EC must review the need for inclusion or exclusion of vulnerable persons and if the steps have been planned to protect them. The documentation of informed consent process should be done carefully and extra steps should be adopted if required, such as audio-visual/audio recording of consent/ reconsent /assent on suggestions of EC. Whenever possible, ancillary care may be provided such as referring them to a healthcare unit, setting up of a facility, helping with schools for unattended children of the participants or a hospital, or guiding for a counselling centre etc. Community representatives may also be invited to EC meetings to make sure the research is responsive to their needs. Exclusion of any particular group due to their vulnerability would also be unjustified. Taking example of women, it may be noted that research benefits should reach women and exclusion of women of child bearing age in general from participation in research would deprive them of the anticipated benefits and if this is done, there should be appropriate reasons for doing so. In case of research in children, EC approved written or verbal/oral assent from children of 7–18 years of age should be obtained in addition to consent from parents/LARs. It is suggested that when research is conducted on any marginalized population or for example on a tribal group, it would be useful to involve or seek help from agencies or groups that may be closely working with tribal groups, and also try to involve local and governmental bodies.

Section 7: Clinical Trials of Drugs and Other Interventions

Clinical trials are well controlled studies necessary for the development of new drugs, medical devices, vaccines, biosimilars etc. Clinical trials seeking regulatory approval for marketing must be conducted in accordance to the Drugs and Cosmetics Act and Rules and applicable amendments from time to time. An investigator should determine if the clinical trial requires regulatory approvals and if so, ensure that the trial follows all requirements as per notifications from Central Drug Standards and Control Organisation (CDSCO) from time to time. Prospective registration of all such clinical trials is mandatory with Clinical Trial Registry of India (CTRI). In case of clinical trials conducted by students as part of their thesis, the responsibilities of the sponsor should be taken up by the guides/and institutions. Precautions should be taken to protect the trial participants from harm when a placebo is used. Trials involving stem cells must be approved by Institutional Committee for Stem Cell Research (IC-SCR) which should be registered with National Apex Committee for Stem Cell Research and Therapy (NAC-SCRT). In a placebo or active-controlled trial in oncology, the current standard of care to which the IP, placebo or active-control is added must be given to all the groups. It is important to have provisions for medical management and payment of compensation in case of research related injury. Ancillary care may be provided to the participants for illnesses which are non-study/trial related and that arise during the study period. Ethical requirements that apply for drug trials also apply to research involving traditional and folk medicines on human participants.

Section 8: Public Health Research

Public health research comes with a number of challenges since there is a thin line of distinction between research and public health practice. This section addresses the ethical issues related to research conducted in public health setting, such as implementation research, data analysis from disease registries, epidemiological surveys, surveillance programs, data and program evaluations, demonstration projects, community trials, and so on. While reviewing public health research, an EC should consider the scientific soundness of the objectives of the study for achieving public health goals. In public health setting, the requirement of individual written informed consent has to be reviewed carefully as at times it may not be feasible or may alter the research outcomes. Appropriate consent processes may be considered by the EC, such as verbal/oral consent; broad consent; group consent; waiver of consent and reconsent. Reconsenting may be required in case there are any changes in the study protocol/intervention/ new information that might jeopardize the safety of participants. The other important fact is that the study may have societal benefits rather than individual benefits alone and therefore, these larger societal benefits may override the individual harm. Data security, confidentiality of information, etc., should be protected and safeguards should be in place for participants and communities. All stakeholders (researchers, Govt. agencies, ECs, NGOs, etc.) should make every effort in order to ensure post study interventions, use of research findings and make sure that public health action is sustained.

There is limited understanding about the ethical requirements for socio-behavioral research related to health and therefore, this section has been introduced to describe the

considerations related to scientific design, conduct, ethical review and benefit-risk assessment that needs to be looked at while reviewing such proposals. Risks are often non measurable and dynamic and the researcher has obligations related to sharing back research benefits and incidental findings to the population. Researchers may often come across situations or finding which are inappropriate or even illegal and the guidelines have suggested that the researchers should not interrupt but depending on its importance, plan next steps such as document findings on unacceptable practices (legally, socially, medically, etc.) and suitably reporting or dissemination for greater social benefit. It is necessary to have an appropriate expert in the social and behavioural science domain as EC member to address the specific ethical challenges like community consent, privacy and confidentiality and data sharing as well as risk assessment and mitigation. Safety measures should also be in place to safeguard the research teams. The EC should carefully review studies using deception and consider debriefing the research participants after completion of the study. Appropriate arrangements such as police protection, counselling and rehabilitation centres, etc. may be required for sensitive studies. It should be ensured by the EC that appropriate measures are taken by the researcher to maintain data security, confidentiality of information, disclosure permissions, and appropriate use of the data.

Section 10: Human Genetics Testing and Research

This section describes the ethical, legal and social issues (ELSI) pertaining to human genetics testing as well as research. Genetic test results have familial/societal implications if some sensitive genetic information reaches other members of family. There is a huge potential for labelling and stigmatization as genetic diseases are usually a taboo. Therefore, maintaining

confidentiality and providing counselling both pre- and post-test by trained individuals is important. Written consent should be obtained for routine genetic investigations and also for genetic screening, pre-symptomatic testing, confirmatory tests, specific interventions, next generation sequencing, genomic studies, prenatal or carrier testing, use of embryos/foetal tissue, if the data is to be used for research. There is also a need to obtain informed consent from family members for preparing family pedigrees as all members of family become secondary subjects. Often there is a need to publish photographs of affected individuals and informed consent should be obtained before any publication of photographs or other identifying information. Quality checks and accreditation is desirable for laboratories offering genetic testing. Since there are long-term implications and potential for misuse, careful review is required. Genetic screening should be purposive, with established provisions for disease management, treatment and counselling. Adequate care should be taken while undertaking research involving new technologies. Needful consent from both the parents and their conselling is required when research is planned on embryos or on material obtained from foetal autopsy.

Section 11: Biological Materials, Biobanking and Datasets

This section would be useful to most researchers, since they are usually involved with collection or analysis or storage of some or the other kinds of biological samples or data or both. Ethical issues such as ownership of samples or data, transfer of biospecimens, custodianship, secondary use, return of results, etc., are important and often not well

understood. However, these are important considerations and [Table 4] categorises the types of samples on the basis of identifying information available with samples or datasets.

Table 4: Samples types

Anonymous or unidentified	Identifiers are not present	
Anonymized	Involves systematic de-identification, reversible or irreversible	
	Coded or reversibly anonymized	**Irreversibly anonymized**
	Indirect link of identity of the sample/data is linked indirectly. Could be relinked if required	Removal of Link to the identity of the participant. re-link cannot be done
Identifiable	Participant's identity to the sample/data is directly linked	

Informed consent is important if the clinical samples are needed for future research and have to be stored or even if there is potential for use of linked data, or sample sharing with other researchers. Based on requirements the type of consent could be broad or blanket, tiered with opt-in option for future use, specific, delayed, dynamic and provision for withdrawal, waiver and reconsent for secondary use of stored samples/ datasets. The informed consent should provide information about the commercial value of samples or data, if applicable, with clarity about benefit sharing. The researchers or biobanks or institutes are only custodians of the samples, participants are the actual owners of the biological samples and associated data collected. If there is any transfer of biological material within or outside the country a material transfer agreement (MTA) must be signed between the involved parties. Return of research results to individuals/ groups, financial or non-financial benefits sharing with donors, their families, or communities is important but

the concept is usually not well understood. It is important to make efforts for sharing the results and the derived benefits with providers of research material wherever possible. EC of the institution or the biorepository should review all such proposals, which require transfer of biological materials or of available data sets. The review of the data sets and repositories must be done with care as there is enormous potential for research as well as commercialization. The institutions are advised to develop contingency plans for sustainability of the biobanks so that the precious samples can be used in future for further research to improve health.

Section 12: Research during Humanitarian Emergencies and Disasters

This is a new section in the revised guidelines and some suggestions are given for the conduct of research during disasters and humanitarian emergencies. Safeguarding the interest of participants who are affected in emergency situations is critical. In an emergency situation the entire framework including infrastructure, governance, communication may be affected and conduct of research and close oversight may not be easy. Prime attention has to be given to maintain the safety as well as right to privacy and confidentiality of people who are affected. Pre-emptive preparation for disaster of cyclical frequency such as floods can be done to identify research questions, study design, collection of samples and data, etc., beforehand. These can also be reviewed in advance so that there is no last-minute rush and adequate safeguards are built into the study to protect the affected persons who may become part of research. Investigators should aim to minimise the risk, ensure equitable distribution of benefits and warrant fair selection of participants. Since the decisional

capacity of participants would be low, obtaining a valid informed consent may be a huge challenge and this may require adequate counselling, psychological help etc. Identifying information of individuals and/or communities should be protected to prevent stigmatization and exploitation by anyone at that time or even later. EC must play an important role by reviewing research through expedited review or unscheduled meetings or through tele-conferencing as per feasibility and requirements. The local ECs should oversee the site requirements to the extent possible to ensure safety of participants. When research involves a foreign researcher/institution in a humanitarian emergency situation, it must involve local partner(s) to make the study more acceptable and to also customize it to local requirements.

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