

**ETHICS IN BIOMEDICAL RESEARCH
&
CLINICAL PRACTICE**

THE POLICY DOCUMENT

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INTRODUCTION

The shocking details of the post Second World War (1939-45) trial of German medical practitioners accused of conducting experiments on human participants without their consent and exposing them to grave risk of death or permanent impairment of their faculties raised grave concern about subjecting human subjects to medical research. Thus, the first International Statement on the ethics of medical research using human subjects namely, the **Nuremberg Code** was formulated in 1947. Although informed consent for participation in research was recorded in 1900, the Nuremberg Code highlighted the essentiality of voluntariness of this consent. In 1948, **Universal Declaration of Human Rights** (adopted by the General Assembly of the United Nations) expressed concern about rights of human beings being subjected to involuntary maltreatment. In 1966, the **International Covenant on Civil and Political Rights** specifically stated, *'No one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment. In particular, no one shall be subjected without his consent to medical or scientific treatment.'* Based on the preliminary efforts of the Council for International Organisations of Medical Sciences (CIOMS) in 1964 at Helsinki, the World Medical Association formulated general principles and specific guidelines on use of human subjects in medical research, known as the **Helsinki Declaration**, which was revised from time to time.

In February 1980, the Indian Council of Medical Research released a **'Policy Statement on Ethical Considerations involved in Research on Human Subjects'** for the benefit of all those involved in clinical research in India and in 1997, it brought out the draft of **"Consultative Document on Ethical Guidelines on Biomedical Research Involving Human Subjects"**.. In 1982, the World Health Organisation (WHO) and the CIOMS issued the **'Proposed International Guidelines for Biomedical Research involving Human Subjects.'** Subsequently the CIOMS brought out the **'International Guidelines for Ethical Review in Epidemiological studies'** in 1991 and **'International Ethical Guidelines for Biomedical Research involving Human Subjects'** in 1993. Over the years, various bioethics advisory bodies in national jurisdictions like Nuffield Council of Bioethics and European Commission on Ethics have also laid down general and specific principles in specific areas of scientific research involving human beings as subjects in medical research. These 'national' Codes drawn from the international codes and the universal principles therein provide the 'guidelines' that should be followed in their respective jurisdictions. Meanwhile the international studies conducted in developing countries sponsored or funded by developed countries highlighted the global health divide and the ethical issues related to the 10/90 gap according to which the majority of biomedical research has been predominantly motivated by concern for the benefit of already privileged communities. This is reflected by the fact that the WHO estimates that 90% of the resources devoted to research and development on medical problems are applied to diseases causing less than 10% of the present global suffering. The establishment of international guidelines that assist in strengthening the capacity for the ethical review of biomedical research in all countries contributes to redressing this imbalance.

National Bioethics Advisory Bodies and Funding organizations of developed nations took note of this and to rectify the situation revised guidelines which had relevance to developing countries as evident from Report of National Bioethics Advisory Committee, USA, by 2000 and Guidelines by Nuffield Council of Bioethics, UK and CIOMS, Geneva by 2002. The Helsinki Declaration underwent changes five times, the last one being in 2004. Still the controversy about use of placebo and post-trial access as described in it is being debated. The most recent documents on ethics are those of UNESCO's **"The Universal Declaration on Human Genome and Human Rights"** (1997), **"The International**

Declaration on Human Gene Data” (2003) and “Universal Declaration on Bioethics and Human Rights” (2005).

National Committee for Ethics in Social Science Research in Health (NCESSRH)

Ethics is concerned with the conduct of human beings. All scientific activities, including those by the social scientists, are conducted with the participation of human beings or have an impact on human beings or on the wider society and environment. Therefore, it is essential that scientists/researchers understand ethical issues and the implications of their scientific work and act accordingly. For making ethical judgment, the scientists/researchers rely upon various standards of ethics, which could be universal or specific to the culture(s) or localities. Indeed, it is essential that researchers share and discuss the ethical issues in their work and evolve collective standards of their own.

The issue of ethics in social sciences, unlike in medical research, has been given less prominence in India. Although many social scientists have paid serious attention to the appropriate conduct of research and set personal examples, they are often not discussed as ethics and no efforts are made to formalize some guidelines based on such experience(s). Our national councils for social science research and their institutions have many guidelines either as administrative orders or for improving the quality of research but enough efforts have not been made to bring them together as comprehensive ethical guidelines. Besides, in the absence of such comprehensive guidelines, ethics are hardly there in the social science education curriculum.

But this situation in India is definitely not due to lack of attention to ethics in social sciences as in other countries. In fact, in the post World War period, there has been growing pressure on social science professionals to self regulate and evolve their own codes of conduct. There has been a continuing debate between the view of making the social sciences "value free" and "objective" and the view that social scientists could not remain value free simply because they deal with contemporary society and because there is an explicit connection between research and social action or political viewpoint. The former tries to make social scientists attain a status of professionals and often puts them in ivory tower situations, while the latter tries to make them aware of the impact of their activities on the society. However, in both cases the ethics of the social inquiry and the application of the expertise of social science to current social problem need to be dealt with.

Internationally, the associations of applied anthropology and the psychologists formulated their codes as early as in 1940s and 1950s. The controversy around the Project Camelot and its cancellation in 1965 led to increased discussion on ethics among the social scientists and eventually prompted most of the major social science associations to formulate their guidelines (Barnes 1979). The universities have also tried to establish formal guidelines to protect student research and their exploitation by the teachers.

The present effort to formulate ethical guidelines for research in social sciences and health in India began in 1998. After a rigorous documentation of the guidelines for medical as well as social science research in India and outside, a multi-disciplinary national committee was constituted in 1999. The committee met twice to prepare the drafts of the guidelines and the final draft was mailed to over 100 researchers and institutions in different parts of the country to get their feed back. Besides, it was directly presented at six institutions to teachers, researchers and students. The feedback thus obtained from all over the country was summarized in a paper, which, along with the draft of the guidelines were then thoroughly discussed in a national meeting of researchers and activists from social science and health

fields in May 2000. The draft of the guidelines discussed at this meeting was again revised, discussed and adopted by the committee after the meeting.

Lastly, the development of organizational mechanism for ethics in social science research in health has been kept as an open process to be evolved by the community of researchers and institutions. The national meeting of researchers in May 2000 correctly felt that such a mechanism could be different for different types of institutions and projects; and that only by practicing ethics within institutions could we arrive at appropriate models for the organizational mechanism. Indeed, such a process would also create a critical mass of individuals and institutions having experience in integrating ethics and guidelines in their institutional environment and the research process. Of course, this is a collective endeavor of networking, sharing, discussing and providing assistance to each other.

The ethical principles and guidelines for research in health, given in this document, are developed for the following purpose:

(i) To sensitize and protect researchers who are often under pressures from various quarters/forces while undertaking research.

(ii) To preserve and promote the autonomy of research through the observance of ethics, ethical values and ethical self-regulation.

(iii) To protect and promote the human rights of participants and to sensitize and encourage researchers to respect participants' rights and needs.

(iv) To improve quality, legitimacy and credibility of research in health.

(v) To make ethics an integral part of the planning and methodology of research, and to enable individuals to develop appropriate mechanisms for ethical self-regulation.

The experiences in using this document may be shared. Keeping in mind the immediate and long-term interests of the larger sections of people and the autonomy of researchers, the ethical guidelines given in this document may be refined through periodic reviews.

ETHICAL PRINCIPLES FOR RESEARCH

1. Four well-known moral principles constitute the basis for ethics in research. They are:

(i) The Principle of Non-maleficence: Research must not cause harm to the participants in particular and to people in general.

(ii) The Principle of Beneficence: Research should also make a positive contribution towards the welfare of people.

(iii) The Principle of Autonomy: Research must respect and protect the rights and dignity of participants.

(iv) The Principle of Justice: The benefits and risks of research should be fairly distributed among people.

GENERAL STATEMENT

Medical and related research using human beings as research participants must necessarily ensure that -

(i) The **PURPOSE**, of such research is that it should be directed towards the increase of knowledge about the human condition in relation to its social and natural environment, mindful that the human species is one of the many species in a planet in which the well being of all species is under threat, no less from the human species as any other, and that such research is for the betterment of all, especially the least advantaged.

(ii) Such research is **CONDUCTED** under conditions that no person or persons become a mere means for the betterment of others and that human beings who are subject to any medical research or scientific experimentation are dealt with in a manner conducive to and consistent with their dignity and well being, under conditions of professional fair treatment and transparency; and after ensuring that the participant is placed at no greater risk other than such risk commensurate with the well being of the participant in question in the light of the object to be achieved.

(iii) Such research must be subjected to a regime of **EVALUATION** at all stages of the proposal i.e., research design and experimentation, declaration of results and use of the results thereof, and that each such evaluation shall bear in mind the objects to be achieved, the means by which they are sought to be achieved, the anticipated benefits and dangers, the potential uses and abuses of the experiment and its results, and above all, the premium that civilised society places on saving and ensuring the safety of each human life as an end in itself.

STATEMENT OF GENERAL PRINCIPLES

Any research using the human beings as participants shall follow the principles given below –

I. Principles of essentiality whereby the research entailing the use of human participants is considered to be absolutely essential after a due consideration of all alternatives in the light of the existing knowledge in the proposed area of research and after the proposed research has been duly vetted and considered by an appropriate and responsible body of persons who are external to the particular research and who, after careful consideration, come to the conclusion that the said research is necessary for the advancement of knowledge and for the benefit of all members of the human species and for the ecological and environmental well being of the planet.

II. Principles of voluntariness, informed consent and community agreement whereby research participants are fully apprised of the research and the impact and risk of such research on the research participant and others; and whereby the research participants retain the right to abstain from further participation in the research irrespective of any legal or other obligation that may have been entered into by such human participants or someone on their behalf, subject to only minimal restitutive obligations of any advance consideration received and outstanding. Where any such research entails treating any community or group of persons as a research participant, these principles of voluntariness and informed consent shall apply, *mutatis mutandis*, to the community as a whole and to each individual member who is the participant of the research or experiment. Where the human participant is incapable of giving consent and it is considered essential that research or experimentation be conducted on such a person incompetent to give consent, the principle of voluntariness and informed consent shall continue to apply and such consent and voluntariness shall be obtained and exercised on behalf of such research participants by someone who is empowered and under a duty to act on their behalf. The principles of informed consent and voluntariness are cardinal principles to be observed throughout the research and experiment, including its aftermath and applied

use so that research participants are continually kept informed of any and all developments in so far as they affect them and others. However, without in any way undermining the cardinal importance of obtaining informed consent from any human participant involved in any research, the nature and form of the consent and the evidentiary requirements to prove that such consent was taken, shall depend upon the degree and seriousness of the invasiveness into the concerned human participant's person and privacy, health and life generally, and, the overall purpose and the importance of the research. Ethics committee shall decide on the form of consent to be taken or its waiver based on the degree of risk that may be involved.

III. Principles of non-exploitation whereby as a general rule, research participants are remunerated for their involvement in the research or experiment; and, irrespective of the social and economic condition or status, or literacy or educational levels attained by the research participants kept fully apprised of all the dangers arising in and out of the research so that they can appreciate all the physical and psychological risks as well as moral implications of the research whether to themselves or others, including those yet to be born. Such human participants should be selected so that the burdens and benefits of the research are distributed without arbitrariness, discrimination or caprice. Each research shall include an in-built mechanism for compensation for the human participants either through insurance cover or any other appropriate means to cover all foreseeable and unforeseeable risks by providing for remedial action and comprehensive aftercare, including treatment during and after the research or experiment, in respect of any effect that the conduct of research or experimentation may have on the human participant and to ensure that immediate recompense and rehabilitative measures are taken in respect of all affected, if and when necessary.

IV. Principles of privacy and confidentiality whereby the identity and records of the human participants of the research or experiment are as far as possible kept confidential; and that no details about identity of said human participants, which would result in the disclosure of their identity, are disclosed without valid scientific and legal reasons which may be essential for the purposes of therapeutics or other interventions, without the specific consent in writing of the human participant concerned, or someone authorised on their behalf; and after ensuring that the said human participant does not suffer from any form of hardship, discrimination or stigmatisation as a consequence of having participated in the research or experiment.

V. Principles of precaution and risk minimisation whereby due care and caution is taken at all stages of the research and experiment (from its inception as a research idea, its subsequent research design, the conduct of the research or experiment and its applicative use) to ensure that the research participant and those affected by it including community are put to the minimum risk, suffer from no known irreversible adverse effects, and generally, benefit from and by the research or experiment; and that requisite steps are taken to ensure that both professional and ethical reviews of the research are undertaken at appropriate stages so that further and specific guidelines are laid down, and necessary directions given, in respect of the conduct of the research or experiment.

VI. Principles of professional competence whereby the research is conducted at all times by competent and qualified persons who act with total integrity and impartiality and who have been made aware of, and are mindful of, preferably through training, the ethical considerations to be borne in mind in respect of such research or experiment.

VII. Principles of accountability and transparency whereby the research or experiment will be conducted in a fair, honest, impartial and transparent manner after full disclosure is made by those associated with the research or experiment of each aspect of their interest in the research, and any conflict of interest that may exist; and whereby, subject to the principles of privacy and confidentiality and the rights of the researcher, full and complete records of

the research inclusive of data and notes are retained for such reasonable period as may be prescribed or considered necessary for the purposes of post-research monitoring, evaluation of the research, conducting further research (whether by the initial researcher or otherwise) and in order to make such records available for scrutiny by the appropriate legal and administrative authority, if necessary.

VIII. Principles of the maximisation of the public interest and of distributive justice whereby the research or experiment and its subsequent applicative use are conducted and used to benefit all human kind and not just those who are socially better off but also the least advantaged; and in particular, the research participants themselves and or the community from which they are drawn.

IX. Principles of institutional arrangements whereby there shall be a duty on all persons connected with the research to ensure that all the procedures required to be complied with and all institutional arrangements required to be made in respect of the research and its subsequent use or application are duly made in a bonafide and transparent manner; and to take all appropriate steps to ensure that research reports, materials and data connected with the research are duly preserved and archived.

X. Principles of public domain whereby the research and any further research, experimentation or evaluation in response to, and emanating from such research is brought into the public domain so that its results are generally made known through scientific and other publications subject to such rights as are available to the researcher and those associated with the research under the law in force at that time.

XI. Principles of totality of responsibility whereby the professional and moral responsibility, for the due observance of all the principles, guidelines or prescriptions laid down generally or in respect of the research or experiment in question, devolves on all those directly or indirectly connected with the research or experiment including the researchers, those responsible for funding or contributing to the funding of the research, the institution or institutions where the research is conducted and the various persons, groups or undertakings who sponsor, use or derive benefit from the research, market the product (if any) or prescribe its use so that, inter alia, the effect of the research or experiment is duly monitored and constantly subject to review and remedial action at all stages of the research and experiment and its future use.

XII. Principles of compliance whereby, there is a general and positive duty on all persons, conducting, associated or connected with any research entailing the use of a human participant to ensure that both the letter and the spirit of these guidelines, as well as any other norms, directions and guidelines which have been specifically laid down or prescribed and which are applicable for that area of research or experimentation, are scrupulously observed and duly complied with.

ETHICAL REVIEW PROCEDURES

The need for evaluation of research proposals has been emphasized under the Statement of General Principles at item no. 5 pertaining to precaution and risk minimisation. It is mandatory that all proposals on biomedical research involving human participants should be cleared by Institutional Ethics Committee (IEC), to safeguard the welfare and the rights of the participants. The Institutional Ethics Committees is entrusted not only with the initial review of the proposed research protocols prior to initiation of the projects but also have a continuing responsibility of regular monitoring of the approved programmes to foresee the compliance of the ethics during the period of the project.

1. Basic responsibilities of IEC

The basic responsibility of this Institutional Ethics Committee (IEC) is to ensure a competent review of all ethical aspects of the project proposals received by it in an objective manner. IECs would provide advice to the researchers on all aspects of the welfare and safety of the research participants after ensuring the scientific soundness of the proposed research itself or through appropriate Scientific Review Committee.

Responsibilities of this IEC can be defined as follows:-

1. To protect the dignity, rights and well being of the potential research participants.
2. To ensure that universal ethical values and international scientific standards are expressed in terms of local community values and customs.
3. To assist in the development and the education of a research community responsive to local health care requirements.

Another responsibility of Ethics Committee is to ensure that ethics and etiquettes are followed in day to day practice by medical practitioners as laid down in “Code of Ethics Regulations, 2002 (Published in part III, section 4 of the Gazette of India, dated 6th April, 2002) and subsequent amendments” of Medical Council of India and “Indian Medical Council (Professional Conduct, Etiquette and Ethics) (Amendment) Regulations 2002”.

2. Role of IEC

IEC will review and approve all types of research proposals involving human participants with a view to safeguard the dignity, rights, safety and well being of all actual and potential research participants. The goals of research, however important, should never be permitted to override the health and well being of the research subjects.

The IEC will take care that all the cardinal principles of research ethics viz. Autonomy, Beneficence, Non - maleficence and Justice are taken care of in planning, conduct and reporting of the proposed research. For this purpose, it will look into the aspects of informed consent process, risk benefit ratio, distribution of burden and benefit and provisions for appropriate compensations wherever required. It will review the proposals before start of the study as well as monitor the research throughout the study until and after completion of the study through well documented procedures of half yearly reports, annual reports, final reports and site visits etc.

The committee will also examine compliance with all regulatory requirements, applicable guidelines and laws. The mandate of the IECs will be to review all research projects involving human subjects to be conducted at the Institute, irrespective of the funding agency.

3. Composition of IEC

IECs shall be multidisciplinary and multisectorial in composition. Independence and competence will be two hallmarks of the IEC.

The number of persons in the ethical committee will be kept fairly small (7-9 members). There will never be more than 13 permanent members in the committee. The Chairperson of the Committee will be from outside the Institution and not from the Institution to maintain the independence of the Committee. The Member Secretary will be from the Institution and will conduct the business of the Committee. Other members shall be a mix of medical / non-medical, scientific and non-scientific persons including lay public to reflect the differed viewpoints. It will be ensured that there is at least one pharmacologist in the committee.

The composition may be as follows:

1. Chairperson
2. 1-2 basic medical scientists.
3. 1-2 clinicians from various Institutes
4. One legal expert or retired judge
5. One social scientist / representative of non-governmental voluntary agency
6. One philosopher / ethicist / theologian
7. One lay person from the community
8. Member-Secretary

4. Authority under which IEC is constituted:

The Institutional Head will constitute the IEC. All the members will be appointed by the Head of the Institute based on their competencies and integrity, and could be drawn from any public or private Institute from anywhere in the country. The committee may subsequently be notified by the State Government.

5. Membership requirements:

- a. The duration of appointment is initially for a period of 3 years
- b. At the end of 3 years, the committee is reconstituted, and 50% of the members will be replaced by a defined procedure.
- c. A member can be replaced in the event of death or long-term non-availability or for any action not commensurate with the responsibilities laid down in the guidelines deemed unfit for a member.
- d. A member can tender resignation from the committee with proper reasons to do so to the appointing authority who can accept it after recommendation from the Chairperson.
- e. All members will maintain absolute confidentiality of all discussions during the meeting and sign a confidentiality form.
- f. Conflict of interest will be declared by members of the IEC.
- g. A statement of the conditions of appointment will be drawn up that will include the following:
 1. A member shall be willing to publicize his/her full name, profession, and affiliation;
 2. All reimbursement for work and expenses, if any, within or related to an EC will be recorded and made available to the public upon request;
 3. A member shall sign a confidentiality agreement regarding meeting deliberations, applications, information on research participants, and related matters; in addition, all EC administrative staff shall sign a similar confidentiality agreement.

6. Quorum requirements:

The minimum of 50% of the permanent members will be required to compose a quorum. All decisions shall be taken in meetings and not by circulation of project proposals. No quorum shall consist entirely of members of one profession or one gender; a quorum shall include at least one member whose primary area of expertise is in a non-scientific area and at least one member who is independent of the institution/research site.

7. Offices

The Chairperson will conduct all meetings of the IEC. If for reasons beyond control, the Chairperson is not available, an alternate Chairperson will be elected from the members by the members present, who will conduct the meeting. The Member Secretary will be responsible for organizing the meetings, maintaining the records and communicating with all concerned. He/she will prepare the minutes of the meetings and get it approved by the Chairperson before communicating to the researchers.

8. Independent consultants

IEC may call upon subject experts as independent consultants who may provide special review of selected research protocols, if need be. These experts may be specialists in ethical or legal aspects, specific diseases or methodologies, or represent specific communities; patient groups or special interest groups e.g. Cancer patients, HIV/AIDS positive persons or ethnic minorities. They are required to give their specialized views but do not take part in the decision making process which will be made by the members of the IEC.

9. Application Procedures:

- a. All proposals shall be submitted in the prescribed application form, the details of which are given under Documentation.
- b. All relevant documents should be enclosed with application form.
- c. Required number of copies of the proposal along with the application and documents in prescribed format duly signed by the Principal Investigator (PI) and Co-investigators / Collaborators shall be forwarded by the Head of the Departments to the ethics committee along with a soft copy.
- d. The date of meeting will be intimated to the researcher, who should be present, if necessary to offer clarifications.
- e. The decision will be communicated in writing. If revision is to be made, the revised document in required number of copies should be submitted within a stipulated period of time as specified in the communication or before the next meeting.

10. Documentation:

For a thorough and complete review, all research proposals should be submitted with the following documents:

1. Name of the applicant with designation
2. Name of the Institute/ Hospital / Field area where research will be conducted
3. Approval of the Head of the Department / Institution
4. Protocol of the proposed research
5. Ethical issues in the study and plans to address these issues
6. Proposal should be submitted with all relevant enclosures like proformae, case report forms, questionnaires, follow - up cards, etc.
7. Informed consent process, including patient information sheet and informed consent form in local language(s).
8. For any drug / device trial, all relevant pre-clinical animal data and clinical trial data from other centres within the country / countries, if available.
9. Curriculum vitae of all the investigators with relevant publications in last five years.
10. Any regulatory clearances required.
11. Source of funding and financial requirements for the project.
12. Other financial issues including those related to insurance or reimbursement.
13. An agreement to report Serious Adverse Events (SAE) to IEC.

14. Statement of conflicts of interest, if any.
15. Agreement to comply with the relevant guidelines.
16. A statement describing any compensation for study participation (including expenses and access to medical care) to be given to research participants; a description of the arrangements for indemnity, if applicable (in study-related injuries); a description of the arrangements for insurance coverage for research participants, if applicable; all significant previous decisions (e.g., those leading to a negative decision or modified protocol) by other ECs or regulatory authorities for the proposed study (whether in the same location or elsewhere) and an indication of the modification(s) to the protocol made on that account. The reasons for negative decisions should be provided.
17. Plans for publication of results – positive or negative, while maintaining the privacy and confidentiality of the study participants.
18. Any other information relevant to the study

11. Review procedures:

- a. The meeting of the IEC shall be held quarterly and additional meetings may be held as and when the proposals are received for review.
- b. The proposals will be sent to members at least 2 weeks in advance.
- c. Decisions will be taken by consensus after discussions, and whenever needed voting will be done.
- d. Researchers will be invited to offer clarifications if need be.
- e. Independent consultants/Experts will be invited to offer their opinion on specific research proposals if needed.
- f. The decisions will be minuted and Chairperson's approval taken in writing.

12. Element of review

The primary task of the IEC lies in the review of research proposals and their supporting documents, with special attention given to the informed consent process, documentation, and the suitability and feasibility of the protocol. IECs shall take into account prior scientific reviews, if any, and the requirements of applicable laws and regulations. The following shall be considered, as applicable:

A. Scientific Design and Conduct of the Study

- A.1 The appropriateness of the study design in relation to the objectives of the study, the statistical methodology (including sample size calculation), and the potential for reaching sound conclusions with the smallest number of research participants;
- A.2 The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants and the concerned communities;
- A.3 The justification for the use of control arms;
- A.4 Criteria for prematurely withdrawing research participants;
- A.5 Criteria for suspending or terminating the research as a whole;
- A.6 The adequacy of provisions made for monitoring and auditing the conduct of the research;
- A.7 The adequacy of the site, including the supporting staff, available facilities, and emergency procedures;
- A.8 The manner in which the results of the research will be reported and published;

B. Recruitment of Research Participants

- B.1 The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status, and ethnicity);
- B.2 The means by which initial contact and recruitment is to be conducted;

B.3 The means by which full information is to be conveyed to potential research participants or their representatives;

B.4 Inclusion criteria for research participants;

B.5 Exclusion criteria for research participants;

C. Care and Protection of Research Participants

C.1 The suitability of the investigator(s)'s qualifications and experience for the proposed study;

C.2 Any plans to withdraw or withhold standard therapies for the purpose of the research, and the justification for such action;

C.3 The medical care to be provided to research participants during and after the course of the research;

C.4 The adequacy of medical supervision and psycho-social support for the research participants;

C.5 Steps to be taken if research participants voluntarily withdraw during the course of the research;

C.6 The criteria for extended access to, the emergency use of, and/or the compassionate use of study products;

C.7 The arrangements, if appropriate, for informing the research participant's general practitioner (family doctor), including procedures for seeking the participant's consent to do so;

C.8 A description of any plans to make the study product available to the research participants following the research;

C.9 A description of any financial costs to research participants;

C.10 The rewards and compensations for research participants (including money, services, and/or gifts);

C.11 The provisions for compensation/treatment in the case of the injury/disability/death of a research participant attributable to participation in the research;

C.12 The insurance and indemnity arrangements;

D. Protection of Research Participant Confidentiality

D.1 A description of the persons who will have access to personal data of the research participants, including medical records and biological samples;

D.2 The measures taken to ensure the confidentiality and security of personal information concerning research participants;

E. Informed Consent Process

E.1 A full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent;

E.2 The adequacy, completeness, and understandability of written and oral information to be given to the research participants, and, when appropriate, their legally acceptable representative(s);

E.3 Clear justification for the intention to include in the research individuals who cannot consent, and a full account of the arrangements for obtaining consent or authorization for the participation of such individuals;

E.4 Assurances that research participants will receive information that becomes available during the course of the research relevant to their participation (including their rights, safety, and well-being);

E.5 The provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project;

E.6 The manner in which the results of the research will be made available to the research participants and the concerned communities.

13. Provisional Approval

Member Secretary shall examine the project and after satisfying himself with necessary information may allow the investigators to proceed provisionally subject to final approval by the committee which shall be taken in the immediate next scheduled meeting. The Investigator(s) shall give the undertaking that the suggestions and/ or amendments made by the committee shall be incorporated immediately and if the committee feels so the project shall be terminated immediately.

14. Protocol Review Committee

The Institution shall have a Protocol Review Committee which should see the scientific aspects of the protocol before it is submitted for ethical approval. The Member Secretary of Ethics Committee shall preferably be the Member Secretary of the PRC also, so as to make the Ethics Committee aware of the proceedings and of any scientific considerations that may be required for ethical approval.

15. Decision-making

In making decisions on applications for the ethical review of biomedical research, The IEC shall take the following into consideration:

15.1 All the decisions shall be made by consensus. When consensus is unlikely, voting will be done;

15.2 A member shall withdraw from the meeting for the decision procedure concerning an application where there arises a conflict of interest; the conflict of interest shall be indicated to the chairperson prior to the review of the application and recorded in the minutes;

15.3 A decision shall only be taken when sufficient time has been allowed for review and discussion of an application in the absence of non-members (e.g., the investigator, representatives of the sponsor, independent consultants) from the meeting, with the exception of IEC staff;

15.4 Decisions will be made only in meetings where quorum is complete;

15.5 The documents required for a full review of the application shall be complete and the relevant elements mentioned above shall be considered before a decision is made;

15.6 Only members who participate in the review shall participate in the decision, the expert consultants will only offer their opinions;

15.7 Decision may be to approve, reject or revise the proposals. Specific suggestions for modifications and reasons for rejection shall be given.

15.8 In cases of conditional decisions, clear suggestions for revision and the procedure for having the application re-reviewed shall be specified.

15.9 Modified proposals may be reviewed by an expedited review through identified members.

16. Communicating the decision

A decision shall be communicated in writing to the applicant by Member Secretary of the IEC within two weeks' time of the meeting at which the decision was made. The communication of the decision shall include, but is not limited to, the following:

16.1 The exact title of the research proposal reviewed;

16.2 The clear identification of the protocol of the proposed research or amendment, on which the decision is based;

16.3 The names and (where possible) specific identification numbers of the documents reviewed, including the potential research participant information sheet/material and informed consent form;

- 16.4 The name and title of the applicant;
- 16.5 The name of the site(s) where proposed research is to be carried out;
- 16.6 The date and place of the decision;
- 16.7 The name of the IEC taking the decision;
- 16.8 A clear statement of the decision reached;
- 16.9 Any advice by the IEC;
- 16.10 In the case of a conditional decision, any requirements by the IEC, including suggestions for revision and the procedure for having the application re-reviewed;
- 16.11 In the case of a positive decision, a statement of the responsibilities of the applicant; for example, confirmation of the acceptance of any requirements imposed by the IEC; submission of progress report(s); the need to notify the EC in cases of protocol amendments (other than amendments involving only logistical or administrative aspects of the study); the need to notify the EC in the case of amendments to the recruitment material, the potential research participant information, or the informed consent form; the need to report serious and unexpected adverse events related to the conduct of the study; the need to report unforeseen circumstances, the termination of the study, or significant decisions by other ECs; the information the EC expects to receive in order to perform ongoing review; the final summary or final report;
- 16.12 The schedule/plan of ongoing review by the EC;
- 16.13 In the case of a negative decision, clearly stated reason(s) for the negative decision;
- 16.14 Signature (dated) of the Member Secretary of the IEC.

17. Follow up procedures

- 17.1 Consent forms duly filled and signed shall be submitted at six months intervals.
- 17.2 Reports shall be submitted at six months intervals for review.
- 17.3 Final report shall be submitted at the end of study.
- 17.4 All SAEs and the interventions undertaken shall be intimated.
- 17.5 Protocol deviation, if any, shall be informed with adequate justifications.
- 17.6 Any amendment to the protocol shall be resubmitted for renewed approval.
- 17.7 Any new information related to the study shall be communicated.
- 17.8 Premature termination of study shall be notified with reasons along with summary of the data obtained so far.
- 17.9 Change of investigators / sites shall be informed.
- 17.10 The following instances or events require the follow-up review of a study:
 - a. Any protocol amendment likely to affect the rights, safety, and/or wellbeing of the research participants or the conduct of the study;
 - b. Serious and unexpected adverse events related to the conduct of the study or study product, and the response taken by investigators, sponsors, and regulatory agencies;
 - c. Any event or new information that may affect the benefit/risk ratio of the study;

18. Record keeping and Archiving

- a. Curriculum Vitae (CV) of all members of IEC.
- b. Copy of all study protocols with enclosed documents, progress reports, and SAEs.
- c. Minutes of all meetings duly signed by the Chairperson.
- d. Copy of all existing relevant national and international guidelines on research ethics and laws along with amendments.
- e. Copy of all correspondence with members, researchers and other regulatory bodies.
- f. Final report of the approved projects.
- g. All documents shall be archived for a period of 25 years.

19. Updating IEC members

- a. All relevant new guidelines shall be brought to the attention of the members.
- b. Members shall be encouraged to attend national and international training programs in research ethics for maintaining quality in ethical review and be aware of the latest developments in this area.

20. Reporting the defaulters

In case it is brought to the notice of the committee that the approved protocol is not being followed, the committee through its members or through its authorized representatives shall find out the truth and in case it is proved that the investigators are deliberately overlooking the ethical issues, shall immediately revoke the approval and inform the sponsors, head of the Institution(s) where the research is being conducted, head of the Institution(s) to which the Investigator(s) belong and registering authorities of the Investigator(s) about the decision.

21. Thesis Protocols

If a research protocol is submitted as a thesis protocol for partial fulfilment of requirements of a degree of University then:

- i. The student shall work as Investigator and guide(s) and co-guide(s) will act as Supervisor(s).
- ii. The supervisors shall submit an undertaking that the research work was conducted under their supervision and that all necessary documents, signed consent forms and data related to the study will be preserved for any scrutiny by Ethics Committee or their authorized representatives any time in future, and shall declare their conflict of interest.
- iii. The student shall attach a sheet describing the ethical issues related to the study and how does he/ she plan to address them along with the list of facilities which would be provided free of cost to the research subjects and any remunerations, if planned.

Application for Approval of Research Projects

(All applications should be signed by the head of the Unit and Department)

NAME AND SIGNATURE OF THE INVESTIGATOR(S)

1. Name (with designation and Department) of the Investigator(s)
2. Responsibilities given in the present research project
3. Full Signature(S) of Investigator(s)

DETAILS OF THE RESEARCH PROJECT

(1 soft and 10 hard copies consisting of adequate information must be furnished in a brief but self-contained manner to enable the Committee to assess the project)

1. **Title of the project**
2. **Objectives**
3. **Summary of the proposed research (up to 150 words) indicating overall aims of the research and importance of the research proposal. Application of the work in the context of national priorities of medical research, if any, may also be mentioned.**
4. **Present knowledge and relevant bibliography including full titles of articles relating to the project.**
5. **Preliminary work already done by the Investigator on this problem, e.g. selection of subjects, standardisation of methods, with results, if any.**
6. **Links with other going on projects if any.**
7. **List of important publications of last 5 years of all the investigators in the relevant fields (enclose reprints, if available).**
8. **Detailed research plan. (give here the design of study, indicating the total number of cases/samples/animals to be studied, the mode of selection of subjects specially in experiments involving human beings, equipments and other materials to be used, methodology/techniques to be employed for evaluating the results including statistical methods any potential to obtain patents etc.)**
9. **Facilities in terms of equipment, etc, available at the sponsoring institution for the proposed investigation.**

BIODATA OF THE INVESTIGATORS(S)

- 1 Name
- 2 Designation
- 3 Complete Postal Address, Telephone Number, Fax, e-mail etc.
- 4 Date of Birth
- 5 Educational Qualification
- 6 Research/Training Experience
- 7 Research specialization (Major scientific fields of interest)
- 8 Important recent publications (last 5 years, with titles and References), including papers In press

Informed Consent

1. Checklist for study Subject's informed consent documents
 - 1.1 Essential Elements
 - a. Statement that the study involves research and explanation of the purpose of research
 - b. Expected duration of the Subject's participation
 - c. Description of the procedures to be followed, including all invasive procedures
 - d. Description of any reasonably foreseeable risks or discomforts to the Subject
 - e. Description of any benefits to the Subject or others reasonably expected from research. If no benefit is expected Subject should be made aware of this.
 - f. Disclosure of specific appropriate alternative procedures or therapies available to the Subject.
 - g. Statement describing the extent to which confidentiality of records identifying the Subject will be maintained and who will have access to Subject's medical records.
 - h. Trial treatment schedule(s) and the probability for random assignment to each treatment (for randomized trials)
 - i. Compensation and /or treatment(s) available to the Subject in the event of a study related injury.
 - j. An explanation about whom to contact for study related queries, rights of Subjects and in the event of any injury
 - k. The anticipated payment, if any, to the subject for participating in the study.
 - l. Statement that participation is voluntary, that the subject can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the Subject is otherwise entitled.
 - m. Any other pertinent information
 - 1.2 Additional Elements, which may be required
 - a. Statement of foreseeable circumstances under which the Subject's participation may be terminated by the investigator without the Subject's consent.
 - b. Additional costs to the Subject that may result from participation in the study.
 - c. The consequences of Subject's decision to withdraw from the research and procedures for orderly termination of participation by Subject.
 - d. Statement that the Subject or Subject's representatives will be notified in a timely manner if significant new findings develop during the course of the research which may affect the Subject's willingness to continue participation will be provided.
 - e. A statement that the particular treatment or procedure may involve risks to the Subject (or to the embryo or fetus, if the Subject is or may become pregnant), which are currently unforeseeable.
 - f. Approximate number of Subjects enrolled in the study

**Dr. Rajendra Prasad Governmentt Medical College & Hospital,
Kangra at Tanda**

Informed Consent Form to Participate in the Research Study

Study Title:.....
Subject's Name.....
Date of Birth/ Age.....

Please initial box (Subject)

- (i) I confirm that I have read and understood the information sheet dated
for the above study and have had the opportunity to ask questions. []
- (ii) I understand that my participation in the study is voluntary and that I am free to
withdraw at any time, without giving any reason, without my medical care or legal
rights being affected. []
- (iii) I understand the Sponsor of the study, others working on Sponsor's behalf,
Investigator(s), the Ethics Committee and the regulatory authorities will not need my
permission to look at my health records both in respect of the current study and any
further research that may be conducted in relation to it, even if I withdraw from the
trial. I agree to this access. However, I understand that my identity will not be
revealed in any information released to third parties or published. []
- (iv) I agree not to restrict the use of any data or results that arise from this study provided
such a use is only for scientific purpose(s). []
- (v) I agree to take part in the above study. []

..... Date:/...../.....
Signature (or Thumb Impression) of the Subject/
Legally Acceptable Representative

Signatory's Name:
..... Date:/...../.....
Signature of the Investigator

Investigator's Name:
..... Date:/...../.....
Signature of the Witness

Name of the Witness:

Undertaking by the Principal Investigator(s)

1. Full name, Designation and Address of the Principal Investigator (or Investigator(s) when there is no Principal Investigator)
2. Name and Address of the Medical College, Hospital or other facility where the study will be conducted
3. Education, training and experience that qualify the Investigator to conduct the study (attach details including medical council registration)
4. Name and address of all clinical laboratory facilities to be used in the study.
5. Names of the other members of the research team (co or sub-Investigators) who will be assisting the Investigator in the conduct of the Investigation(s).
6. Title of the study to be conducted by the Investigator(s).
7. Commitments:
 - (i) I have reviewed the protocol and agree that it contains all the necessary information to conduct the study. I will not begin the study until all necessary Ethics Committee and regulatory approvals have been obtained.
 - (ii) I agree to conduct the study in accordance with the current protocol. I will not implement any deviation from or changes of the protocol without agreement by the sponsor and prior review and documented approval/ favourable opinion from the Ethics Committee of the amendment, except where necessary to eliminate an immediate hazard(s) to the trial Subjects or when the change(s) involved are only logistical or administrative in nature.
 - (iii) I agree to personally conduct and/ or supervise the study.
 - (iv) I will ensure that the requirements relating to obtaining informed consent and ethics committee review and approval specified in the GCP guidelines are met.
 - (v) I agree to report to the Ethics Committee all Serious Adverse Events that occur during the course of the study.
 - (vi) I have read and understood all available information related to the study including the potential risks and side effects of the drugs and procedures that will be used in the study.
 - (vii) I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are suitably qualified and experienced and they have been informed about their obligations in meeting their commitments in the study.
 - (viii) I agree to maintain adequate and accurate records and to make those records available for audit by Ethics Committee, Licensing Authority or Sponsors, if asked for.
 - (ix) I agree to promptly report to the Ethics Committee all changes in the study related activities and all the unanticipated problems involving risks to human subjects or others.

- (x) I will maintain confidentiality of the identification of all participants and assure security and confidentiality of study data.
- (xi) I agree to comply with all other requirements, guidelines and statutory obligations as applicable to clinical Investigators participating in the Clinical study.

Signature of the Investigator

Date

Contents of a Submitted Package

Initial Review Submitted Package

- Original Initial Review Application Form
- Undertaking by the Principal Investigator(s)
- Protocol and Protocol-Related Documents
 - information for subjects
 - case report forms (CRF)
 - investigator’s brochure
 - informed consent form
 - study budget
 - others.....

Resubmission for Re-review Submitted Package

- Resubmission or “Correction” Memorandum
- Revised Protocol Summary Sheet (if submitted initially)
- Original Initial Review Application Form
- Undertaking by the Principal Investigator(s)
- Protocol and Protocol-Related Documents
 - information for subjects
 - case report forms (CRF)
 - investigator’s brochure
 - informed consent form
 - study budget
 - others.....

Note: Changes made to the protocol and protocol-related documents should be clearly marked either with the underlining or highlighting feature of the document or the software package used to prepare the documents.

Protocol Amendment Submitted Package

- Request for Amendment Memorandum
- Original Amendment Submission Form
- Undertaking by the Principal Investigator(s)
- Protocol and Protocol-Related Documents

Note: Changes made to the protocol and protocol-related documents should be clearly marked either with the underlining or highlighting feature of the software package used to prepare the document.

Annual Continuing Review Package

- Request for Annual Continuing Review Memorandum
- Original Continuing Review Application Form
- Current Informed Consent Document (last approved by the IEC/IRB)

Protocol Termination Package

- Request for Termination Memorandum
- Original Continuing Review Application Form (Termination Submissions are contained on this form).

Confidentiality / Conflict of Interest Agreement Form

In recognition of the fact, that I....*member's name and his /her affiliation*.....herein referred to as the "Undersigned", has been appointed as a member of the IEC of Dr. R.P. Govt. Medical College, Kangra at Tanda has been asked to assess research studies involving human subjects in order to ensure that they are conducted in a humane and ethical manner, with the highest standards of care according to the applied national, local regulations, institutional policies and guidelines; Whereas, the appointment of the undersigned as a member of the IEC of Dr. R.P. Govt. Medical College, Kangra at Tanda is based on individual merits and not as an advocate or representative of a home province/ territory/ community nor as the delegate of any organization or private interest; Whereas, the fundamental duty of an IEC member is to independently review both scientific and ethical aspects of research protocols involving human subjects and make a determination and the best possible objective recommendations, based on the merits of the submissions under review; Whereas, the IEC of Dr. R.P. Govt. Medical College, Kangra at Tanda must meet the highest ethical standards in order to merit the trust and confidence of the communities in the protection of the rights and well-being of human subjects;

The undersigned, as a member of the IEC of Dr. R.P. Govt. Medical College, Kangra at Tanda, is expected to meet the same high standards of ethical behavior to carry out its mandate.

This Agreement thus encompasses any information deemed Confidential or Proprietary provided to the Undersigned in conjunction with the duties as a member of the IEC of Dr. R.P. Govt. Medical College, Kangra at Tanda. Any written information provided to the Undersigned that is of a Confidential, Proprietary, or Privileged nature shall be identified accordingly.

As such, the Undersigned agrees to hold all Confidential or Proprietary trade secrets ("Information") in trust or confidence and agrees that it shall be used only for contemplated purposes, shall not be used for any other purpose or disclosed to any third party. Written Confidential information provided for review shall not be copied or retained. All Confidential information (and any copies and notes thereof) shall remain the sole property of the IEC.

The Undersigned agrees not to disclose or utilize, directly or indirectly, any Confidential or Proprietary information belonging to a third party in fulfilling this agreement. Furthermore, the

Undersigned confirms that his/her performance of this agreement is consistent with the institute's policies and any contractual obligations they may have to third parties.

Conflict of Interest

It is recognized that the potential for conflict of interest will always exist but has faith in the IEC and its Chairperson to manage the conflict issues so that the ultimate outcome is the protection of human subjects.

It is the policy of the IEC of Dr. R.P. Govt. Medical College, Kangra at Tanda that no member may participate in the review, comment or approval of any activity in which he/she has a conflict of interest except to provide information as requested by the IEC.

The Undersigned will immediately disclose to the Chairperson of the IEC of Dr. R.P. Govt. Medical College, Kangra at Tanda any actual or potential conflict of interest that he/she may have in relation to any particular proposal submitted for review by the Committee, and to

abstain from any participation in discussions or recommendations in respect of such proposals.

If an applicant submitting a protocol believes that an IEC member has a potential conflict, the investigator may request that the member be excluded from the review of the protocol. The request must be in writing and addressed to the Chairperson. The request must contain evidence that substantiates the claim that a conflict exists with the EC member(s) in question. The Committee may elect to investigate the applicant's claim of the potential conflict. When a member has a conflict of interest, the member should notify the Chairperson and may not participate in the IEC review or approval except to provide information requested by the Committee.

Examples of conflict of interest cases may be any of the following:

A member is involved in a potentially competing research program.

Access to funding or intellectual information may provide an unfair competitive advantage.

A member's personal biases may interfere with his or her impartial judgment

Agreement on Confidentiality and Conflict of Interest

Please sign and date this Agreement, if the Undersigned agrees with the terms and conditions set forth above. The original (signed and dated Agreement) will be kept on file in the custody of the IEC of Dr. R.P. Govt. Medical College, Kangra at Tanda. A copy will be given to you for your records.

In the course of my activities as a member of the IEC, I may be provided with confidential information and documentation (which we will refer to as the "Confidential Information"). I agree to take reasonable measures to protect the Confidential Information; subject to applicable legislation, including the Access to Information Act, not to disclose the Confidential Information to any person; not to use the Confidential Information for any purpose outside the Committee's mandate, and in particular, in a manner which would result in a benefit to myself or any third party; and to return all Confidential Information (including any minutes or notes I have made as part of my Committee duties) to the Chairperson upon termination of my functions as a Committee member.

Whenever I have a conflict of interest, I shall immediately inform the Chairperson not to count me toward a quorum for voting.

I,, have read and accept the aforementioned terms and conditions as explained in this Agreement.

Undersigned Signature

Date

Principal, Dr. R.P. Govt. Medical College, Kangra at Tanda

Date

Confidentiality Agreement Form for Guest Attendees to IEC Meetings

I,....., understand that I am allowed to attend the IEC meeting as a guest or an observer. In the course of the meeting of the IEC, some confidential information may be disclosed or discussed.

Upon signing this form, I agree to take reasonable measures to keep the information as Confidential.

Indicate the details of the IEC Meeting to be attended:

.....
.....
.....

Signature of the Guest or Observer

Date

Chairperson/ Member Secretary of IEC

Date

**Confidentiality Agreement Form for
Non-members Requesting Copies of IEC's Documents**

I,....., as a non-member of IEC, understand that the copy (ies) given to me by the IEC is (are) confidential. I shall use the information only for the indicated purpose as described to the IEC and shall not duplicate, give or distribute these documents to any person(s) without permission from the IEC.

Upon signing this form, I agree to take reasonable measures and full responsibility to keep the information as Confidential.

I have received copies of the following IEC documents:

.....
.....
.....
.....

Signature of the recipient

Date

Chairperson/ Member Secretary of IEC

Date

Guidance for reviewing a study protocol

Reviewers should think about and try to find answers to the following questions:

1. How will the knowledge, result or outcome of the study contribute to human wellbeing?
 - ✓ Knowledge from the basic research may possibly benefit.
 - ✓ A new choice of method, drug or device that benefits the subject during the study and others in the future.
 - ✓ Provide safety data or more competitive choices.
2. Does the study design will be able to give answers to the objectives? Whether
 - ✓ The endpoints are appropriately selected.
 - ✓ The participating duration of a study participant is adequate to allow sufficient change in the endpoints.
 - ✓ The control arm is appropriately selected for best comparison.
 - ✓ The placebo is justified.
 - ✓ The number of study participants in non-treatment (or placebo) arm is minimized.
 - ✓ Unbiased assignment (e.g. randomization, etc.) is in practice.
 - ✓ Inclusion and exclusion criteria are carefully selected to eliminate confounding factors as much as possible.
 - ✓ The sample group size appropriate with the given statistical assumptions.
 - ✓ Predictable risks are minimized.
 - ✓ The tests and procedures that are more than minimal risk are cautiously used.
 - ✓ Subject deception is avoided.
 - ✓ Instruction and counseling for study participants are included (if needed) when deception is integral to the study design.
 - ✓ The study participants are adequately assessed and provided follow-up care, if needed.
3. Who will be the participants in the study? Whether
 - ✓ The described population is appropriate for the study.
 - ✓ Predictable vulnerabilities are considered.
 - ✓ It is completely necessary to conduct the study in a vulnerable population. If not, is there any other way to get the study answers?
 - ✓ There will be secondary participants.
4. Do the inclusion and exclusion criteria
 - ✓ Selectively include participants most likely to serve the objective of the study?
 - ✓ Equitably include participants?
 - ✓ Properly exclude participants who can predictably confound the results?
 - ✓ Properly exclude participants who may predictably be at increased risk in the study due to coexisting conditions or circumstances?

5. Does the study design have adequate built-in safeguards for risks?
 - ✓ Appropriate screening of potential participants?
 - ✓ Use of a stepwise dose escalation with analysis of the results before proceeding?
 - ✓ Does the frequency of visits and biological samplings reasonably monitor the expected effects?
 - ✓ Are there defined stopping (discontinuation) /withdrawal criteria for participants with worsening condition?
 - ✓ Is there minimized use of medication withdrawal and placebo whenever possible?
 - ✓ Will rescue medications and procedures be allowed when appropriate?
 - ✓ Is there a defined safety committee to perform interim assessments, when appropriate?
 - ✓ Is appropriate follow-up designed into the study? For instance, gene transfer research may require following the participants for years or for their entire lifetime after they receive the gene transfer agent.
6. Is pre-clinical and/or early clinical studies sufficiently performed before this study?
 - ✓ The animal study and *in vitro* testing results?
 - ✓ Previous clinical results, if done?
 - ✓ Whether the proposed study is appropriately built on the pre-clinical and/or early clinical results.
 - ✓ The selected dose based on adequate prior results?
 - ✓ Monitoring tests designed to detect expected possible risks and side effects?
7. Does the study and the informed consent process include issues of special concern, such as:
 - ✓ Waiver or alteration of consent?
 - ✓ Delayed consent (e.g., emergency treatment, etc.)?
 - ✓ Deception?
 - ✓ Sensitive information of participants that may require a confidentiality statement?

Study Assessment Form

Date (D/M/Y):

1. Assigned Protocol number.....
2. Protocol Title:
3. Principal Investigator(s): Contact No
4. Institute: Contact No.
5. Co – investigator(s): Contact No.
6. Total No. of Participants: No. of Study site:
7. Funding Agency:
8. Duration of the Study:
9. Status: New Revised Amended
10. Reviewer’s name: Contact No.
11. Type of the Study:

<input type="checkbox"/> Intervention	<input type="checkbox"/> Epidemiology
<input type="checkbox"/> Document based	<input type="checkbox"/> Individual based
<input type="checkbox"/> Social Survey	<input type="checkbox"/> Others, specify.....
12. Description of the Study in brief: Mark whatever applied to the study.

<input type="checkbox"/> Randomized	<input type="checkbox"/> Stratified Randomized	<input type="checkbox"/> Open-labeled
<input type="checkbox"/> Double blinded	<input type="checkbox"/> Placebo controlled	<input type="checkbox"/> Treatment controlled
<input type="checkbox"/> Cross-over	<input type="checkbox"/> Parallel	<input type="checkbox"/> Interim Analysis
<input type="checkbox"/> Use of Tissue samples	<input type="checkbox"/> Use of Blood samples	<input type="checkbox"/> Use of genetic materials
<input type="checkbox"/> Multicenter study	<input type="checkbox"/> Screening	<input type="checkbox"/> Descriptive
13. Brief the study design and the statistic used:
14. Study Objectives:

.....

.....

.....

.....

.....

.....

Mark and comment on what ever items applicable to the study.

1. Objectives of the Study

<input type="checkbox"/> clear	<input type="checkbox"/> unclear	What should be improved?
--------------------------------	----------------------------------	--------------------------
2. Need for Human Participants

<input type="checkbox"/> Yes	<input type="checkbox"/> No	Comment:
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3. Methodology:

<input type="checkbox"/> clear	<input type="checkbox"/> unclear	What should be improved?
--------------------------------	----------------------------------	--------------------------
4. Background Information and Data

<input type="checkbox"/> sufficient	<input type="checkbox"/> insufficient	Comment:
-------------------------------------	---------------------------------------	----------
5. Risks and Benefits Assessment

<input type="checkbox"/> acceptable	<input type="checkbox"/> unacceptable	
-------------------------------------	---------------------------------------	--
6. Inclusion Criteria

<input type="checkbox"/> appropriate	<input type="checkbox"/> inappropriate	Comment:
--------------------------------------	--	----------
7. Exclusion Criteria

<input type="checkbox"/> appropriate	<input type="checkbox"/> inappropriate	Comment:
--------------------------------------	--	----------
8. Discontinuation and Withdrawal Criteria

<input type="checkbox"/> appropriate	<input type="checkbox"/> inappropriate	Comment:
--------------------------------------	--	----------

9. Involvement of Vulnerable Participants
 Yes No Comment:
10. Voluntary, Non-Coercive Recruitment of Participants
 Yes No Comment:
11. Sufficient number of participants?
 Yes No Comment:
12. Control Arms (placebo, if any)
 Yes No Comment:
13. Are Qualification and experience of the Participating Investigators appropriate?
 Yes No Comment:
14. Disclosure or Declaration of Potential Conflicts of Interest
 Yes No Comment:
15. Facilities and infrastructure of Participating Sites
 Appropriate Inappropriate Comment:
16. Community Consultation
 Yes No Comment:
17. Involvement of Local Researchers and Institution in the Protocol Design, Analysis and Publication of Results
 Yes No Comment:
18. Contribution to Development of Local Capacity for Research and Treatment
 Yes No Comment:
19. Benefit to Local Communities
 Yes No Comment:
20. Availability of similar Study/ Results
 Yes No Comment:
21. Are blood/tissue samples sent abroad?
 Yes No Comment:
22. Are procedures for obtaining Informed Consent appropriate?
 Yes No Comment:
23. Contents of the Informed Consent Document
 clear unclear Comment:
24. Language of the Informed Consent Document
 clear unclear Comment:
25. Contact Persons for Participants
 Yes No Comment:
26. Privacy & Confidentiality
 Yes No Comment:
27. Inducement for Participation
 Unlikely Likely Comment:
28. Provision for Medical / Psychosocial Support
 appropriate inappropriate Comment:
29. Provision for Treatment of Study-Related Injuries
 appropriate inappropriate Comment:
30. Provision for Compensation
 appropriate inappropriate Comment:

Assessment Report

Review Date (D/M/Y):.....

Assigned Protocol number.....

Protocol Title:

Elements Reviewed

Attached Not attached

Review of Revised Application

Yes No

Date of Previous review:

DECISION:

Approved Approved with Recommendation
 Resubmission Disapproved

Comment:

Signature:

Date:

IEC Decision

Meeting No.:/..... Date (D/M/Y):.....
Assigned Protocol number.....
Protocol Title:

Principal Investigator(s):
Institute:

Elements Reviewed (FF 01-008):
 Attached Not attached
Review of Revised Application:
 Yes No
Date of Previous review:
Decision of the meeting:
 Approved Approved with Recommendation
 Resubmission Disapproved

Decision: Unanimous

No, Voting IEC members AP AR RES DA
Note: AP - Approved; AR – Approved with recommendation; RES – Resubmission for re-review; DA – Disapproved

Signature:

Chairperson

Date

**Approval of Institutional Ethics Committee
Dr. Rajendra Prasad Government Medical College & Hospital,
Kangra at Tanda**

IEC No

To
Dr.

Dear Dr..... (Name of the Principal Investigator).....
The Institutional Ethics Committee of Dr. Rajendra Prasad Government Medical College, Kangra at Tanda reviewed and discussed your application to conduct the Research Work entitled“” in the meeting of the committee held on(Date, Time & Place) that was submitted for the first time to the committee/ that was submitted earlier also on(Date) but was returned by the committee for revision.

The following Members of the Ethics Committee were present in the meeting.
..... (Chairperson of the Ethics Committee)
..... (Member Secretary of the Ethics Committee)
..... (Name of each Member with Designation)

We approve the Research work to be conducted in its presented form/ We approve the Research work to be conducted with following suggestions/ We suggest that you make following amendments and again submit your protocol for review/ We reject your protocol because of the following reasons.
Suggestions/ Amendments/Reasons for Rejection.....

The Institutional Ethics Committee expects to be informed about
Copy of all consent forms, filled and signed
The Half Yearly Progress of the study
Any Serious Adverse Event occurring during the study
Any changes in the protocol, Patient Information, Informed consent, Site of study or Investigator
A Copy of the Final Report of the study

Please Note that Members of IEC have the right to monitor the trial with prior intimation.

Yours Sincerely,

Member Secretary, Ethics Committee

**Institutional Ethics Committee
Dr. Rajendra Prasad Government Medical College & Hospital,
Kangra at Tanda
Provisional Approval**

IEC No

To
Dr.

Dear Dr..... (Name of the Principal Investigator).....
The Member Secretary of the Institutional Ethics Committee of Dr. Rajendra Prasad Government Medical College, Kangra at Tanda reviewed your application to conduct the Research Work entitled“.....” that was submitted for the first time to the committee/ that was submitted earlier also on(Date) but was returned by the committee for revision and provisionally approve the Research work to be conducted in its presented form/ provisionally approve the Research work to be conducted with following suggestions/ provisionally suggest that you make following amendments and again submit your protocol for review, **subject to the final Approval of the committee.**

Suggestions/ Amendments.....

You shall have to incorporate all the suggestions made by the committee in its final approval without delay and shall immediately stop the project if the committee decides so.

Yours Sincerely,

Member Secretary, Ethics Committee

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

Ethical Principles for Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the:

29th WMA General Assembly, Tokyo, Japan, October 1975

35th WMA General Assembly, Venice, Italy, October 1983

41st WMA General Assembly, Hong Kong, September 1989

48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996

52nd WMA General Assembly, Edinburgh, Scotland, October 2000

53rd WMA General Assembly, Washington 2002 (Note of Clarification on paragraph 29 added)

55th WMA General Assembly, Tokyo 2004 (Note of Clarification on Paragraph 30 added)

59th WMA General Assembly, Seoul, October 2008

A. INTRODUCTION

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

The Declaration is intended to be read as a whole and each of its constituent paragraphs should not be applied without consideration of all other relevant paragraphs.

2. Although the Declaration is addressed primarily to physicians, the WMA encourages other participants in medical research involving human subjects to adopt these principles.

3. It is the duty of the physician to promote and safeguard the health of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.

4. The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."

5. Medical progress is based on research that ultimately must include studies involving human subjects. Populations that are underrepresented in medical research should be provided appropriate access to participation in research.

6. In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests.

7. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best current interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

8. In medical practice and in medical research, most interventions involve risks and burdens.

9. Medical research is subject to ethical standards that promote respect for all human subjects and protect their health and rights. Some research populations are particularly vulnerable and need special protection. These include those who cannot give or refuse consent for themselves and those who may be vulnerable to coercion or undue influence.

10. Physicians should consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

B. PRINCIPLES FOR ALL MEDICAL RESEARCH

11. It is the duty of physicians who participate in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects.

12. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.

13. Appropriate caution must be exercised in the conduct of medical research that may harm the environment.

14. The design and performance of each research study involving human subjects must be clearly described in a research protocol. The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest, incentives for subjects and provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study. The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits.

15. The research protocol must be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins. This committee must be independent of the researcher, the sponsor and any other undue influence. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration. The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No change to the protocol may be made without consideration and approval by the committee.

16. Medical research involving human subjects must be conducted only by individuals with the appropriate scientific training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional. The responsibility for the protection of research subjects must always rest with the physician or other health care professional and never the research subjects, even though they have given consent.

17. Medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community and if there is a reasonable likelihood that this population or community stands to benefit from the results of the research.

18. Every medical research study involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and communities involved in the research in comparison with foreseeable benefits to them and to other individuals or communities affected by the condition under investigation.

19. Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject.

20. Physicians may not participate in a research study involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily

managed. Physicians must immediately stop a study when the risks are found to outweigh the potential benefits or when there is conclusive proof of positive and beneficial results.

21. Medical research involving human subjects may only be conducted if the importance of the objective outweighs the inherent risks and burdens to the research subjects.

22. Participation by competent individuals as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no competent individual may be enrolled in a research study unless he or she freely agrees.

23. Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information and to minimize the impact of the study on their physical, mental and social integrity.

24. In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information. After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

25. For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse. There may be situations where consent would be impossible or impractical to obtain for such research or would pose a threat to the validity of the research. In such situations the research may be done only after consideration and approval of a research ethics committee.

26. When seeking informed consent for participation in a research study the physician should be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent should be sought by an appropriately qualified individual who is completely independent of this relationship.

27. For a potential research subject who is incompetent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the population represented by the potential subject, the research cannot instead be performed with competent persons, and the research entails only minimal risk and minimal burden.

28. When a potential research subject who is deemed incompetent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected.

29. Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research population. In such circumstances the physician should seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee.

Consent to remain in the research should be obtained as soon as possible from the subject or a legally authorized representative.

30. Authors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. They should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results should be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest should be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE

31. The physician may combine medical research with medical care only to the extent that the research is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.

32. The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention, except in the following circumstances:

- The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists; or
- Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of an intervention and the patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm. Extreme care must be taken to avoid abuse of this option.

33. At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.

34. The physician must fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never interfere with the patient-physician relationship.

35. In the treatment of a patient, where proven interventions do not exist or have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, this intervention should be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information should be recorded and, where appropriate, made publicly available.

GLOSSARY

The definitions provided within this glossary apply to terms as they are used in these Guidelines. The terms may have different meanings in other contexts.

Advice

Non-binding considerations adjoined to a decision intended to provide ethical assistance to those involved in the research.

Applicant

A qualified researcher undertaking the scientific and ethical responsibility for a research project, either on his/her own behalf or on behalf of an organization/firm, seeking a decision from an ethics committee through formal application.

Community

A community is a group of people understood as having a certain identity due to the sharing of common interests or to a shared proximity. A community may be identified as a group of people living in the same village, town, or country and, thus, sharing geographical proximity. A community may be otherwise identified as a group of people sharing a common set of values, a common set of interests, or a common disease.

Conflict of interest

A conflict of interest arises when a member (or members) of the EC holds interests with respect to specific applications for review that may jeopardize his/her (their) ability to provide a free and independent evaluation of the research focused on the protection of the research participants. Conflicts of interests may arise when an EC member has financial, material, institutional, or social ties to the research.

Decision

The response (positive, conditional, or negative) by an EC to an application following the review in which the position of the EC on the ethical validity of the proposed study is stated.

Investigator

A qualified scientist who undertakes scientific and ethical responsibility, either on his/her own behalf or on behalf of an organization/firm, for the ethical and scientific integrity of a research project at a specific site or group of sites. In some instances a coordinating or principal investigator may be appointed as the responsible leader of a team of sub investigators.

Protocol

A document that provides the background, rationale, and objective(s) of a biomedical research project and describes its design, methodology, and organization, including ethical and statistical considerations. Some of these considerations may be provided in other documents referred to in the protocol.

Protocol amendment

A written description of a change to, or formal clarification of, a protocol.

Requirements

In the context of decisions, requirements are binding elements that express ethical considerations whose implementation the ethics committee requires or views as obligatory in pursuing the research.

Research participant

An individual who participates in a biomedical research project, either as the direct recipient of an intervention (e.g., study product or invasive procedure), as a control, or through observation. The individual may be a healthy person who volunteers to participate in the research, or a person with a condition unrelated to the research carried out who volunteers to participate, or a person (usually a patient) whose condition is relevant to the use of the study product or questions being investigated.

Sponsor

An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a research project.