INSTITUTIONAL REVIEW BOARD POLICIES AND PROCEDURES

COORG INSTITUTE OF DENTAL SCIENCES

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FOREWORD

Research involving human subjects can be very rewarding with lots of data that can be used to benefit mankind in many ways. In the urge to get the required results, very often there are chances that fundamental principles governing the patient rights may be violated. Coorg Institute of Dental Sciences is committed to ensuring good research practices by ensuring that research involving human subjects is carried out in a safe environment abiding by all the ethical rules that are applied nationally and internationally. The Indian populace is a rich and diverse mix of several cultures and subcultures with different systems of belief. This manual has been prepared after thought to protect the interests of those who are subjected to research at CIDS. It is mandatory that all personnel at CIDS, the graduate, the postgraduate and the faculty researcher ensure that these guidelines are understood and followed.

I wish all the members of CIDS many years of fruitful research aimed at taking patient care to the next level and for our students to become responsible researchers. Good luck!

Dr. Sunil Muddaiah

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PROLOGUE

SYNONYMS

Institutional Review Board - Ethical Clearance - Ethical Review Board

ETHICAL AND REGULATORY MANDATES FOR CONDUCTING RESEARCH

Coorg Institute of Dental Sciences (CIDS) is committed to ensuring that all the Research Projects are conducted in accordance with the ethical principles stated in the **ICMR Ethical Guidelines 2006 Centre for studies in Ethics & Rights, Mumbai** and **Clinical Trials Registry-India (CTRI).** CIDS is interested to assist in the development and education of a research community responsive to local health care requirements. All CIDS personnel involved in the conduct and supervision of human subject research must abide by the fundamental principles set forth in the **ICMR 2006, CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals),** Centre for studies Ethics & Rights, Mumbai, which include:

RESPECT FOR PERSONS

- Individuals should be treated as autonomous agents afforded the right to make decisions for them. Those with diminished autonomy (e.g. minors, prisoners, persons who are mentally disabled) are entitled to additional protections. Application of this principle requires that human subjects be enrolled into research studies only under the conditions of effective informed consent. This involves a process in which participation in the research is acknowledged by the research subject (or by a legally authorized representative) as a voluntary act, free from coercion or undue influence from the investigator or members of the research team.

BENEFICENCE AND NON-MALEFICENCE

- The word '*beneficence'* originated from Latin meaning 'to do good'. This principle puts the onus on the researchers to protect the physical, mental and social well-being of the research participant. In healthcare our efforts are to help others must carefully assess the risky conditions we may put the participant in. Thus, there is an obligation to balance benefits against risks. The minimal standard of this principle is '*nonmaleficence*'. Derived from the Latin phrase *Primum non nocere*, means 'first, do no harm'. The obligation is to provide net benefits to the participants

JUSTICE

- The possibility for benefits and the potential burdens of the research should be equitably distributed among the potential research subjects. Application of this principle requires the close scrutiny of the enrollment process to ensure that particular classes (welfare patients, racial and ethnic minorities, or persons confined to institutions) are not selected for their compromised position or convenience to the research investigator.

GENERAL PRINCIPLES TO BE FOLLOWED

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 authorized on their behalf; and after ensuring that the said human participant does not suffer from any form of hardship, discrimination or stigmatization as a consequence of having participated in the research or experiment.

V. Principles of precaution and risk minimization 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 maximization 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.

These 12 principles laid down under Statement on General Principles are common to all areas of biomedical research. The specific issues are mentioned under relevant topics.

COMPOSITION OF THE IRB

At CIDS, the IRB committee is multidisciplinary and multi-sectorial in composition. Independence and competence are the two hallmarks of the IRB. Based on the ICMR 2006 guidelines, the number of persons in the IRB is kept fairly small (8 - 12 members). A minimum of five persons are required to form the quorum without which a decision regarding the research should not be taken. The IRB should appoint from among its members a Chairman who is from outside the Institution and not head of the same Institution to maintain the independence of the Committee. The Member Secretary should is from the same Institution and will conduct the business of the Committee. Other member are a mix of medical/non-medical, scientific and non-scientific persons including laypersons to represent the differed points of view.

The composition may be as follows: -

1. Chairperson
2. Co-chair
3. Member Secretary
4. One/two clinicians from various Institutes
5. One/two persons from basic medical science area
6. One philosopher/ ethicist/ theologian
7. One lay person from the community
8. One legal expert or retired judge
9. One social scientist/representative of non-governmental voluntary agency.
10. If required, subject experts and consultants could be invited to offer views.

TERMS OF REFERENCE FOR IRB MEMBERS

The Terms of References will include Terms of Appointment with reference to the duration of the term, the policy for removal, replacement, resignation procedure, frequency of meetings, and payment of processing fee to the IRB for review, honorarium/consultancy to the members/ invited experts *etc.* and these should are specified in the SOP which is made available to each member. Our Institute has written SOPs according to which the Committee does its function. The SOPs will be updated periodically based on the changing requirements. The term of appointment of members could be extended for another term and a defined percentage of members could be changed on regular basis. It would be preferable to appoint persons trained in bioethics or persons conversant with ethical guidelines and laws of the country. Substitute member may be nominated if meetings have been continuously missed by a member due to illness or other unforeseen circumstances. For this the criteria for number of missed meetings may be defined in the SOP.

TRAINING OF IRB MEMBERS

The IRB members are encouraged to keep abreast of all national and international developments in ethics through orientation courses on related topics by its own members or regular training organized by constituted body (ies), so that they become aware of their role and responsibilities. For drug trial review our IRB members are given training in Good Clinical Practice. Any change in the regulatory requirements are brought to their attention and they should be aware of local, social and cultural norms, as this is the most important social control mechanism.

REGULATION OF IRB

Once the legislation of guidelines occurs which is currently under active consideration by the Ministry of Health, a Biomedical Research Authority will be set up under the proposed Bill on Biomedical Research on Human

Participants(Promotion and Regulation) which would require that all IRBs register with this Authority. It will also evaluate and monitor functioning of the IRB, and develop mechanisms for enforcing accountability and transparency by the institutions.

GENERAL ETHICAL ISSUES

All the research involving human participation should be conducted in accordance with the four basic ethical principles, namely

- autonomy (respect for person/participant)
- beneficence,
- non-malfeasance (do no harm) and
- justice.

The guidelines laid down are directed at application of these basic principles to research involving human participants. The Principal Investigator is the person responsible for not only undertaking research but also for observance of the rights, health and welfare of the participants recruited for the study. She/he should have qualification and competence in biomedical research methodology for proper conduct of the study and should be aware of and comply with the scientific, legal and ethical requirements of the study protocol.

INFORMED CONSENT PROCESS

1. Informed Consent of Participants:

For all biomedical research involving human participants, the investigator must obtain the informed consent of the prospective participant or in the case of an individual who is not capable of giving informed consent, the consent of a legal guardian. Informed consent protects the individual's freedom of choice and respect for individual's autonomy and is given voluntarily to participate in research or not. Adequate information about the research is given in a simple and easily understandable unambiguous language in a document known as the Informed Consent Form with Participant/ Patient Information Sheet. The latter should have following components as may be applicable:

1. Nature and purpose of study stating it as research

2. Duration of participation with number of participants

3. Procedures to be followed

4. Investigations, if any, to be performed

5. Foreseeable risks and discomforts adequately described and whether project involves more than minimal risk

6. Benefits to participant, community or medical profession as may be applicable

7. Policy on compensation

8. Availability of medical treatment for such injuries or risk management

9. Alternative treatments if available

10. Steps taken for ensuring confidentiality

11. No loss of benefits on withdrawal

12. Benefit sharing in the event of commercialization

13. Contact details of PI or local PI/Co-PI in multicentric studies for asking more information related to the research or in case of injury

14. Contact details of Chairman of the IRB for appeal against violation of rights

15. Voluntary participation

16. If test for genetics and HIV is to be done, counseling for consent for testing must be given as per national guidelines

17. Storage period of biological sample and related data with choice offered to participant regarding future use of sample, refusal for storage and receipt of its results A copy of the participant/patient information sheet should be given to the participant for her/his record. The informed consent should be brief in content highlighting that it is given of free will or voluntarily after understanding the implications of risks and benefits and s/he could withdraw without loss of routine care benefits. Assurance is given that confidentiality would be maintained and all the investigations/interventions would be carried out only after consent is obtained. When the written consent as signature or thumb impression is not possible due to sensitive nature of the project or the participant is unable to write, then verbal consent can be taken after ensuring its documentation by an unrelated witness. In some cases ombudsman (a third party) can ensure total accountability for the process of obtaining the consent. Audio-visual methods could be adopted with prior consent and adequate precaution to ensure confidentiality, but approval of IRB is required for such procedures. For drug trials, if the volunteer can give only thumb impression then another thumb impression by the relative or

legal custodian cannot be accepted and an unrelated witness to the project should then sign.

FRESH OR RE-CONSENT IS TAKEN IN FOLLOWING CONDITIONS

1. Availability of new information which would necessitate deviation of protocol.

2. When a research participant regains consciousness from unconscious state or is mentally competent to understand the study. If such an event is expected then procedures to address it should be spelt out in the informed consent form.

3. When long term follow-up or study extension is planned later.

4. When there is change in treatment modality, procedures, site visits.

5. Before publication if there is possibility of disclosure of identity through data presentation or photographs (which should be camouflaged adequately)?

WAIVER OF CONSENT

Voluntary informed consent is always a requirement for every research proposal. However, this can be waived if it is justified that the research involves not more than minimal risk or when the participant and the researcher do not come into contact or when it is necessitated in emergency situations elaborated in the previous Chapter. If such studies have protections in place for both privacy and confidentiality, and do not violate the rights of the participants then IRB may waive off the requirement for informed consent in following instances:

i. When it is impractical to conduct research since confidentiality of personally identifiable information has to be maintained throughout

research as may be required by the sensitivity of the research objective, *e.g.*, study on disease burden of HIV/AIDS.

ii. Research on publicly available information, documents, records, works, performances, reviews, quality assurance studies, archival materials or third party interviews, service programs for benefit of public having a bearing on public health programs, and consumer acceptance studies.

iii. Research on anonymised biological samples from deceased individuals, left over samples after clinical investigation, cell lines or cell free derivatives like viral isolates, DNA or RNA from recognized institutions or qualified investigators, samples or data from repositories or registries *etc*.

iv. In emergency situations when no surrogates consent can be taken.

2. Obligations of investigators regarding informed consent:

The investigator has the duty to:

i. Communicate to prospective participants all the information necessary for informed consent. Any restriction on participant's right to ask any questions related to the study will undermine the validity of informed consent;

ii. Exclude the possibility of unjustified deception, undue influence and intimidation. Although deception is not permissible, if sometimes such information would jeopardize the validity of research it can be withheld till the completion of the project, for instance, study on abortion practices;

iii. Seek consent only after the prospective participant is adequately informed. The investigator should not give any unjustifiable assurances

to prospective participant, which may influence her/his decision to participate;

iv. Obtain from each prospective participant a signed form as an evidence of informed consent (written informed consent) preferably witnessed by a person not related to the trial, and in case the participant is not competent to do so, a legal guardian or other duly authorized representative;

v. Take verbal consent when the participant refuses to sign or give thumb impression or cannot do so. This can then be documented through audio or video means;

vi. Take surrogate consent from the authorized relative or legal custodian or the institutional head in the case of abandoned institutionalized individuals or wards under judicial custody;

vii. Renew or take fresh informed consent of each participant under circumstances described earlier in this chapter;

viii. If participant loses consciousness or competence to consent during the research period as in Alzheimer or psychiatric conditions, surrogate consent may be taken from the authorized person or legal custodian.

ix. The investigator must assure prospective participants that their decision to participate or not will not affect the patient - clinician relationship or any other benefits to which they are entitled.

3. Essential information for prospective research participants:

Before requesting an individual's consent to participate in research, the investigator must provide the individual with the following information in the language she or he is able to understand which should not only be scientifically accurate but should also be sensitive/ adaptive to their social and cultural context:

i. The aims and methods of the research;

ii. The expected duration of the participation;

iii. The benefits that might reasonably be expected as an outcome of research to the participant or community or to others;

iv. Any alternative procedures or courses of treatment that might be as advantageous to the participant as the procedure or treatment to which she/he is being subjected;

v. Any foreseeable risk or discomfort to the participant resulting from participation in the study;

vi. Right to prevent use of her/his biological sample (DNA, cell-line, etc.) at any time during the conduct of the research;

vii. The extent to which confidentiality of records could be maintained i.e., the limits to which the investigator would be able to safeguard confidentiality and the anticipated consequences of breach of confidentiality;

viii. Responsibility of investigators;

ix. Free treatment for research related injury by the investigator and/ institution and sponsor(s);

x. Compensation of participants for disability or death resulting from such injury;

xi. Insurance coverage if any, for research related or other AEs;

xii. Freedom of individual/family to participate and to withdraw from research any time without penalty or loss of benefits which the participant would otherwise be entitled to;

xiii. The identity of the research teams and contact persons with address and phone numbers;

xiv. Foreseeable extent of information on possible current and future uses of the biological material and of the data to be generated from the research and if the material is likely to be used for secondary purposes or would be shared with others, clear mention of the same;

xv. Risk of discovery of biologically sensitive information and provision to safeguard confidentiality;

xvi. Publication, if any, including photographs and pedigree charts. The quality of the consent of certain social and marginalized groups requires careful consideration as their agreement to volunteer may be unduly influenced by the Investigator.

COMPENSATION FOR PARTICIPATION

Participants may be paid for the inconvenience and time spent, and should be reimbursed for expenses incurred, in connection with their participation in research. They may also receive free medical services. When this is reasonable then it cannot be termed as benefit. During the period of research if the participant requires treatment for complaints other than the one being studied necessary free ancillary care or appropriate referrals may be provided. However, payments should not be so large or the medical services so extensive as to make prospective participants consent readily to enroll in research against their better judgment, which would then be treated as undue inducement. All payments, reimbursement and medical services to be provided to research participants should be approved by the IRB. Care should be taken:

i. When a guardian is asked to give consent on behalf of an incompetent person, no remuneration should be offered except a refund of out of pocket expenses;

ii. When a participant is withdrawn from research for medical reasons related to the study the participant should get the benefit for full participation;

iii. When a participant withdraws for any other reasons s/he should be paid an amount proportionate to the amount of participation.

CONFLICT OF INTEREST

A set of conditions in which professional judgment concerning a primary interest like patient's welfare or the validity of research tends to be or appears to be unduly influenced by a secondary interest like non-financial (personal, academic or political) or financial gain is termed as Conflict of Interest (COI). Academic institutions conducting research in alliance with industries/commercial companies require a strong review to probe possible conflicts of interest between scientific responsibilities of researchers and business interests. *g* **(**.ownership or part-ownership of a company developing a new product). In cases where the review board/ committee determines that a conflict of interest may damage the scientific integrity of a project or cause harm to research participants, the board/committee should advise accordingly. Significant financial interest means anything of monetary value that would reasonably appear to be a significant consequence of such research including salary or other payments for services like consulting fees or honorarium per participant; equity interests in stocks, stock options or other ownership interests; and intellectual property rights from patents, copyrights and royalties from such rights. The investigators should declare such conflicts of interest in the application submitted to IRB for review. Institutions and IRBs need self-regulatory processes to monitor, prevent

and resolve such conflicts of interest. The IRB can determine the conditions for management of such conflicts in its SOP manual. Prospective participants in research should also be informed of the sponsorship of research, so that they can be aware of the potential for conflicts of interest and commercial aspects of the research. Those who have also to be informed of the secondary interest in financial terms should include the institution, IRB, audience when presenting papers and should be mentioned when publishing in popular media or scientific journals.

Undue inducement through compensation for individual participants, families and populations should be prohibited. This prohibition however, does not include agreements with individuals, families, groups, communities or populations that foresee technology transfer, local training, joint ventures, provision of health care reimbursement, costs of travel and loss of wages and the possible use of a percentage of any royalties for humanitarian purposes. Undue compensation would include assistance to related person(s) for transport of body for cremation or burial, provision for insurance for unrelated conditions, free transportation to and fro for examination not included in the routine, free trip to town if the participants are from rural areas, free hot meals, freedom for prisoners, free medication which is generally not available, academic credits and disproportionate compensation to researcher/ team/institution. However, in remote and inaccessible areas some of the features mentioned above may be a necessity and culture specific. Therefore, the IRB should examine this on a case-by-case basis, as some of these elements may be justifiable for collecting vital data for national use or necessary to find if some interventions may significantly have direct impact on health policies.

SELECTION OF SPECIAL GROUPS AS RESEARCH PARTICIPANTS

i. *Pregnant or nursing women*: Pregnant or nursing women should in no circumstances be the participant of any research unless the research carries no more than minimal risk to the fetus or nursing infant and the object of the research is to obtain new knowledge about the foetus, pregnancy and lactation. As a general rule, pregnant or nursing women should not be participants of any clinical trial except such trials as are designed to protect or advance the health of pregnant or nursing women or foetuses or nursing infants, and for which women who are not pregnant or nursing would not be suitable participants.

a. The justification of participation of these women in clinical trials would be that they should not be deprived arbitrarily of the opportunity to benefit from investigations, drugs, vaccines or other agents that promise therapeutic or preventive benefits. Example of such trials are, to test the efficacy and safety of a drug for reducing prenatal transmission of HIV infection from mother to child, trials for detecting foetal abnormalities and for conditions associated with or aggravated by pregnancy etc. Women should not be encouraged to discontinue nursing for the sake of participation in research and in case she decides to do so, harm of cessation of breast-feeding to the nursing child should be properly assessed except in those studies where breast feeding is harmful to the infant. Compensation in terms of supplying supplementary food such as milk formula should be considered in such instances.

b. Research related to termination of pregnancy: Pregnant women who desire to undergo Medical Termination of Pregnancy (MTP) could be made participants for such research as per The Medical Termination of Pregnancy Act, GOI, 1971.

c. Research related to pre-natal diagnostic techniques: In pregnant women such research should be limited to detect the foetal abnormalities or genetic disorders as per the Prenatal Diagnostic Techniques (Regulation and Prevention of Misuse) Act, GOI, 1994 and not for sex determination of the foetus.

ii. *Children*: Before undertaking trial in children the investigator must ensure that -

a. Children will not be involved in research that could be carried out equally well with adults;

b. The purpose of the research is to obtain knowledge relevant to health needs of children. For clinical evaluation of a new drug the study in children should always be carried out after the phase III clinical trials in adults. It can be studied earlier only if the drug has a therapeutic value in a primary disease of the children;

c. A parent or legal guardian of each child has given proxy consent;

d. The assent of the child should be obtained to the extent of the child's capabilities such as in the case of mature minors from the age of seven years up to the age of 18 years.;

e. Research should be conducted in settings in which the child and parent can obtain adequate medical and psychological support;

f. Interventions intended to provide direct diagnostic, therapeutic or preventive benefit for the individual child participant must be justified in relation to anticipated risks involved in the study and anticipated benefits to society;

g. The child's refusal to participate in research must always be respected unless there is no medically acceptable alternative to the therapy

provided/ tested, provided the consent has been obtained from parents / guardian;

h. Interventions that are intended to provide therapeutic benefit are likely to be at least as advantageous to the individual child participant as any available alternative interventions;

i. The risk presented by interventions not intended to benefit the individual child participant is low when compared to the importance of the knowledge that is to be gained.

iii. *Vulnerable groups*: Effort may be made to ensure that individuals or communities invited for research be selected in such a way that the burdens and benefits of the research are equally distributed.

a. Research on genetics should not lead to **racial inequalities**;

b. Persons who are **economically or socially disadvantaged** should not be used to benefit those who are better off than them;

c. Rights and welfare of **mentally challenged and mentally differently able persons** who are incapable of giving informed consent or those with behavioral disorders must be protected. Appropriate proxy consent from the legal guardian should be taken after the person is well informed about the study, need for participation, risks and benefits involved and the privacy and confidentiality procedures. The entire consent process should be properly documented;

d. Adequate justification is required for the involvement of participants such as prisoners, students, subordinates, employees, service personnel etc. who have **reduced autonomy** as research participants, since the consent provided may be under duress or various other compelling reasons.

ESSENTIAL INFORMATION ON CONFIDENTIALITY FOR PROSPECTIVE

RESEARCH PARTICIPANTS

Safeguarding confidentiality - The investigator must safeguard the confidentiality of research data, which might lead to the identification of the individual participants.

Data of individual participants can be disclosed under the following circumstances:

a. Only in a court of law under the orders of the presiding judge or

b. There is threat to a person's life or

c. In cases of severe adverse reaction may be required to communicate to drug registration authority or

d. If there is risk to public health it takes precedence over personal right to privacy and may have to be communicated to health authority. Therefore, the limitations in maintaining the confidentiality of data should be anticipated and assessed and communicated to appropriate individuals or authorities as the case may be.

COMPENSATION FOR ACCIDENTAL INJURY

Research participants who suffer physical injury as a result of their participation are entitled to financial or other assistance to compensate them equitably for any temporary or permanent impairment or disability. In case of death, their dependents are entitled to material compensation.

Obligation of the sponsor to pay :- The sponsor whether a pharmaceutical company, a government, or an institution, should agree, before the research begins, in the *a priori* agreement to provide

compensation for any physical or psychological injury for which participants are entitled or agree to provide insurance coverage for an unforeseen injury whenever possible. An Arbitration committee or appellate authority could be set up by the institution to decide on the issue of compensation on a case-by-case basis for larger trials where such a step is feasible. Alternately an institution can also establish such a committee to oversee such claims, which would be common for projects being undertaken by it.

Compensation for **ancillary care** for unrelated illness as free treatment or appropriate referrals may also be included in the *a priori* agreement with the sponsors whenever possible.

Special Concerns:

1. Given the magnitude and severity of the health problems in different countries, capacity building to address ethical issues that arise out of collaborative research must be promoted on a priority basis. Strategies should be implemented so that various countries and communities can practice meaningful self-determination in health development and can ensure the scientific and ethical conduct of research.

2. The collaborating investigators, institutions and countries can function as equal partners with sponsors even when in a vulnerable position by building appropriate safeguards. Community representatives should be involved early enough while designing the protocol and in a sustained manner during the development, implementation, monitoring and dissemination of results of research.

3. Careful consideration should be given to protect the dignity, safety and welfare of the participants when the social contexts of the proposed research can create foreseeable conditions for exploitation of the participants or increase their vulnerability to harm. The steps to be taken

to overcome these should be described and approval taken from concerned IRB/IndEC.

4. Every adult participant in the research should voluntarily give informed consent and child her/his assent as may be applicable.

5. As different kinds of research (epidemiological studies, clinical trials, product development, behavioral and social science oriented research *etc.*) have their own particular scientific requirements and specific ethical challenges, the choice of study populations for each type of study should be justified in advance in scientific and ethical terms regardless of the place from where the study population is selected. Generally, early clinical phases of research, particularly of drugs, vaccines and devices, should be conducted in communities that are less vulnerable to harm or exploitation. However, for valid scientific and public health reasons, if sufficient scientific and ethical safeguards are ensured it may be conducted in any phase after obtaining relevant regulatory clearances.

6. The nature, magnitude, and probability of all foreseeable harms resulting from participation in a collaborative research programme should be specified in the research protocol and explained to the participants as fully as can be reasonably done. Moreover, the modalities by which to address these, including **provision for the best possible nationally available care** to participants who experience adverse reactions to a vaccine or drug under study, compensation for injury related to the research, and referral for psychosocial and legal support if necessary, need to be described.

7. The research protocol should outline the benefits that persons/communities/countries participating in such research should experience as a result of their participation. Care should be taken so that these are not presented in a way that unduly influences freedom of

choice in participation. The burden and the benefit should be equally borne by the collaborating countries.

8. Guidelines, rules, regulations and cultural sensitivities of all countries participating in collaborative research projects should be respected, especially by researchers in the host country and the sponsor country. These could be with reference to intellectual property rights, exchange of biological materials (human, animal, plant or microbial), data transfer, security issues, and issues of socially or politically sensitive nature. In this context, it is essential for researchers to follow the GOI notification on “Exchange of Human Biological

Material for Biomedical Research” issued on 19.11.97 and obtains appropriate regulatory clearances as prevalent in the country for international collaboration and IRB approval from all trial sites before the initiation of research.

RESPONSIBILITIES OF THE IRB CHAIRPERSON/ALTERNATE MEMBERS

The IRB Chairperson will hold leadership responsibility for IRB review and approval of all the research in accordance with current guidelines, institutional policies, and Indian research regulatory bodies.

In addition, the IRB Chair will:

- Oversee the recruitment, orientation, continuing education and retention of IRB members;

- Oversee the development and implementation of appropriate policies, procedures and guidelines directed at human subject protections and the functions and activities of the IRB. The IRB Chair is responsible for reviewing the IRB's policies and procedures for accuracy and consistency on an ongoing basis but not less than every three years. Ad hoc committees will be formed to review guidance issued by regulatory agencies to determine whether updates to the policies and procedures are required.

- Have the authority to suspend some or all research activities if exceptional human subject safety issues are identified. (Note that this authority is only exercised if an action is required prior to a convened meeting and it is not feasible to assemble an emergency meeting)

- Approve written correspondence to state and central regulatory agencies having jurisdiction over human subject research prior to final approval and signature of the Institutional Official

Responsibilities of IRB Members

General Responsibilities of all IRB Members include:

- Reviewing research study proposals and evaluating them from the

perspective of the regulatory criteria and any other relevant ethical, scientific or compliance considerations;

- Reviewing informed consent documents and evaluating them from the perspective of addressing the required and additional elements of informed consent and any other relevant ethical or compliance considerations;

- Attending at least 70% of IRB meetings in person, unless exigent circumstances prevent such attendance on an occasional basis; reporting promptly at the designated time that the meeting convenes; and remaining in attendance at the meeting until the full agenda has been addressed;

- Participating in IRB deliberations concerning issues inherent to proposed research studies and related informed consent documents, and making recommendations for reducing risk and improving the informed consent process and otherwise for improving human subject protections;

- Voting for full approval, approval subject to modification(s), reconsideration, or disapproval of the human subject research;

- Evaluating the risk level (i.e., minimal or greater than minimal) of the proposed research. In performing this evaluation, IRB members will use the following absolute definition for "minimal risk"

- Deciding, for research studies of greater than minimal risk, if IRB continuing review of the research is warranted on a more frequent basis than the requisite annual review.

- Deciding, for research studies involving greater than minimal risk, complexity, or conflict-of-interest concerns, if the informed consent process and/or other aspects of the research study should be audited;

- Deciding, for research studies involving an unapproved device, if the device and its proposed use constitute a non-significant or significant risk to research subjects;

- Deciding, for research studies subject to IRB continuation approval, if verification is required from sources other than the investigator that no material changes have occurred since previous IRB review;

- Recommending improvements to IRB policies and procedures so as to enhance the IRB review process and/or human subject protections;

- Informing the IRB Chair of human subject research noncompliance problems or ethical issues of which they become aware;

- Conforming, at all times, their behavior to be within legal and ethical principles accepted by the IRB; including, but not limited to, maintaining confidentiality/non-disclosure of human subject research submitted for IRB review and approval, and good faith participation in IRB deliberations without appearance of discrimination or conflict-of-interest.

RESEARCH TEAM

PRINCIPAL INVESTIGATOR REQUIREMENTS AND RESPONSIBILITIES

The Principal Investigator (PI) is ultimately responsible for assuring compliance with applicable CIDS-IRB policies and procedures and the informed consent process. Although the PI may delegate tasks to members of his/her research team, she retains the ultimate responsibility for the conduct of the study.

WHO MAY SERVE AS A PRINCIPAL INVESTIGATOR (PI)?

Because PI responsibilities involve direct interaction and supervision of the research team, the PI must be a current faculty or student of the CIDS, who is operating within CIDS to oversee the conduct of the study. PIs leaving the institution are responsible for notifying the IRB well in advance of their departure so that they can make arrangements to either close the study or name another appropriately qualified individual currently at the institution to serve as the PI.

The following individuals may serve as PI:

- **Faculty members:** All categories of faculty members may serve as PI if the respective HOD allows them to serve as Principal Investigator on applications.
- **Outside faculty:** No outside faculty may serve in this role even if they have appropriate qualifications to conduct the research or if they have obtained approval to conduct the research from their immediate supervisor.
- **Students:** Students may serve as principal investigators for their own research projects and are responsible for submitting the IRB

application. However, when a student is listed as the PI, a faculty guide must be listed on the protocol submission.

Note: *The IRB reviews and holds student research projects to the same standards as human subject research conducted by faculty. IRB approval or exemption must be obtained prior to initiating any research activity under IRB oversight. "Retroactive" IRB approval or exemption is not permitted under CIDS policy. Failure to obtain IRB approval for research with human subjects may preclude the use of the previously collected data and could result in other sanctions.*

GENERAL RESPONSIBILITIES OF PRINCIPAL INVESTIGATORS

As a general condition for the approval of a research study, the IRB holds the principal investigator of the study responsible for ensuring that:

- Risks to research subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose the subjects to risk; and, whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes;

- Risks to human research subjects are reasonable in relation to the anticipated benefits (if any) to the individual, and the importance of the knowledge that may be expected to result

- Selection of human subjects and patients for research participation is equitable;

- Individuals are adequately informed of the risks and benefits of research participation and the procedures that will be involved in the research, and that informed consent will be obtained from each prospective human research subject, or his/her legally authorized representative, in accordance with, and to the extent required, by

University policies and Indian research regulation bodies

- Informed consent of human research subjects will be obtained in advance of research participation and appropriately documented in accordance with, and to the extent required, by University policies and Indian research regulation bodies

- Where appropriate, there is routine monitoring of the data collected to the ensure the safety of human research subjects

- The privacy of human research subjects is protected and the confidentiality of data is maintained;

- Appropriate additional safeguards are included in the study to protect the rights and welfare of human research subjects who are likely to be vulnerable to coercion or undue influence (e.g., children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons).

SPECIFIC RESPONSIBILITIES OF PRINCIPAL INVESTIGATORS

The IRB holds the principal investigator of an approved research study responsible for:

- Promptly responding to all requests for information or materials solicited by the IRB Office, including the timely submission of the research study for IRB renewal;
- Ensuring that adequate resources and facilities are available to carry out the proposed research study;
- Abstaining from enrolling any individual in a research study
    i. until such study is approved in writing, by the IRB;
    ii. during any period when the IRB or sponsor/principal investigator has suspended study activities; or
    iii. following IRB-or sponsor/principal investigator-directed termination of the study;
- Ensuring that all associates, colleagues, and other personnel assisting in the conduct of the research study are appropriately informed of
    i. the study procedures;
    ii. informed consent requirements;
    iii. the potential adverse events associated with study participation and the steps to be taken to reduce potential risks;
    iv. adverse event reporting requirements; and
    v. data collection and record-keeping criteria;
- Conducting the study in strict accordance with the current IRB-approved research protocol except where a change may be necessary to eliminate an apparent immediate hazard to a given human research subject;
- Reporting promptly to the IRB Office any deviations from the currently approved research protocol;

- Requesting IRB approval of any proposed modification to the research protocol or informed consent documents prior to implementing such modifications;
- Obtaining prospectively and documenting informed consent in accordance with the current IRB-approved informed consent documents (i.e., unless the IRB has granted a waiver of the consent process) maintaining adequate, current, and accurate records of research data, outcomes, and adverse events to permit an ongoing assessment of the risk/benefit ratio of study participation;
- Reporting promptly to the IRB any internal or external adverse event that is considered to be
  i. unexpected;
  ii. serious and
  iii. possibly or definitely related to the study;
- Reporting promptly to the IRB any significant changes in the risk/benefit of study participation;
- Ensuring that, in the event a research subject experiences a significant adverse event, every reasonable effort is made to provide the subject with adequate care to correct or alleviate the consequences of the adverse event to the extent possible;
- Ensuring that human research subjects are kept fully informed of any new information that may affect their willingness to continue to participate in the research study;
- Ensuring that all listed investigators have the appropriate credentials to conduct the portion of the study in which they are involved;
- Ensuring submission of final report/intimation towards completion of project

SPECIFIC PRINCIPLES TO BE FOLLOWED FOR EPIDEMIOLOGICAL STUDIES

INTRODUCTION

Epidemiology is defined as the study of the distribution and determinants of health related states or events in specified populations and the application of this study to control health problems. Epidemiological studies are of primary importance in a large developing country like ours where the natural history, incidence, prevalence and impact on morbidity and mortality of a variety of diseases are not known. Such studies are on large scale and assist in improving the public health, which includes both patients and healthy people and communities.

It has usually been considered that epidemiology of infectious diseases is of prime importance in our country. However, the evolving pattern of change in the society with upward economic mobility and increasing number of middle class population would mean that a significant number of life style related diseases such as Ischaemic Heart Disease are increasing. The Framingham Heart Studies in USA illustrates how epidemiological data collected on risk factors for cardiovascular diseases helped in planning measures to prevent and control them. Such information in India could be undertaken as long term cohort studies in different population groups.

Epidemiological studies are generally considered in two categories – observational and experimental. Designs of these studies are based on cross-sectional, case-control or cohort approaches. Epidemiological studies cover research, programme evaluation and surveillance. Ethics in epidemiological studies is multidimensional covering clinical medicine, public health and the social milieu. The code of ethics is much better

understood for clinical research, where the interaction between a patient and a clinical researcher is of supreme importance. In epidemiological research the researcher is dealing with a group of individuals and the questions faced by an epidemiologist are more of a professional nature. These questions would pertain to interactions with individual participants, sources of funding or employer, fellow epidemiologist and the society at large. Need for a code of ethics for epidemiologists is being recognized globally and the issues for such a code in the context of epidemiological research in India deserve attention.

Epidemiological research differs from clinical research in the context of the large number of study participants and generally a long time frame. If some mistakes or aberrations get detected during the course of conduct of such studies, repeating the whole exercise will be expensive, time consuming and may not even be feasible. Hence utmost care needs to be taken for various aspects - technical, practical and ethical.

DEFINITIONS

1. Observational Epidemiology: In observational studies predefined parameters in a defined population group over a specified period and frequency are recorded for studying exposure to risks affecting health. These may be of the following types:

a. Cross Sectional Studies (Surveys): This is primarily population based and involves selecting an entire population or random samples of the representative population based on census data and then using questionnaires to understand the prevalence of various diseases. Its aim is to assess aspects of the health of a population or to test hypotheses about possible cause of disease or suspected risk factors. The study participants are directly contacted only once in the defined period for which informed consent is required to be taken.

b. Case Control Studies: This usually compares the past history of exposure to risks among patients who have a specified condition/disease (cases) with the past history of exposure to this among persons who resemble the cases in such respects as age, sex socioeconomic status, geographic location, but who do not have the disease (controls). Case control studies can be done by following up available records, usually records in a hospital, but in the context of a country like ours it may require direct contact between research workers and study participants and informed consent to participate in the study is necessary. However, if it entails only a review of medical records, informed consent may not be required and indeed may very often not be feasible. But for such waiver of consent approval from IEC would be necessary.

c. Cohort Studies: These are longitudinal or prospective studies of a group of individuals with differing exposure levels to suspected risk factors. They are observed over a long period usually several years. The rate of occurrence of the condition of interest is measured and compared in relation to identified risk factors. It requires a study of large number of participants for a long time and involves asking questions, checking of records, routine medical examination and sometimes laboratory investigations. Individuals are being followed up as the cohort and it is essential to identify precisely every individual to be studied.

2. Experimental Epidemiology: In experimental epidemiology the investigators alter one or more parameters under controlled conditions to study the effects of the intervention on health. These are usually randomized controlled trials done to test a preventive or therapeutic regimen or the efficacy of a diagnostic procedure. Although these are strictly speaking epidemiological studies they come under the purview of clinical evaluation of drugs/devices/products/vaccines etc. The possibility of use of placebo as one of the arm of the trial should be explained and informed consent taken in such studies.

GENERAL PRINCIPLES

General ethical principles of respect for persons, duty to maximize possible benefits and minimize possible harm are important considerations in ethical guidelines. At the same time it is essential that all individuals in an epidemiological research are treated alike keeping in mind the rules of distributive justice. The welfare of the individual has to be balanced against the welfare of the community and society at large. The C.I.O.M.S/W.H.O Guidelines for Epidemiological Research assume that the individuals or populations being studied are capable of giving informed consent understanding the implications of the study. With large segments of our population, given their level of education, the full understanding in the sense of industrialized countries may not be achievable. How the principle of "do no harm" is ensured under such circumstances without being paternalistic is a major issue that has to be taken into consideration in ethical guidelines. In cohort or survey techniques for incidence and prevalence of various diseases, a major issue that has to be considered is how much of intervention is justified and whether one is justified in withholding interventions. For example, if you are looking at longitudinal morbidity in a population group, should you give them health education that is well established with regard to preventive aspects, or should you leave them alone so that the natural evolution of the disease can be studied? Health education or other interventions including non-health interventions can be quite expensive. An alternate strategy that may be followed is to make curative therapy available to the population at their own request. This usually involves running a clinic, which is readily accessible to the population without any other intervention. However, it is generally considered unethical to withhold intervention or services.

Surveillance studies to obtain true disease burden rates most likely give rise to ethical dilemmas regarding maintenance of confidentiality and

prevention of stigmatization. So is the case with studies on post – disaster events, mental health and evaluation of health programs. Wherever applicable anonymisation could solve these problems the information is required to be placed in public domain.

SPECIFIC PRINCIPLES

1. Informed Consent: When individuals are to be included as participants of any epidemiological studies, the purpose and general objectives of the study has to be explained to them keeping in mind their level of understanding. It needs to be ensured that privacy will be maintained. In the context of developing countries, obtaining informed consent has been considered many times as difficult/ impractical / not meeting the purpose on various grounds such as incompetence to comprehend the meaning or relevance of the consent and culturally being dependent on the decision of the head of the family or village/ community head. However, there is no alternative to obtaining individual's informed consent but what should be the content of the informed consent is also a crucial issue. In spite of obtaining informed individual consent, it is quite likely that the participants/ patients may not be fully aware of their rights. In this context, the role of investigator is crucial and s/he should remain vigilant and conscious of her/ his obligations towards the participants/ patients, all through the course of the studies.

2. In most epidemiological research it would be necessary to have the **consent of the community,** which can be done through the Village Leaders, the Panchayat head, the tribal leaders *etc*. who are considered to be gate keepers of the society/ community

3. In obtaining the consent of individuals or communities it is important to keep in mind that working through peer groups or through Panchayat etc. may mean that the individuals or community would feel reluctant to

disagree and refuse to give consent because of **societal pressures**. This is something that has **to be carefully avoided**.

4. Particularly in a country like India, with the level of poverty that is prevalent it is easy to use inducements, especially financial inducements, to get individuals and communities to consent. **Such inducements are not permissible**. However, it is necessary to provide for adequate compensation for loss of wages and travel / other expenses incurred for participating in the study.

5. **All risks involved** including the risk of loss of privacy must be explained to the participants in an epidemiological study. Steps should be taken to maintain utmost privacy which should be informed to the community.

6. **Maintaining confidentiality** of epidemiological data is absolutely essential. A particular concern is the fact that some population based data may also have implications on issues like national security and these need to be carefully evaluated at the beginning.

7. All attempts should be made to **minimize harm** to the individuals and society at large. Special consideration for the cultural characteristics of the communities that are being studied is essential to prevent any disturbance to cultural sensitivities because of the investigation.

8. The design of the study should ensure that the **benefits of the study are maximized** for the individuals and communities taking part in the study. This means that at the onset itself the investigators should design the way in which the results of the study are going to be communicated and also decide whether individuals identified at particular risk during the course of the studies would be informed. It may also be necessary in some instances to inform the concerned family members about the results, for instance, as in AIDS, STD etc. It may not always be possible

to communicate study results to individuals but research findings and advice should be publicized by appropriate available means. It is also important that the beneficial results of epidemiological studies are fed into the health system and necessary training modules should be developed as part of the epidemiological project.

9. In all situations where there is likely to be **conflicts of interest** it must be ensured that the interest of the individuals involved in the study are protected at all cost, for *eg.,* studies on outbreaks, epidemics, disasters and calamities, and epidemiological studies undertaken by providers of relief and rehabilitation.

10. Scientific objectivity should be maintained with honesty and impartiality, both in the design and conduct of the study and in presenting and interpreting findings. Selective withholding of data and similar practices are unethical.

11. Benefits: When epidemiological studies (like those on mortality and morbidity as a result of exposure to an agent) lead to long associations with the community, the results if released in timely manner could give improved health care facilities or educate the community to reduce the impact of adverse environment on health and tackle the problem at their end in time.

12. Ethical Review Procedures: In all Ethical Committees at least one or two individuals with an understanding of the principles of epidemiological ethics have to be included. These Committees should be independent and comprise of epidemiologists, clinicians, statisticians, social scientists, philosophers, legal experts and representatives from community/voluntary groups who should be aware of local, social and cultural norms, as this is the most important social control mechanism.

13. Distinction between research and programme evaluation: It is difficult to make a distinction between epidemiological research and programme evaluation. Whenever a programme evaluation and surveillance is launched, the monitoring and evaluating mechanisms should clearly be planned and cleared by IRB before initiation as is done in all epidemiological studies.

It is not always possible to know what will happen to the participants as unexpected results or undesirable events can sometimes occur. Very often the benefits and risks of the research pertain not only to the individual participants, but also the community from which they are drawn. Therefore, the participation of local community representatives in planning, conducting and monitoring research is important to avert circumstances which may be detrimental to the participants' welfare. This also helps in improving the vision of the researcher regarding the objectives and the design of study. The inclusion of a community representative to act on behalf of all participants involved in a research study Communities should be informed of the research, possible outcomes (positive and negative), and the results of the research. Research findings belong to participants and their communities as well as the researchers and the research community. Community representatives and researchers can work together to make sure that research is conducted in the most appropriate way and the benefits if any, could be shared in a reasonable or workable manner.

COMMUNITY PARTICIPATION

A community can be defined as a group of people sharing the same location, beliefs, culture, ideals, goals, age, gender, profession, lifestyle, common interests, geographical locations or settings or disease. When research participants are drawn from a specific community, members of that community can be involved to discuss any concerns it may have

regarding the research. In different ways such a dialogue can be facilitated. If an ethics committee does not have a member from the community, it may ask a local community representative to be the voice for all participants. On the other hand, community representatives can formally join together to form a group termed as Community Advisory Board, Community Working Group, or Community Advisory Group, which takes part in the research at all stages of the study. In international studies, particularly on issues involving communities, representation from this body ensures that the community's health needs and expectations are addressed, informed consent is appropriate, and access to research benefits is provided through research that is designed and implemented in the best interests of science and community.

Community representation should be involved before, during and after the study. Before the study is initiated the community is informed to see if it agrees that the research addresses a need or problem relevant to that community and to confirm that the design is culture specific and brings some benefits to research participants or the community. Since some risk may be associated the community representation is needed to assist in developing appropriate ways to protect the participants. During the study, the association with community representatives continues to educate others about the research and to alert the researcher to ethical issues related to the research. After the study is completed, community representatives can help in making the results known to the entire community. However, application of research findings may take a long time, which the community representatives should be made to understand. The benefits may be participants' and community's access to intervention. Whose responsibility and conditions under which this would be done, duration of availability of intervention, methods of improving the quality of health care in the community and any expected

desirable behavioral change in the community should be clearly explained to community by the Ethics Committee or community representatives.

DECISION MAKING PROCESS

The IRB should be able to provide complete and adequate review of the research proposals submitted to them. It should meet periodically at frequent intervals to review new proposals, evaluate annual progress of ongoing ones, review serious adverse event (SAE) reports and assess final reports of all research activities involving human beings through a previously scheduled agenda, amended wherever appropriate.

The following points should be considered while doing so:

1. The decision must be taken by a broad consensus after the quorum requirements are fulfilled to recommend/reject/suggest modification for a repeat review or advice appropriate steps. The IRB chairperson should communicate the decision in writing to the PI.
2. If a member has conflict-of-interest (COI) involving a project then he/she should submit this in writing to the chairperson before the review meeting, and it should also be recorded in the minutes.
3. If one of the members has her/his own proposal for review or has any COI then s/he should withdraw from the IRB while the project is being discussed.
4. A negative decision should always be supported by clearly defined reason.
5. An IRB may decide to reverse its positive decision on a study if it receives information that may adversely affect the risk/ benefit ratio.
6. The discontinuation of a trial should be ordered if the IRB finds that the goals of the trial have already been achieved midway or unequivocal results are obtained.
7. In case of premature termination of study, notification should include the reasons for termination along with the summary of results conducted till date.
8. The following circumstances require the matter to be brought to the

attention of IRB:

a. Any amendment to the protocol from the originally approved protocol with proper justification;
b. Serious and unexpected adverse events and remedial steps taken to tackle them;
c. Any new information that may influence the conduct of the study.

9. If necessary, the applicant/investigator may be invited to present the protocol or offer clarifications in the meeting. Representative of the patient groups or interest groups can be invited during deliberations to offer their view point.
10. Consultants (Subject experts) may be invited to offer their views, but should not take part in the decision making process. However, her/his opinion must be re-considered.
11. Meetings are to be minuted which should be approved and signed by the Chairperson/Member Secretary of the Board.

THE DECISIONS:

- Out right approval- at most only very minor changes required are suggested. The application contained all necessary information.
- Approval with modification- there is enough information to judge the study, but clarifications or changes are needed.
- Resubmit with more information- there is not enough information to judge the application appropriately.
- Outright disapproval- there is no way the researchers can ethically do the study.

The Member secretary communicates these decisions to the researchers by issuing:

Any matter that is researched after the approval of the IRB cannot and

shall not be published in any journal/book either in internationally, nationally or institutionally without the prior approval of the Heads of the Institution through protocol no: 75 D

ISSUING OF CLEARANCE CERTIFICATE:

Ethical clearance certificate will be issued after the research proposal is accepted in the review meetings by the Chairperson, in their absence by Member Secretary.

REVIEW PROCEDURES

The IRB should review every research proposal on human participants before the research is initiated. It should ensure that a scientific evaluation has been completed before ethical review is taken up. The Committee should evaluate the possible risks to the participants with proper justification, the expected benefits and adequacy of documentation for ensuring privacy, confidentiality and the justice issues.

The IRB member from the respective department from where proposal has been submitted shall screen the proposals for their completeness and depending on the risk involved categorize them into three types, namely, exemption from review, expedited review and full review.

However, in some cases like surgery, chemotherapy or radiation therapy, great risk would be inherent in the treatment itself, but this may be within the range of minimal risk for the research participant undergoing these interventions since it would be undertaken as part of current everyday life.

An investigator cannot decide that her/his protocol falls in the exempted category without approval from the IRB. All proposals will be scrutinized to decide under which of the following three categories it will be considered:

EXEMPTION FROM REVIEW:

Proposals, which present less than minimal risk fall under this category as, may be seen in following situations:

- Research on educational practices such as instructional strategies or
- Effectiveness of or the comparison among instructional techniques, curricular or
- Classroom management methods.

EXCEPTIONS:

I. When research on use of educational tests, survey or interview procedures or observation of public behavior can identify the human participant directly or through identifiers, and the disclosure of information outside research could subject the participant to the risk of civil or criminal or financial liability or psychosocial harm.

II. When interviews involve direct approach or access to private papers.

EXPEDITED REVIEW:

The proposals presenting no more than minimal risk to research participants may be subjected to expedited review. The Member-Secretary and the Chairperson of the IRB or designated member of the IRB may expedited review only if the protocols involve –

1. Minor deviations from originally approved research during the period of approval (usually of one year duration).
2. Revised proposal previously approved through full review by the IRB or continuing review of approved proposals where there is no additional risk or activity is limited to data analysis.
3. Research activities that involve only procedures listed in one or more of the following categories:

   Clinical studies of drugs and medical devices only when -

   i. Research is on already approved drugs except when studying drug interaction or conducting trial on vulnerable population.
   ii. Serious Adverse Event (SAE) or unexpected Adverse Drug Reaction (ADR) of minor nature is reported.
4. Research involving clinical materials (data, documents, records, or specimens) that have been collected for non-research (clinical) purposes. When in emergency situations like serious outbreaks or disasters a full review of the research is not possible, prior written

permission of IRB may be taken before use of the test intervention. Such research can only be approved for pilot study or preliminary work to study the safety and efficacy of the intervention and the same participants should not be included in the clinical trial that may be initiated later based on the findings of the pilot study.

5. Research on interventions in emergency situation

When proven prophylactic, diagnostic, and therapeutic methods do not exist or have been ineffective; physicians may use new intervention as: Investigational drug (IND)/devices/vaccine to provide emergency medical care to their patients in life threatening conditions. Research in such instance of medical care could be allowed in patients –

i. When consent of person/patient/responsible relative or custodian/ designated doctors for such an event is not possible. However information about the intervention should be given to the relative/ legal guardian when available later.
ii. When the intervention has undergone testing for safety prior to its use in emergency situations and sponsor has obtained prior approval of Drugs Controller General of India (DCGI).
iii. Only if the local IRB reviews the protocol since institutional responsibility is of paramount importance in such instances.
iv. If Data Safety Monitoring Board (DSMB) is constituted to review the data.

FULL REVIEW:

All research presenting with more than minimal risk, proposals/ protocols that do not qualify for exempted or expedited review and projects that involve vulnerable population and special groups, shall be subjected to full review by all the members.

While reviewing the proposals, the following situations may be carefully assessed against the existing facilities at the research site for

risk/benefit analysis:

1. Collection of blood samples by finger prick or venipuncture:
    a. From healthy adults and non-pregnant women who weigh normal for their age and not more than 500 ml blood is drawn in an 8 week period and frequency of collection is not more than 2 times per week;
    b. From other adults and children, where the age, weight, and health of the participants, the collection procedure, the amount of blood to be collected and the frequency with which it will be collected has been considered and not more than 50 ml or 3 ml per kg, whichever is lesser is drawn inan 8 week period and not more than 2 times per week;
2. Prospective collection of biological specimens for research purposes by noninvasive means.
3. Dental treatment procedures - deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction of permanent teeth; supra and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth;
4. Use of intracanal medicaments or analyzing different obturating materials
5. Comparison of different surgical or treatment techniques
6. Collection of data through noninvasive procedures routinely employed in clinical practice. Where medical devices are employed, they must be cleared/approved for marketing, for instance –
    a. Physical sensors that are applied either to the surface of the body for radiographic purposes
    b. Electromyography, electrocardiography, ultrasound, diagnostic infrared imaging, CT imaging, etc.
7. Research involving clinical materials (data, documents, records, or

specimens) that will be collected solely for non-research (clinical) purposes.

STEPS IN REVIEW PROCESS OF IRB

Step 1: Prefixed dates

- Need to be finalized in advance
- Submission made by researchers in keeping with the requirements of the IRB's SOP
- Finalizing primary and secondary reviewers
- The proposals circulated to members giving sufficient time for review

Step 2: Submissions to the IRB

- The members undertake the review
- The meeting of the IRB
- Discussions at the IRB
- Decisions made
- The process and decisions are documented
- These decisions and the reasons are communicated to the researchers

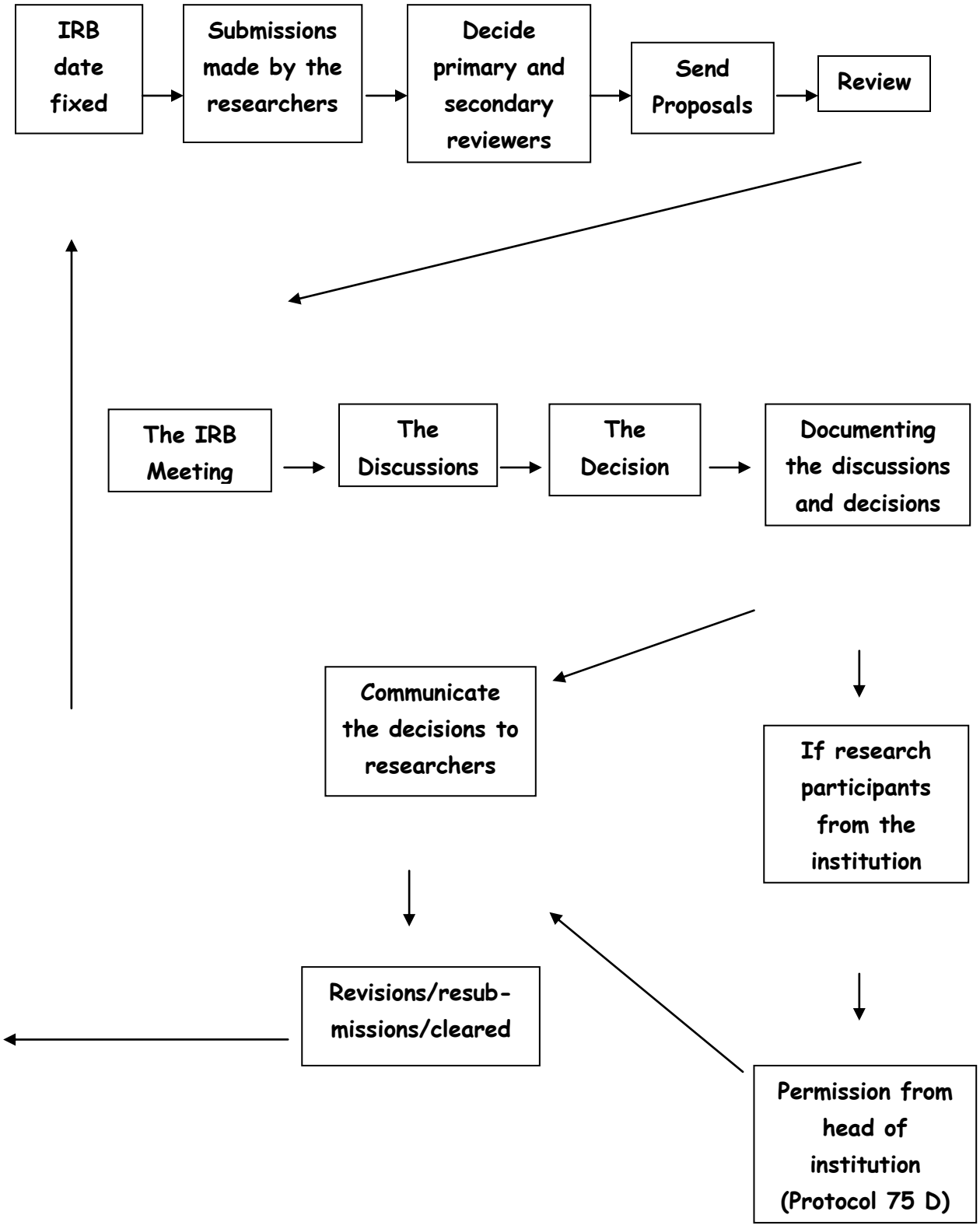
Step 3: Primary and secondary reviewers

- The Member secretary of IRB sorts through the proposals, allocates primary and secondary reviewers for the proposals that need full review

Step 4: Sending of proposals

- Proposals are mailed to all members

FIGURE 1: STEPS IN IRB REVIEW



REVIEW PROCESS

The method of review should be stated in the SOP whether the review should be done by all reviewers or by primary reviewer(s) in which case a brief summary of the project with informed consent and patient information sheet, advertisements or brochures, if any, should be circulated to all the other members. The ethical review should be done in formal meetings and IRB should not take decisions through circulation of proposals**.** The committee should meet at regular intervals and should not keep a decision pending for more than 3 - 6 months, which may be defined in the SOP.

PERIODIC REVIEW

The ongoing research may be reviewed at regular intervals of six months to one year as may be specified in the SOP of the ethics committee.

CONTINUING REVIEW

The IRB has the responsibility to continue reviewing approved projects for continuation, new information, adverse event monitoring, follow-up and later after completion if need be.

INTERIM REVIEW

Each IRB should decide the special circumstances and the mechanism when an interim review can be resorted to by a sub-committee instead of waiting for the scheduled time of the meeting like re-examination of a proposal already examined by the IRB or any other matter which should be brought to the attention of the IRB. However, decisions taken should be brought to the notice of the main committee.

MONITORING

Once IRB gives a certificate of approval it is the duty of the IRB to monitor the approved studies, therefore an oversight mechanism should be in place. Actual site visits can be made especially in the event of

reporting of adverse events or violations of human rights. Additionally, periodic status reports must be asked for at appropriate intervals based on the safety concerns and this should be specified in the SOP of the IRB. SAE reports from the site as well as other sites are reviewed by IRB and appropriate action taken when required. In case the IRB desires so, reports of monitoring done by the sponsor and the recommendations of the DSMB may also be sought.

ADMINISTRATION AND MANAGEMENT

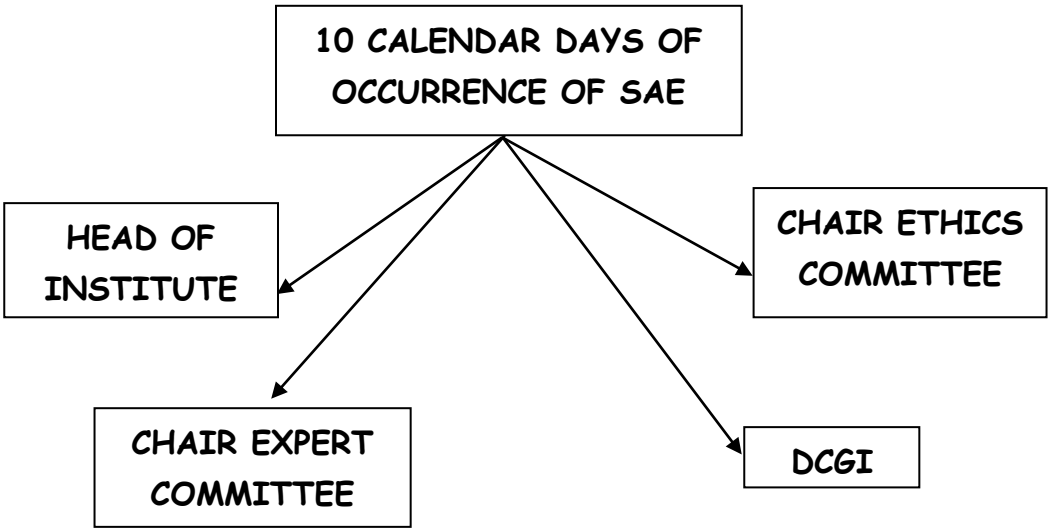
A full time secretariat and space for keeping records is required for a well functioning IRB. The members could be given a reasonable compensation for the time spared for reviewing the proposals. A reasonable fee can be charged to cover the expenses related to review and administrative processes. Every institution should allocate reasonable amount of funds for smooth functioning of the IRB.

SPECIAL CONSIDERATIONS

While all the above requirements are applicable to biomedical research as a whole irrespective of the specialty of research, there are certain specific concerns pertaining to specialized areas of research which require additional safe guards/ protection and specific considerations for the IRB to take note of. Examples of such instances are research involving children, pregnant and lactating women, vulnerable participants and those with diminished autonomy besides issues pertaining to commercialization of research and international collaboration. The observations and suggestions of IRB should be given in writing in unambiguous terms in such instances.

SERIOUS ADVERSE EVENTS (SAE)

Reports from the site as well as other sites are reviewed by IRB and appropriate action taken when required.


10 CALENDAR DAYS OF OCCURRENCE OF SAE
HEAD OF INSTITUTE
CHAIR ETHICS COMMITTEE
CHAIR EXPERT COMMITTEE
DCGI

SUBMISSION OF APPLICATION

The researcher should submit an application in a prescribed format along with the study protocol as prescribed in SOP of IRB concerned. The protocol should include the following:-

1. The title with signature of Principal Investigator (PI) and Co-investigators as attestation for conducting the study.
2. Clear research objectives and rationale for undertaking the investigation in human participants in the light of existing knowledge. Recent curriculum vitae of the investigators indicating qualification and experience.
3. Participant recruitment procedures and brochures, if any.
4. Inclusion and exclusion criteria for entry of participants.
5. Precise description of methodology of the proposed research, including sample size (with justification), type of study design (observational, experimental, pilot, randomized, blinded *etc.*), intended intervention, dosages of drugs, route of administration, duration of treatment and details of invasive procedures if any.
6. Plan to withdraw or withhold standard therapies in the course of research.
7. Plan for statistical analysis of the study.
8. Procedure for seeking and obtaining informed consent with sample of patient information sheet and informed consent forms in English and local languages.
9. Safety of proposed intervention and any drug or vaccine to be tested, including results of relevant laboratory, animal and human research.
10. For research involving more than minimal risk, an account of management of such risk or injury.

11. Proposed compensation and reimbursement of incidental expenses and management of research related and unrelated injury/ illness during and after research period.
12. An account of storage and maintenance of all data collected during the trial.
13. Plans for publication of results - positive or negative - while maintaining the privacy and confidentiality of the study participants.
14. A statement on probable ethical issues and steps taken to tackle the same like justification for washout of standard drug, or the use of placebo control.
15. All other relevant documents related to the study protocol like investigator's brochure for trial on drugs/devices/vaccines/herbal remedies and statement of relevant regulatory clearances.
16. Agreement to comply with national and international Good Clinical Practices (GCP) protocols for clinical trials.
17. Details of Funding agency/Sponsors and fund allocation.
18. For international collaborative study details about foreign collaborators and documents for review of Health Ministry's Screening Committee(HMSC) or appropriate Committees under other agencies/ authority like Drug Controller General of India (DCGI)
19. For exchange of biological material in international collaborative study a
20. MoU/Material Transfer Agreement between the collaborating partners.
21. A statement on conflict-of-interest (COI), if any.

CLINICAL TRIALS REGISTRY-INDIA (CTRI)

Registration of clinical trials in the Clinical Trials Registry-India (CTRI) is now mandatory. As per notification of the Drugs Controller General (India), trials registered in the CTRI are freely searchable, both from CTRI site (www.ctri.nic.in) as well as the International Clinical Trials Registry Platform.

Any researcher who plans to conduct a trial involving human participants of any intervention such as drugs, surgical procedures, preventive measures, life style modifications, devices, educational, behavioral, treatment rehabilitation strategies as well as trial being conducted in purview of the Department of AYUSH (http://indianmedicine.nic.in) is expected to register the trial in CTRI before the enrollment of first participant. Trial registration involves public declaration and identification of trial investigators, sponsors interventions, patient population etc before the enrollment of first patient. Submission of ethics approval and DCGI approval (if applicable) is essential for trial registration in CTRI. Multi country trials are applicable if India is a participating country and the trials have been registered in CTRI. In the CTRI, details of Indian investigators, trial sites, Indian target sample size and date of enrollment are captured. After trial is registered, trialists are expected to regularly update the trial status and other aspects as the case may be. After the trial is registered all updates and changes will be recorded and available for public display register.

Being a primary of the International Clinical Trials Registry (ICTRP) (http://www.who.int/ictrp/search/en/), registered trials are freely searchable both from WHO's search portal, ICTRP as well as form the CTRI.

The researcher to verify the following

1. All other relevant documents related to the study protocol like investigator's brochure for trial on drugs/devices/vaccines/herbal medicines and statement of relevant regulatory clearances.
2. Agreement to comply with national and international Good Clinical Practices (GCP) protocols for clinical trials.
3. Details of Funding agency/ Sponsors and fund allocation.
4. For international collaborative study details about foreign collaborators and documents for review.
5. Where applicable, committee (HMSC) or appropriate Committees under other agencies/authority like Drug Controller General of India (DCGI)
6. For exchange of biological material in international collaborative study a MoU/Material Transfer Agreement between the collaborating partners, if applicable.
7. A statement on conflict-of-interest (COI), if any.

RECORD KEEPING

All documentation and communication of an IRB must be dated, filed and preserved according to written procedures.

Strict confidentiality is to be maintained during access and retrieval procedures. The following records should be maintained for the following:

1) The Constitution and composition of the IRB;
2) Signed and dated copies of the latest curriculum vitae of all IRB members with records of training if any;
3) Standing operating procedures of the IRB;
4) National and International guidelines;
5) Copies of protocols submitted for review;
6) All correspondence with IRB members and investigators regarding application, decision and follow up;
7) Agenda of all IRB meetings;
8) Minutes of all IRB meetings with signature of the Chairperson or designee;
9) Copies of decisions communicated to the applicants;
10) Record of all notification issued for premature termination of a study with a summary of the reasons.

It is recommended that all records must be safely maintained after the completion/termination of the study for a period of 3 years if it is not possible to maintain the same for more than that due to resource crunch and lack of infrastructure.

PROPOSAL FOR PUBLICATION OF RESEARCH

All the research is to be published. The principal author for this would be on the basis of ICMJE qualification criteria “an author is to be someone who has made substantive intellectual contributions

This includes

1. Conception, design, acquisition of data, treatment, diagnosis etc
2. Drafting the article and revising it for important intellectual content

Thus any person who has diagnosed, treated or investigated case should always be given priority to be one of the authors. When more than one department are involved and have made contributions in diagnosis and treatment of cases, the principal authorship for consecutive publications will be done in rotatory basis. The principal author from each department shall have the freedom to suggest the name of another staff member as a joint author based on these considerations again. The concerned post graduate from the department will be included as co-author. This would give the due credits to all contributors and avoid the sense of victimization of people deserving to be authors.

INSTITUTIONAL RESEARCH SPONSOR

The research by the faculty on the topics of either social obligation or regional prevalence of oral and para-oral diseases or basic research and testing of indigenous medicaments after approved by the IRB will receive complete sponsor from the Institution. (CIDS)

The collaborative studies from the Institution (CIDS) with the eminent Indian and foreign universities will be considered for the sponsor from the Institution.

Sponsors available from other institutions are Rajiv Gandhi University of Health Sciences (RGUHS), Indian Council of Medical Research (ICMR).

INSTITUTIONAL ANIMAL ETHICS COMMITTEE (IAEC)

RESPONSIBILITIES

- Review and approve research projects
- Prevent unnecessary suffering to animals during experimentation
- Proper accommodation/ veterinary care
- Humane disposal after termination of study
- Midterm termination if unnecessary suffering
- Adequate skilled personnel to do the experiment

MEMBERS

- A biological scientist
- Two scientist from different biological disciplines
- A veterinarian involved in care of animal
- Scientist in charge of animals facility of the establishment concerned
- A scientist from outside the institute
- A non-scientific socially aware member
- A nominee of CPCSEA

'R's of animal use in research:

Replacement (alternate method)- refers to method which avoid or replace the use of animals and these can be absolute by using in silico (computer based programs) and in vitro methods (human volunteers) or relative replacement (invertebrates, such as fruit flies and nematode worms

Reduction (number, species) - refers to method which allow researchers to obtain comparable levels of information from fewer animals thereby minimizing animal use (improved experimental design, modern imaging techniques, sharing data and resources)

Refinement- refers to improvements in procedures, which minimize pain, suffering and distress and allow general improvement of animal welfare (improvement in the living conditions of research animals, anesthesia and analgesia for pain relief)

Rehabilitation- refers to after care and/ or rehabilitation of animals post-experimentation. All researchers using experimental animals have a moral responsibility to animals after use. Rehabilitation of experimental animals is a legal requirement in India

CPCSEA- Committee for Purpose of Control and Supervision of Experiments on Animals

Committee comprises of nominated members and representatives from national regulatory agencies

- Ministry of Health and Family welfares
- Ministry of Environment and Forest
- National Academic and Research Councils
- Research Institutes, eminent scientists
- Animal welfare organizations (PETA, Blue Cross)

Main functions of CPCSEA

- Registration of establishments conducting animal experimentation or breeding of animals for this purpose
- Selection and appointment of nominees in IAEC of registered establishments
- Approval of animal house facilities on basis of reports of inspections conducted by CPCSEA
- Permission for conducting experiments involving use of animals
- Recommendations for import of animals for use in experiments Action against establishments in case of violation of any legal norm/ stipulation.

APPENDIX

APPENDIX I: DEFINITIONS

Research: A systematic investigation, including research development, testing and evaluations, designed to develop or contribute to generalize knowledge. Any experiment that involves a test article and one or more human subjects and that is either subject to requirements for prior submission to the IRB. The terms "research," "clinical research," "clinical study," "study," and "clinical investigations" are deemed to be synonymous for purposes of this part.

Systematic Investigation: An activity that involves a prospective plan, which incorporates data collection, either quantitative or qualitative, and data analysis to answer a question.

Generalizable: Knowledge that may be justifiably transferred or extrapolated to a broader population or situation than from which it was initially derived.

Human Subject: An individual who is or becomes a participant in research, either as a recipient of a test article or as a control. A subject may be either a healthy individual or a patient. A living individual about whom an investigator (whether professional or student) conducting research obtains

1. Data through intervention or interaction with the individual, or
2. Identifiable private information.
3. The clinical investigations involving medical devices and the results of which are intended to be submitted to the IRB, or held for inspection.

Or human subject also means a human who participates in an

investigation, either as an individual on whom or on whose specimen, an investigational device is used or as a control.

1. Intervention includes both physical procedures by which data are gathered (for example venipuncture) and manipulation of the subject or the subject's environment that are performed for research purposes.
2. Interaction includes communication or interpersonal contact between investigator and subject.
3. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public.

Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

Minimal risk- means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life (i.e., of the general population) or during the performance of routine physical or psychological examinations or tests.

APPENDIX II: CONFIDENTIALITY AND CONFLICT OF INTEREST DECLARATION FORM

To, Date:

The Chairperson,

Institutional Review Board,

Coorg Institute of Dental Sciences,

Virajpet.

Sir/Madam,

I,_____ consent to be a _____Member to the Institutional Review Board, Coorg Institute of Dental Sciences, Virajpet.

- I will cooperate in conducting the IRB meetings with confidentiality
- I shall declare if there is any conflict of interest in the research proposal before the IRB

SIGNATURE

APPENDIX III: APPLICATION FOR ETHICAL CLEARANCE AND RESEARCH PROPOSAL

To, Date:

The Chairperson,

Institutional Review Board,

Coorg Institute of Dental Sciences,

Virajpet.

(CONFIDENTIAL)

1. TITLE OF THE RESEARCH PROPOSAL:

2. NAME OF APPLICANT/CHIEF INVESTIGATOR:
   DESIGNATION:
   DEPARTMENT:
   CONTACT NUMBER:

3. NAME(S) OF THE COINVESTIGATOR(S)
   DESIGNATION:
   DEPARTMENT:

4. NAME OF THE GUIDE/CO-GUIDE
   DESIGNATION:
   DEPARTMENT:

5. NEED OF THE STUDY: (in 100 words)

6. TYPE OF RESEARCH:
   a. Clinical trial/In-vitro study

b. Involves patients/Bio-samples
    i. If used then specific the Biosamples
c. Involves vulnerable persons

7. STUDY PROTOCOL TO BE FOLLOWED: (In 250 words)

8. INFORMED CONSENT:

   Enclose the informed consent form format

   Does the informed consent used in the proposal includes the following

   a. Number of participants involved in the study :
   b. Duration of the participation of the participants:
   c. Any investigations to be performed on the participants: YES/NO
   d. Foreseeable risks adequately described to the participants: YES/NO

      If YES specify
   e. Benefits to the participants appropriately described: YES/NO

      (Including monetary benefits)

9. COMPENSATION FOR PARTICIPATION:

   a. Participants are reimbursed for their expenses YES/NO
   b. Minimal risks of the research is considered YES/NO

      If YES. Plans for compensation (In 50 Words)
   c. Any serious adverse effects involved in the study to the participants YES/NO

      If YES explain
   d. Management of adverse effects planned YES/NO

10. PRIVACY AND CONFEDENTIALLY IS MAINTAINED: YES/NO

11. FUNDINGSOURCE: YES/NO
If YES specify

12. ANY CONFLICT OF INTEREST: YES/NO

Note: Please note that the IRB should be notified of any adverse or unforeseen circumstances arising out of this study

Signature of Applicant
Date:

TO BE COMPLETED BY HEAD OF DEPARTMENT

It is the responsibility of the HOD to peer review and discuss the ethical implications of the research in the department. And to inform the IRB if any adverse or unforeseen circumstances arising out of this study or of any emerging ethical concerns after the research have been commenced.

Name, Signature and Seal of HOD
Date:

APPENDIX IV: FORMAT FOR INFORMED CONSENT FROM SUBJECTS

Study Title:

Subject's Initials: _____

Subject's Name: _____

Date of Birth/ Age: _____

(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 that the Sponsor of the study, others working on the college's behalf, 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.

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____

Signature:

APPENDIX V: APPLICATION FOR THE POST GRADUATES RESEARCH/THESIS/TERM PAPER

From, Date:

To,

The Chairperson,
Institutional Review Board,
Coorg Institute of Dental Sciences,
Virajpet.

Sir/Madam,

Subject: Request for ethical clearance.

This is to state that I_____, Post Graduate Student at the Department of _____, intend to conduct a study titled___ _____ _____ _____as a _____ _____. This study involves_____ _____.

I request the Institutional review board (IRB) to consider this study for the ethical clearance.

Yours Faithfully

Name of the Guide:

Guides signature:

APPENDIX VI: APPLICATION FOR RENEWAL

From, Date:

_____

_____

_____

_____

To,

The Chairperson,

Institutional Review Board,

Coorg Institute of Dental Sciences,

Virajpet.

Sir/Madam

Subject: Request to renewal of the proceedings of IRB/ ethical clearance certificate

This is to state that _____, faculty/Post Graduate Student from Department of _____, had received the proceedings of the IRB/ the ethical clearance certificate for the study _____

_____

_____.

I request you to issue a continuing review of IRB certificate.

Yours Faithfully,

APPENDIX VII: ABSENTEE FORM FOR THE IRB MEMBER

To, Date:

The Chairperson,

Institutional Review Board,

Coorg Institute of Dental Sciences,

Virajpet.

Sir

I, ... am unable to attend the meeting to be held on.....at.....due to .....(reason)

I agree with the decisions arrived on consensus in this meeting.

Or

I have enclosed suggestions regarding the agenda of the meeting

SIGNATURE

APPENDIX VIII: MODEL FORMAT TO BE FOLLOWED BY IRB MEMBERS WHILE REVIEWING RESEARCH PROPOSALS

Proposed Title

Principal Investigator: Co-Investigator: 1.
2.
3.

Supporting Agency: ICMR? NON-ICMR

If NON-ICMR, name of agency

Project Status: Proposed Ongoing

Review Reviewed

Before First Review

Date of Review

1. *Research Design*
   a. *Scientifically sound enough to expose subjects to risk* *Yes/ No*
   b. *Relevant to contribute to further knowledge* *Yes /No*
   c. *Of some importance to society* *Yes/No*

2. *Risks*
   a. *Is there physical/social/psychological risk/discomfort?* *Yes/No*
   b. *Is the overall risk/ benefit ratio* *Acceptable/Unacceptable*

3. *Benefits*
   Direct Reasonable Undue None

   Indirect: Improvement in social/ Knowledge

   Any Other

4. *Subject selection*
   a. *Inclusion/exclusion criteria addressed?* *Yes/No*

b. *Vulnerable subject (women, child, mentally challenged, seriously or terminally ill, fetus, economically or socially backward and healthy volunteers) adequately protected? Yes/ No*
c. *Special group subjects (captives, students, nurses& dependent staff) adequately protected? Yes/ No*

5. *Privacy & Confidentiality maintained? Yes/ No*

6. *Patient Information sheet Adequate/ Inadequate*

7. *Consent form components addressed adequately? Yes/ No*

8. *Compensation,(If any applicable) addressed adequately Yes/ No*

9. *Is there a Conflict of Interest? Yes/ No*
   If Yes, Acceptable/ Unacceptable

10. *Budget Appropriate/ Inappropriate/ Not available*

11. *Decision of review*

    Recommended Recommended with suggestions

    Revision Rejected

12. *Any other remarks/ Suggestions.*

Reviewer's name and signature

(Modified from Indian council of Medical Research format)

APPENDIX IX: EVOLUTION OF ETHICS AND REGULATORY GUIDELINES

- *1947 : Nuremberg code*
- *1964 : Declaration of Helsinki*
- *1979 : Belmont Report*
- *1996 : ICH Guidelines*
- *2000 : ICMR guidelines*
- *2001 : Indian GCP guidelines*
- *2005 : Revision of Schedule Y*
- *2006 : Revision of ICMR Guidelines*
- *2008 : Revision Declaration of Helsinki*
- *2010 : GCP for ASU Medicines*
- *2011-12 : CDSCO guidelines*
- *2013 : Compensation / EC Registration*

APPENDIX X: IMPORTANT LINKS

- *Indian Journal of Medical Ethics (www.ijme.in)*
- *Centre for studies in Ethics and Rights (www.cser.in)*
- *A .TCG.life science Enterorise (www.clininvent.com)*
- *Clinical Trials Registry-India (www.ctri.nic.in)*

APPENDIX XI: REFERENCES

(http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm)

ICMR 2006

Centre for Studies in Ethics and Rights, Mumbai