

**Christian Medical College  
Vellore  
Tamil Nadu  
India**

**Institutional Review Boards  
(Research and Ethics Committees)**



**Policies and Standard Operating Procedures**

**2016**

## **General information:**

The policies and standard operating systems of the Institutional Review Board (IRB) of the Christian Medical College (CMC) Vellore were revised in April 2016 to include updated information and to ensure the CMC's IRB complies with Indian regulatory norms and the guiding principles of the institution. The revised document reflects the changes made and approved by the Senatus of CMC in October 2010.

## **This document is organized in four sections:**

**Section 1** describes the general principles and regulations that guide biomedical research in India.

**Section 2** details the policies and procedures of the Institutional Review Boards of CMC Vellore.

**Section 3** details the policies for specific situations adapted from the ICMR Ethical Guidelines for Biomedical Research on Human Participants (2006) and Schedule Y of the Drugs and Cosmetics Act (1940) and Rules (1945) as amended up to 30 June 2005 and further revised in October 2008 (Further revisions that have been published in the Gazette of India become applicable as notified by the Government of India). It also includes policies adopted by CMC Vellore that are covered in other international guidelines or by administrative approval that are specific for the institution.

**Section 4** provides forms to be used for IRB submissions for different study designs and for providing interim reports, final reports, adverse events reports and other relevant forms. Where available, these forms conform to national and international guidelines governing specific research designs.

This document will be available for download from the CMC intranet. In addition, relevant guidelines and policy documents will also be available on the Research Website.

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## Section 1

# GENERAL PRINCIPLES AND REGULATIONS GOVERNING CONTEMPORARY BIOMEDICAL RESEARCH IN INDIA

## 1. BACKGROUND AND HISTORY

The ethical principles that guide contemporary research in human participants stem from guidance from various organizations through the years. The earliest such attempt was the *Nuremberg Code* formulated in 1947 in the wake of Nazi atrocities of experiments with prisoners during World War II. This code clearly delineated the need for, and parameters of, informed consent in research; the need for a favorable risk benefit ratio and the need for qualified research staff and appropriate research designs. This was backed by the *Universal Declaration of Human Rights* (adopted by the General Assembly of the United Nations) in 1948.

### 1.1 INTERNATIONAL ETHICAL GUIDELINES

In 1964 at Helsinki, the World Medical Association formulated general principles and specific guidelines on use of human participants in medical research, known as the *Declaration of Helsinki*, which has undergone several revisions. In 1978, the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research submitted its report entitled "*The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*", named after the Belmont Conference Center at the Smithsonian Institute. The Belmont Report sets forth the basic ethical principles underlying the acceptable conduct of research involving human participants; these principles, *respect for the autonomy of persons, beneficence, non-maleficance and justice*, are now accepted as the quintessential requirements for the ethical conduct of research involving human participants.

In 1982, the World Health Organisation (WHO) and the Council for International Organisations of Medical Sciences (CIOMS) issued the '*Proposed International Guidelines for Biomedical Research involving Human Subjects*.' Subsequently the CIOMS brought out the '*International Guidelines for Ethical Review in Epidemiological studies*' in 1991 and '*International Ethical Guidelines for Biomedical Research involving Human Subjects*' in 1993. More recent documents on ethics include those of UNESCO's "*The Universal Declaration on Human Genome and Human Rights*" (1997), "*The International Declaration on Human Gene Data*" (2003) and "*Universal Declaration on Bioethics and Human Rights*" (2005).

Many national and regional bioethics advisory bodies such as the Nuffield Council of Bioethics (UK) and the European Commission on Ethics have general and specific principles in specific areas of scientific research involving human beings that should be followed in their respective jurisdictions, and that are updated or added to, periodically.

### 1.2 ETHICAL GUIDELINES AND REGULATORY PROCEDURES IN INDIA

In India, the Indian Council of Medical Research (ICMR) brought out the 'Policy Statement on Ethical Considerations involved in Research on Human Subjects' in 1980 and revised these guidelines in 2000 as the '*Ethical guidelines for Biomedical Research on Human Subjects*'. Due to further rapid developments in science and technology in India after the release of the

second version, globalization leading to increasing research being conducted in the developing world, and the revised CIOMS guidelines in 2002 and the Nuffield Council guidelines (Research ethics related to healthcare in developing countries) in 2002, focusing on observance of ethical norms relevant to the protection of research participants in the pluralistic cultural environments in these countries, the ICMR issued its revised guidelines in 2006 ([http://www.icmr.nic.in/human\\_ethics.html](http://www.icmr.nic.in/human_ethics.html)).

The revised guidelines take into account the challenges faced by Indian researchers in applying universal ethical principles to biomedical research in a multicultural Indian society with a multiplicity of health-care systems of variable standards. In keeping with the national policies and the demands of Indian culture, the revised ICMR guidelines address ethical issues in specific situations, keeping in mind the twin dictates of not violating any universally applicable ethical standards, and the need to consider local cultural values when it comes to the application of the ethical principles to individual autonomy and informed consent. The ICMR guidelines acknowledge the need in India to balance the primacy of autonomy, as a guiding principle, with harmony of the environment of the research participant.

Other regulations relevant to research in India include the *Drugs and Cosmetics Act (1940) and Rules (1945)* as amended up to June 2005 (<http://www.cdscsco.in>). These provide regulations on the import, manufacture, distribution and sale of drugs and cosmetics in India. *Schedule Y* (revised in January 2005), of the Act, in particular, lays down requirements and guidelines for permission to import and / or manufacture of new drugs for sale, or to undertake clinical trials. Schedule Y covers human and animal experimentation. It delineates the responsibilities of investigators, ethics committees and the procedures to be followed in all clinical trials, particularly for drugs that are to be licensed for manufacture in India, but it also covers drugs to be used for experimental indications for the first time in India, or for new indications, even though approved for marketing in India. The *Indian Good Clinical Practice (GCP) guidelines* (<http://www.cdscsco.nic.in/html/GCP1.html>) lay down more detailed guidance on the conduct of clinical trials. Schedule Y requires all researchers to abide by the ICMR guidelines, as well as the Declaration of Helsinki and the Indian GCP guidelines.

Regulations for export of biological materials are laid down by the Director General of Foreign Trade (<http://dgftcom.nic.in/>) and the material transfer agreement of the ICMR. For clinical trials, permission for shipment of biological materials to overseas central laboratories may be included in the approval from the Drugs Controller General of India. All internationally funded research needs approval by the Health Ministry's Screening Committee (HMSC); this is to screen such research for potential violations of national security and intellectual property rights.

### 1.3 CARDINAL ETHICAL PRINCIPLES IN RESEARCH

The Declaration of Helsinki recognizes that medical progress is based on research which ultimately must rest in part on experimentation involving human participants. The Declaration asserts that medical research involving human participants must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation; in short for research to be meaningful, it should be scientifically sound.

It also recognizes that in medical research on human participants, considerations related to the well-being of the human participant should take precedence over the interests of science and society. A basic principle enunciated in the Declaration is that it is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human participant. These can best be achieved by adherence to the four cardinal ethical principles that govern all physician-patient encounters: *Respect for the autonomy of the individual, beneficence, non-maleficance, and justice.*

**Respect for the autonomy of the individual** recognizes the personal dignity and autonomy of individuals to make decisions for themselves, and special protection of those persons with diminished autonomy. The derivative principles, which flow from respect for autonomy, are respect for the *confidentiality* of information and identity of the individual, *telling the truth* and obtaining valid *informed consent* before enrolling participants in research.



**Informed consent** contains three essential elements: information, comprehension (and competence), and voluntariness. First, participants must be given sufficient information on which to decide whether or not to participate, including the research procedure(s), their purposes, risks and anticipated benefits, alternative procedures (where therapy is involved), and a statement offering the participant the opportunity to ask questions and to withdraw at any time from the research. The amount of information to be disclosed is often a matter of debate with researchers often claiming that participants are unlikely to require or understand too much information. The Belmont report suggests that in deciding what constitutes adequate information a "reasonable volunteer" standard be used: "the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the participants should understand clearly the range of risk and the voluntary nature of participation." Incomplete disclosure is justified only if it is clear that: (1) the goals of the research cannot be accomplished if full disclosure is made; (2) the undisclosed risks are minimal; and (3) when appropriate, participants will be debriefed and provided the research results.

Second, participants must be able to comprehend the information that is given to them and be competent to make informed choices. The presentation of information must be adapted to the participant's capacity to understand it and can be through conversation, information sheets and brochures, group discussion, video presentations, and consent forms. Testing to ensure that participants have understood the essentials of the research, potential risks and benefits may be warranted. Where persons with limited ability to comprehend are involved, they should be given the opportunity to choose whether or not to participate to the extent they are able to do so, and their objections should not be overridden, unless the research entails providing them a therapy unavailable outside of the context of research. However, their choices should be supplemented by permission to participate from a responsible relative or legally authorized guardian. Each such class of persons should be considered on its own terms (*e.g.*, minors, persons with impaired mental capacities, the terminally ill, and the comatose). Respect for persons requires that the permission of third persons also be given in order to further protect them from harm.

Thirdly, consent to participate must be voluntarily given, free from coercion and from unfair persuasions and inducements. Consent forms are thus only evidence of a process and not the process itself. To ensure that consent is free and thus valid to the greatest extent, researchers should give attention to the setting and timing under which consent is obtained, the manner in which consent is invited and to how other persons impinge on the decision. IRBs should be especially sensitive to these factors when vulnerable participants are involved.

**Beneficence and non-maleficence:** These two cardinal principles emphasize *risk/benefit assessments* that are concerned with the probabilities and magnitudes of possible harms and anticipated benefits. This involves defining the nature and scope of the risks and benefits, and systematically assessing the risks and benefits. All possible harms, not just physical or psychological pain or injury, should be considered. These principles require both protecting individual participants against risk of harm and consideration of not only the benefits for the individual, but also the societal benefits that might be gained from the research.

It is recommended that the IRB should: (1) determine the "validity of the presuppositions of the research;" (2) distinguish the "nature, probability and magnitude of risk with as much clarity as possible;" and (3) "determine whether the investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies."

Five basic principles or rules apply when making the risk/benefit assessment: (1) "brutal or inhumane treatment of human participants is never morally justified;" (2) risks should be minimized, including the avoidance of using human participants if at all possible; (3) IRBs must be scrupulous in insisting upon sufficient justification for research involving "significant risk of serious impairment" (*e.g.*, direct benefit to the participant or "manifest voluntariness of the participation") (4) the appropriateness of involving vulnerable



populations must be demonstrated; and (5) the proposed informed consent process must thoroughly and completely disclose relevant risks and benefits.

**Justice:** The principle of justice mandates that the selection of research participants must be the result of fair selection procedures and must also result in fair outcomes. The "justness" of participant selection relates both to the participant as an individual and to the participant as a member of social, racial, sexual, or ethnic groups.

With respect to their status as individuals, participants should not be selected either because the researcher favors them or because they are held in disdain (*e.g.*, involving "undesirable" persons in risky research). Further, "social justice" indicates an "order of preference in the selection of classes of participants (*e.g.*, adults before children, non-pregnant women before pregnant women) and that some classes of potential participants (*e.g.*, people with reduced capacity to consent or prisoners) may be involved as research participants, if at all, only on certain conditions.

Investigators, institutions, or IRBs may consider principles of distributive justice relevant to determining the appropriateness of proposed methods of selecting research participants that may result in unjust distributions of the burdens and benefits of research. Such considerations may be appropriate to avoid the injustice that "arises from social, racial, sexual, and cultural biases institutionalized in society."

Participants should not be selected simply because they are readily available in settings where research is conducted, or because they are "easy to manipulate as a result of their illness or socioeconomic condition." Care should be taken to avoid overburdening institutionalized persons who "are already burdened in many ways by their infirmities and environments." Non-therapeutic research that involves risk should use other, less burdened populations, unless the research "directly relate[s] to the specific conditions of the class involved."

#### 1.4 THE STATEMENT OF GENERAL PRINCIPLES FOR RESEARCH OF THE ICMR

The ICMR, in its *Ethical Guidelines for Biomedical Research in Human Participants*, has formulated a Statement on General Principles that are common to all areas of biomedical research.

"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, participant 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 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 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. The ethics committee shall decide on the form of consent to be taken or its waiver based on the degree of risk that may be involved.

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

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

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

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

**VII. Principles of accountability and transparency** whereby the research or experiment will be conducted in a fair, honest, impartial and transparent manner after full disclosure is made by those associated with the research or experiment of each aspect of their interest in the research, and any conflict of interest that may exist; and whereby, subject to the principles of privacy and confidentiality and the rights of the researcher, full and complete records of the research inclusive of data and notes are retained for such reasonable period as may be prescribed or considered necessary for the purposes of post-research monitoring, evaluation of the research, conducting further research (whether by the initial researcher or otherwise) and in order to make such records available for scrutiny by the appropriate legal and administrative authority, if necessary.

**VIII. Principles of the maximisation of the public interest and of distributive justice** whereby the research or experiment and its subsequent applicative use are conducted and used to benefit all human kind

and not just those who are socially better off but also the least advantaged; and in particular, the research participants themselves and or the community from which they are drawn.

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

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

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

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

### 1.5 RESEARCH COMBINED WITH CLINICAL CARE

Special concerns have been raised when research is conducted in settings where normal clinical care is provided. This is due to the ‘therapeutic misconception’ that arises in the minds of patients recruited as research participants who are often unable to comprehend the differences between participating in a study and receiving treatment in the clinical setting. Rather than understanding these differences, study participants tend to believe that therapy and research were governed by the same primary goal, to advance the individual patient's best interests. Therapeutic misconception is particularly relevant to clinical trials and refers to the belief that the purpose of a clinical trial is to benefit the individual patient rather than to gather data for the purpose of scientific research. This can take the form of therapeutic mis-estimation, which is an overestimation of the potential for benefit from the research; therapeutic optimism, which is the unwarranted hope for the most positive outcome, and therapeutic mis-assignment, which refers to the tendency for participants to over-estimate their chances of being assigned the active or experimental intervention over placebo or standard care.

The **Declaration of Helsinki** has laid down the following guidelines to govern such situations:

- “The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research participants.
- The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.

- At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.
- **The physician should fully inform the patient which aspects of the care are related to the research** (emphasis added). The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.
- In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgement, it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published” (Clauses 28-32).

**In the final analysis, it is the investigator’s moral and ethical duty to convey, through the process of informed consent, to participants that the sole purpose of research is to contribute to scientific knowledge and not the specific treatment of an individual patient.** This is particularly important in research that is unlikely to directly benefit participants. IRBs have an obligation to ensure that this information is incorporated in the information sheet that accompanies the consent form.

## 1.6 RESEARCH ON VULNERABLE PARTICIPANTS

Vulnerable research participants are individuals whose willingness to volunteer in a research such as clinical trial may be duly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate, or those whose consent may not be valid due to a variety of reasons. Vulnerable participants include those who are economically disadvantaged, those with mental disorders that impair their capacity to consent, children, pregnant and nursing women, the institutionalised, those in a dependant and relatively un-empowered relationship such as students, employees, military and prisoners, and patients with life threatening diseases.

Research using vulnerable participants is not prohibited by international ethical codes or regulations but their inclusion needs to be justified and special precautions need to be implemented for their protection.

### Research using children and adolescents

The purpose of including children in research is to gain knowledge relevant to the health needs of children. The ICMR guidelines state:

“Before undertaking trial in children the investigator must ensure that

- i. Children will not be involved in research that could be carried out equally well with adults;
- ii. 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;
- iii. A parent or legal guardian of each child has given proxy consent;
- iv. 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.;
- v. Research should be conducted in settings in which the child and parent can obtain adequate medical and psychological support;
- vi. 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;



- vii. 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;
- viii. 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;
- ix. 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."

### **Research in the economically disadvantaged**

Persons who are economically or socially disadvantaged should not be used to benefit those who are better off than them. The economically disadvantaged have limited access to health care, may enrol in research to receive treatment, or enrol for compensation, are often educationally disadvantaged too with limitations in understanding and the potential for undue influence or manipulation. It is, therefore, important that the informed consent process uses simple language and enlists the help of family and significant others to explain the potential for risks, the uncertainty of personal health benefits, if appropriate, and clearly delineates those aspects of the study that are purely for research and those that are part of standard care. Undue financial inducements should be avoided. Particularly for illiterate and vulnerable participants in research, the informed consent process should be witnessed by an impartial witness, who is not part of the research team.

### **Research using students and employees**

Research involving trainees of any description or employees including faculty often confers no therapeutic advantage for the participant. However, students and employees have the same rights as any other potential recruit to participate in a research project, irrespective of the degree of risk, provided certain conditions are met:

- The research must not bestow upon participating employees or students any competitive academic or occupational advantage over other staff and students who do not volunteer, and the researchers must not impose any academic or occupational penalty on those or staff who do not volunteer.
- Students and employees must not be systematically treated differently from non-employee or non-student participants as part of the project.
- Due to the potential for perceived or real coercion to participate, students and employees who desire to participate in the research (especially those under the direct supervision of the principal investigator or listed research collaborators) should ideally have a witness of their choice present during the informed consent process to ensure that participation was voluntary. A suitable representative may be invited to be present during the ethics review of the proposal.

The Declaration of Helsinki states that, "When obtaining informed consent for the research project the physician should be particularly cautious if the participant is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship" (Clause 23). If at all possible, this approach is to be preferred to the immediately previous suggestion.

### **Research involving people with life threatening diseases or who are medically vulnerable**

Prospective participants in a study which has a therapeutic component who are by reason of mental or behavioural disorders not capable of giving adequately informed consent, persons with serious, potentially disabling, or life-threatening diseases, and persons rendered incapable of informed consent by an acute condition [emergency], are also vulnerable to exploitation, as are people who by virtue of progressive cognitive impairment may become vulnerable during the process of research (e.g., long term studies of those with cognitive decline who develop dementia).

Participants with serious medical diseases are vulnerable to (possibly) misplaced therapeutic optimism. For such participants, attempts should be made to include them only if there is minimal risk if non - therapeutic research; for therapeutic research potential risks should be emphasized, as should realistic estimates of benefits. If the disease cannot otherwise be treated, a “compassionate use” of the experimental intervention is ethically justified.

*The Declaration of Helsinki* states that, “For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons (Clause 24).

Being mentally ill does not automatically render a person incompetent to consent and this must be ascertained for every participant. In people with major mental disorders such as schizophrenia, severe depression, mania, or people with mental retardation, even if the patient consents to participate, consent to permit participation should be additionally obtained from a responsible relative or legal guardian.

*The Declaration of Helsinki* also states, that “Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research participants with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate” (Clause 26).

### **Research on pregnant or nursing women**

The *ICMR guidelines* state, “Pregnant or nursing women should in no circumstances be the subject of any research unless the research carries no more than minimal risk to the foetus 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 subjects 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.

- i. 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 perinatal 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.
- ii. **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.
- iii. **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”.

## **SECTION 2**

# **POLICIES AND PROCEDURES OF THE INSTITUTIONAL REVIEW BOARDS OF THE CHRISTIAN MEDICAL COLLEGE, VELLORE**

## **2. RESEARCH AT CMC, VELLORE**

The Christian Medical College (CMC), Vellore, established and maintained by the Christian Medical College Vellore Association, is a Registered Society formed by over 50 different Indian Christian churches and Christian organizations. It has the aim of "the establishment, maintenance and development of a Christian Medical College and hospitals in India, where women and men shall receive an education of highest grade in the art and science of medicine, nursing, or in related professions, to equip them in the spirit of Christ for service in the relief of suffering and the promotion of health". The motto of the institution is "NOT TO BE MINISTERED UNTO, BUT TO MINISTER".

The Christian Medical College Vellore Council is the highest body that represents this society and is responsible for the formation of institutional policies. In keeping with the goal of imparting the highest grade of education, research is a priority area for this institution. Research is an integral part of the vision and the mission of CMC. Research at the institution has been oriented to areas of need and emphasizes application of knowledge to relevant problems. The inculcation of an attitude of inquiry, acquisition of knowledge of the mechanisms of research and the conduct of research, at various levels of involvement in health care, are encouraged in faculty and students. Research relevant to the country's needs is encouraged with institutional grants as seed money to initiate projects.

CMC has established an Office of Research under the Additional Vice-Principal (Research) to facilitate the conduct and reporting of research and to institute and provide oversight mechanisms. The Office of Research provides support to facilitate and coordinate research activities and education regarding the responsible conduct of research. It also functions as the Office of Research Integrity that has established policies and procedures for investigations of allegations of research misconduct.

CMC has demonstrated a commitment to responsible and ethical medical care and to human participant protection by establishing a clinical ethics committee led by the Medical Superintendent that is separate from the institution's IRBs. This committee deals with all matters pertaining to the ethical clinical care of patients attending the hospital.

### **2.1 INSTITUTIONAL AUTHORITY**

The Council of CMC which met on the 16<sup>th</sup> of June, 1994, authorized the Director to set up the Institutional Review Board (IRB), otherwise called the Ethics Committee (EC) (CMC Council minutes 16<sup>th</sup> June 1994).

The Director, CMC, constitutes the IRBs under the directive of the Christian Medical College Council. All appeals about decisions of the IRBs shall be to the Director, who is not a member of the IRB, but functions as an appellate authority.

#### **2.1.1 The Institutional Review Board (IRB)**

CMC utilizes a centralized program to review all research. Until 2010, CMC operated one Institutional Review Board, but because of the increased workload, in order to conform to national and international requirements of research oversight, from 2011 CMC has operated two Institutional Review Boards (IRB) that each comprise of a Research Committee (RC) charged with reviewing the scientific validity of all research proposals and an Ethics Committee (EC) that specifically addresses ethical concerns. The IRBs review projects in a wide range of medical, biomedical, social, education and behavioral fields. The IRB Silver reviews all external research proposals, all faculty proposals and all clinical trials. The IRB Blue reviews all applications from post-graduate trainees & IRB Green reviews all application from Students and interns (Medical, Nursing & Allied Health). As a part of CMC's continued commitment to human participants' protections, the resources allocated to the IRBs are constantly monitored to ensure the existence of adequate support of IRB functions.



### **2.1.2 Purpose of the Policies and Standard Operating Procedures of the IRB**

The objective of the Policies and Standard Operating Procedures (SOP) document is to protect the rights, dignity, welfare and privacy of human research participants and to contribute to the effective functioning of the IRBs. The IRBs must function such that a responsible and consistent ethical review mechanism for health and biomedical research is put in place for all proposals dealt by the IRBs, as prescribed by the Ethical Guidelines for Biomedical Research on Human Subjects of ICMR and the Drugs and Cosmetics Act and Rules, Government of India. The mechanism is also in keeping with the ICH-GCP, the National Institutes of Health Office for Human Research Protection guidelines and the European Medicines Agency directives.

### **2.1.3 Mandate**

The IRBs will review all types of research proposals, involving human participants, laboratory protocols and animal experimentation, with a view to safeguard the dignity, rights, safety and well being of all actual and potential research participants. The goals of research, however important, should never be permitted to override the health and well being of the research participants. The IRBs will review all research projects involving human participants to be conducted at CMC, irrespective of the funding agency, approve them if all ethical considerations are met, and monitor ongoing studies.

Research proposals involving animals will be reviewed for scientific content by the Research Committee but ethics approval will be obtained from the Animal Experimentation Committee that is separate from the EC of the IRBs.

Ethical issues pertaining to clinical services provided by the institution will normally be dealt with by the Clinical Ethics Committee under the supervision of the Medical Superintendent's office.

As stated above, the IRB Silver reviews all external research proposals, all faculty proposals and all clinical trials. The IRB Blue reviews all applications from post-graduate trainees & IRB Green reviews all application from Students and interns (Medical, Nursing & Allied Health).

#### **The IRBs of CMC have the mandate to**

- i. Require that all research conducted in the institution be presented to the IRBs for assessment in the prescribed format. The IRB can also review research that is conducted off-site at institutions where no IRB exists and the researcher is a member of the faculty of CMC.
- ii. Provide competent and timely review of all research proposals submitted to ensure the scientific validity studies within the standard norms of national and international guidelines, and the ethical conduct of all such research within the ethical norms laid down by the latest revisions of the Ethical Guidelines for Biomedical Research on Human Subjects of the Indian Council for Medical Research (ICMR) and other relevant guidelines. In addition it will ensure that all research it approves will also conform to applicable central, state and local laws and regulations.
- iii. Evaluate the informed consent process and documentation; assess the risk benefit ratio, distribution of burden and benefit and provisions for appropriate compensations, wherever required.
- iv. Suggest strategies to improve research proposals that fall short of the expected scientific and ethical standards.
- v. Refuse approval of research proposals that do not meet the expected scientific and ethical standards.
- vi. Provide ongoing monitoring of all research that it approves, including site visits and audits of procedures and documentation.
- vii. Require periodic reports and final reports of all research that it approves.
- viii. Require that the results be made publically available in the form of research publications.

- ix. Ensure that universal ethical values and international scientific standards are expressed in terms of local community values and customs.
- x. Work towards facilitating the collaborative and multidisciplinary nature of scientific research, maintaining the integrity of the research process, detecting and declaring all conflicts of interest in research conduct and research review, reporting research misconduct, and ensuring research is driven by relevance to local needs and the interests of patient care and scientific advancement over personal motives.
- xi. To assist in the development and the education of a research community responsive to local health care requirements.

## **2.2 COMPOSITION AND ROLE OF IRB**

The IRB Silver reviews all external research proposals, all faculty proposals and all clinical trials. The IRB Blue reviews all applications from post-graduate trainees & IRB Green reviews all application from Students and interns (Medical, Nursing & Allied Health).

The composition and roles of the two committees (Research and Ethics) that make up CMC Vellore's IRBs are as follows:

### **2.2.1 Research Committee Silver**

The Research Committee of the IRB Silver of CMC shall consist of the Chairperson (*ex officio* the Principal of CMC), a member Secretary (*ex officio* the Head of the Department of Biostatistics), a deputy chairperson (*ex officio* the Additional Vice Principal (Research)), Vice-Principal (PG), the Director's representative, and the Medical Superintendent or his/her representative (all *ex-officio* members) and eight members selected by the Senatus of CMC (chosen to represent a mix of specialties and research expertise).

### **Research Committee Blue & Green**

The Research Committee of the IRB Blue & Green of CMC shall consist of the Chairperson (*ex officio* the Principal of CMC), a member Secretary (*ex officio* the Head of the Department of Biostatistics), a deputy chairperson (*ex officio* the Additional Vice Principal (Research)), all the Vice-Principals, the Director's representative, and the Medical Superintendent or his/her representative (all *ex-officio* members) and eight members selected by the Senatus of CMC (chosen to represent a mix of specialties and research expertise).

#### **2.2.1.1 Purpose of the Research Committees**

The Research Committee Blue and Green will discuss and review the design, scientific content, statistical methods and the appropriateness of the study in the setting of CMC, and the budget for requests for funding from the Fluid Research funds of the institution. For externally funded projects, the Research Committee Silver will review the design, methods, scientific content and budget of the project. For studies involving research on animals, if the study is approved by the appropriate research committee, the RC will recommend that the investigators submit the proposal to the Animal Experimentation Committee for approval before commencement of the study.

The primary responsibility of the Research Committee is to provide oversight of the requirements for proper scientific conduct of a research study; ethical issues are not its primary concern but members are encouraged to raise their concerns about potential ethical problems with the proposals that they review at the convened meetings of the IRB or in their reports.

#### **2.2.1.2 Terms of appointment**

- i. The Principal of CMC invites members of the faculty elected by the Senatus of CMC from its members to serve on the Research Committee.

- ii. The duration of appointment for elected members is usually for a period of three years.
- iii. For the ex-officio members, it is for the period that they hold administrative office.
- iv. The Director and the Medical Superintendent may be represented by a nominee who should ideally continually attend meetings of the Research Committee as a permanent representative during their term of office.
- v. Members may be re-appointed for as many terms as deemed by the Principal
- vi. At the end of the term of a member or members, new member(s) are appointed such that at least 50% of the members will remain in the committee to provide continuity.
- vii. A member can be replaced in the event of resignation or non-attendance for three consecutive Research Committee meetings (unless this was intimated in advance to the member secretary on sufficient grounds), or for any action not commensurate with the responsibilities laid down in the guidelines. Disqualification of members for any reason is communicated in writing by the Chairperson (Principal).
- viii. A member who is unable to attend three consecutive meetings and informs the Office of Research in advance may be temporarily replaced by another member of the Senatus selected by the Principal.
- ix. A member can tender his/her resignation from the committee, with approval from the Principal.
- x. Membership of the Research Committee is a position of responsibility and is not a paid position. Members will not be paid an honorarium or compensation for their membership or attendance at the meetings.

### 2.2.1.3 Current members of the Research Committee Silver

S. No	Name	Qualification	Designation	Affiliation	Term period as member
1	Dr. Alfred Job Daniel	D Ortho, MS Ortho, DNB Ortho	Principal, Chairperson-Research Committee, IRB, CMC, Vellore	Internal, Clinician	2011 - 2016
2	Dr. B. Antonisamy	MSc, PhD, FSMS, FRSS	Professor, Biostatistics, Secretary (Research Committee), IRB, CMC, Vellore	Internal, Statistician	2013 - 2016
3	Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal, Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician	2016– 2019
4	Dr. Nihal Thomas	MD, MNAMS, DNB(Endo), FRACP (Endo) FRCP(Edin) FRCP (Glasg)	Professor, Endocrinology, CMC, Vellore	Internal, Clinician	2016 - 2018
5	Dr. Prasanna Samuel	MSc, PhD	Lecturer, Biostatistics,	Internal,	2015 -2017

			CMC, Vellore	Statistician	
6	Dr. D. J. Christopher	BSc, MBBS, DTCD DNB, FRCP(Glasg), FCCP(USA)	Professor, Pulmonary Medicine, CMC, Vellore	Internal, Clinician	2015 - 2016
7	Dr. Asha Mary Abraham	MBBS, MD, PhD	Professor, Virology, CMC, Vellore	Internal, Clinician	2016 - 2018
8	Dr. Anuradha Bose	MBBS, DCH, MD, MRCP, FRCPC	Professor, Child Health, CMC, Vellore	Internal, Clinician	2015 - 2016
9	Dr. RV. Shaji	BSc, MSc, PhD	Professor, Hematology, CMC, Vellore	Internal, Basic Medical Scientist	2016 - 2018
10	Dr. Vinod Joseph Abraham	MBBS, MD, MPH	Professor, Community Medicine, CMC, Vellore	Internal, Clinician	2016 - 2018
11	Dr. Suresh Devasahayam	BE, MS, PhD	Professor of Bio- Engineering, CMC, Vellore	Internal, Basic Medical Scientist	2016 - 2018
12	Dr. Deepak Abraham	MBBS, MS	Professor, Endocrine Surgery, CMC, Vellore	Internal, Clinician	2015 - 2016
13	Dr. Thambu David	MBBS, MD, DNB	Professor, Medicine, CMC, Vellore	Internal, Clinician	2015 - 2016
14	Dr. Anil Kuruvilla	MBBS, MD, DCH	Professor, Child Health, CMC, Vellore	Internal, Clinician	2015 - 2016
15	Dr. Sathya Subramani	MD, PhD	Professor, Physiology, CMC, Vellore	Internal, Clinician	2014 - 2016

In addition for proposals that review related to Stem Cell Research, a nominee of the Director of the CMC-DBT Stem Cell Research Centre is invited to attend, in order to comply with Government of India norms for stem cell research proposals.

### **Institutional Committee for Stem Cell Research and Therapy (IC-SCRT/RED IRB)**

S. No	Name	Qualification	Designation	Affiliation	Term period as member
1	Dr. George Thomas	MBBS, D Ortho, PhD	Orthopaedic Surgeon, St. Isabella Hospital, Chennai, Chairperson, Ethics Committee, IRB, Chennai	External, Clinician	2016 -2018
2	Prof. Keith Gomez	BSc, MA (S.W), M. Phil (Psychiatry Social Work)	Student counselor, Loyola College, Chennai, Deputy Chairperson, Ethics Committee, IRB, Chennai	External, Lay Person & Social Scientist	2016 - 2018
3	Dr. Nihal Thomas	MD, MNAMS, DNB(Endo), FRACP (Endo) FRCP(Edin) FRCP (Glasg)	Professor , Endocrinology., CMC, Vellore	Internal, Clinician	2016 - 2018
4	Dr. Jayaprakash Muliyl	BSc, MBBS, MD, MPH, Dr PH (Epid),	Retired Professor, Vellore	External, Scientist	2016 - 2018

		DMHC		&Epidemiologist	
5	Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Additional Vice Principal (Research), Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician	2016 – 2019
6	Dr. Binu Susan Mathew	MBBS, MD	Associate Professor, Clinical Pharmacology, CMC, Vellore	Internal, Pharmacologist	2016 – 2018
7	Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person	2016 -2018
8	Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert	2016 -2018
9	Rev. Dr. T. Arul Dhas	MSc, BD, DPC, PhD(Edin)	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist	2016 - 2018

### Current membership of the Research Committee Blue

S. No	Name	Qualification	Designation	Affiliation	Term period as member
1	Dr. Alfred Job Daniel	D Ortho, MS Ortho, DNB Ortho	Principal, Chairperson-Research Committee, IRB, CMC, Vellore	Internal, Clinician	2011 - 2016
2	Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Additional Vice Principal (Research), Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician	2016 – 2019
3	Dr. Simon Pavamani	MBBS, MD	Professor, Radiotherapy, CMC, Vellore	Internal, Clinician	2014 - 2016
4	Dr. Vivek Mathew	MD (Gen. Med.) DM (Neuro) Dip. NB (Neuro)	Professor, Neurology, CMC, Vellore	Internal, Clinician	2013 - 2016
5	Dr. Mathew Joseph	MBBS, MCh	Professor, Neurosurgery, CMC, Vellore	Internal, Clinician	2015 - 2016
6	Dr. Ranjith K Moorthy	MBBS, MCh	Professor, Neurological Sciences, CMC, Vellore	Internal, Clinician	2015 - 2016
7	Dr. Anand Zachariah	MBBS, PhD	Professor, Medicine, CMC, Vellore	Internal, Clinician	2015 -2016
8	Dr. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Pulmonary Medicine, CMC, Vellore	Internal, Clinician	2015-2016
9	Dr. Visalakshi. J	MPH, PhD	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician	2016- 2018
10	Dr. Rajesh	MD, PhD.	Professor, Clinical	Internal,	2016 –2017



	Kannangai		Virology, CMC, Vellore	Clinician	
11	Dr. Niranjana Thomas	DCH, MD, DNB (Paediatrics)	Professor, Neonatology, CMC, Vellore	Internal, Clinician	2014 – 2016
12	Dr. Jacob John	MBBS, MD	Associate Professor, Community health, CMC, Vellore	Internal, Clinician	2014 – 2016
13	Dr. Inian Samarasam	MS, FRCS, FRACS	Professor, Surgery, CMC, Vellore	Internal, Clinician	2014 – 2016
14	Ms. Grace Rebekha	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician	2015 – 2017
15	Dr. Rekha Pai	BSc, MSc, PhD	Associate Professor, Pathology, CMC, Vellore	Internal, Basic Medical Scientist	2016 - 2018
16	Dr. Sathish Kumar	MBBS, MD, DCH	Professor, Child Health, CMC, Vellore	Internal, Clinician	2016 – 2018
17	Dr. Thomas V Paul	MBBS, MD, DNB, PhD	Professor, Endocrinology, CMC, Vellore	Internal, Clinician	2016 – 2018

### 2.2.2 Ethics Committees

The ECs of CMC shall consist of a chairman nominated by the Director from outside the institution to maintain the independence of the IRB/EC, the Medical Superintendent, the Dean, College of Nursing, the Nursing Superintendent or their nominees, the Principal, the Head, Chaplaincy Department, Council appointed staff representing different disciplines (including at least one clinical pharmacologist), the Additional Vice-Principal (Research), the Legal Adviser to CMC, a lawyer from outside the institution and at least two Director's nominees (Vellore citizens or lay persons).

The Chairperson of the EC will necessarily be a person of stature with a scientific background and adequate familiarity with the principles of ethics and related issues. The deputy chairperson may be from within the institution and the member secretary will be the Additional Vice-Principal (Research) to ensure the efficient functioning of the EC.

The composition of the EC shall reflect that recommended by the ICMR's guidelines and Schedule Y of the Drugs and Cosmetics Act and include a social scientist, an ethicist/theologian/representative of a non-governmental organization, a legal expert, a lay person from the community, a basic medical scientist (preferably a pharmacologist) and a clinician

#### 2.2.2.1 Purpose of the Ethics Committee

The ECs of CMC shall provide ethical oversight of all research conducted in CMC within the mandate stipulated here. Their primary concern is not the scientific aspects of the research, which will be reviewed and approved by the Research Committee, though EC members may seek clarification in this regard, if needed.

#### 2.2.2.2 Terms of Appointment

1. The Director of CMC (through the Principal's and Medical Superintendent's offices) invites members nominated by the Senatus of CMC to serve on the EC.
2. The duration of appointment for members is usually for a period of three years.
3. For the nominated, or ex-officio members, it would be for the period that they hold administrative office.
4. The Director will be and the Medical Superintendent may be represented by their nominees who should ideally continually attend meetings of the Research Committee as permanent representatives during their term of office.

5. Members may be re-appointed for as many terms as deemed by the Director
6. At the end of the term of a member or members, a new member or members is/are appointed such that at least 50% of the members will remain in the committee to provide continuity and to help in the seamless overview of ongoing research.
7. A member can be replaced in the event of resignation or non-attendance for three consecutive EC meetings (unless this was intimated in advance to the member secretary on sufficient grounds), or for any action not commensurate with the responsibilities laid down in the guidelines. Disqualification of any member is communicated in writing by the Director.
8. A member who is unable to attend three consecutive meetings and informs the Member Secretary in advance may be temporarily replaced by another member of the Senatus selected by the Director and nominated by the Principal's office.
9. A member can tender his/her resignation from the committee, with approval from the Director (through the Principal's office).
10. Membership of the EC is a position of responsibility and is not a paid position for institutional members. Members will not be paid an honorarium or compensation for their membership or attendance at the meetings.

Members of the EC who are from outside the institution shall be provided transport to attend EC meetings or be compensated for their travel expenses and shall be paid an honorarium, as fixed by the Principal's office, for attendance and participation at each EC meeting.

### 2.2.2.3 Compensation Committee and SAE meeting

The Compensation Committee meeting will be held once in a month where the Serious Adverse Events (Death/ Injury) proposals are reviewed. The Compensation committee follows the guidelines provided by the Drug Controller General of India (DCGI) and the Supreme Court that has been recommended is enclosed in the following link:

[Compensation guidelines\Compensation formula for SAEs 2013.pdf](#) where the Committee determines the compensation for the patients' dependents.

#### Procedure for reporting:

All interventional trials approved by the IRB of CMC Vellore will come under the purview of this policy (drugs, devices, and behavioral or educational interventions; single or multiple armed trials, randomized or non-randomized).

#### For all SAE reports:

- ❖ Within **24 hours** of learning about an unanticipated or serious adverse event.
- ❖ The principal investigator is responsible for notifying the **DCGI**, the Study Sponsor (if external)
- ❖ The Ethics Committee ([saeclinpharm@gmail.com](mailto:saeclinpharm@gmail.com)) with a cc to the secretariat at the Office of Research CMC ([research@cmcvellore.ac.in](mailto:research@cmcvellore.ac.in)). A hard copy of this document must also be sent to the IRB SAE co-ordinator, Clinical Pharmacology Unit, CMC Hospital, Vellore 632 004, Tamil Nadu.
- ❖ Within **10 days** the principal investigator is to submit a follow up report to the same list of people as above.
- ❖ IF IT IS A DEATH REPORT THEN THIS MUST ALSO BE SENT TO THE EXPERT COMMITTEE AND THE HEAD OF THE INSTITUTION (both should have a copy of the original report to the DCGI).



**Expert Committee address:**

The Chairman, Expert Committee, The Drug Controller General of India, FDA Bhavan, ITO, Kotla Road, New Delhi -110002

Within 10 days the completed access database should be sent to the IRB SAE Co-ordinator at [saeclinpharm@gmail.com](mailto:saeclinpharm@gmail.com).

**2.2.2.4 Current membership of the Ethics Committee Silver**

S. No	Name	Qualification	Designation	Affiliation	Term period as member
1	Dr. George Thomas	MBBS, D Ortho, PhD	Orthopaedic Surgeon, St. Isabella Hospital, Chennai, Chairperson, Ethics Committee, IRB.	External, Clinician	2016 - 2018
2	Prof. Keith Gomez	BSc, MA (S.W), M. Phil (Psychiatry Social Work)	Student counselor, Loyola College, Chennai, Deputy Chairperson, Ethics Committee, IRB	External, Lay Person & Social Scientist	2016 - 2018
3	Dr. Alfred Job Daniel	D Ortho, MS Ortho, DNB Ortho	Principal, CMC, Vellore	Internal, Clinician	2011 - 2016
4	Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal, Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician	2016 - 2019
5	Mr. Samuel Abraham	MA, PGDBA, PGDPM, M. Phil, BL.	Sr. Legal Officer, CMC, Vellore	Internal, Legal Expert	2016 – 2018
6	Dr. P. Zachariah	MBBS, PhD	Retired Professor, Vellore	External, Clinician	2016 - 2018
7	Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay person	2016 - 2018
8	Dr. Jayaprakash Muliyl	BSC, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, CMC, Vellore	External, Scientist & Epidemiologist	2016 – 2018
9	Dr. Shirley David	MSc, PhD	Professor, Head of Fundamentals Nursing Department, College of Nursing, CMC, Vellore	Internal, Nurse	2014 - 2017
10	Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert	2016 -2018
11	Rev. Dr. T. Arul Dhas	MSc, BD, DPC, PhD(Edin)	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist	2016 -2018
12	Dr. Binu Susan Mathew	MBBS, MD	Associate Professor, Clinical Pharmacology CMC, Vellore	Internal, Pharmacologist	2016 - 2018
13	Dr. Denise H.	BSc (Hons), PhD	Honorary Professor,	Internal,	2016 – 2018

	Fleming		Clinical Pharmacology, CMC, Vellore	Scientist & Pharmacologist	
14	Dr. Vinita Ravindran	PhD (Nursing)	Professor & Addl. Deputy Dean, College of Nursing, CMC, Vellore	Internal, Nurse	2014 - 2016
15	Mrs. Ruma Nayak	M Sc (Nursing)	Professor, Head of Paediatric Nursing & Deputy Nursing Superintendent, College of Nursing, CMC, Vellore	Internal, Nurse	2014 – 2016

### Current membership of the Ethics Committee Blue

S. No	Name	Qualification	Designation	Affiliation	Term period as member
1	Dr. B. J. Prashantham	MA(Counseling Psychology), MA(Theology), Dr. Min(Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore	External, Social Scientist	2016 – 2017
2	Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician	2016 - 2018
3	Mr. Samuel Abraham	MA, PGDBA, PGDPM, M. Phil, BL.	Sr. Legal Officer, CMC, Vellore	Internal, Legal Expert	2016 - 2018
4	Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person	2016 - 2018
5	Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist	2016 – 2018
6	Dr. Jayaprakash Muliyl	BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, CMC, Vellore	External, Scientist &Epidemiologis t	2016 –2018
7	Mrs. Emily Daniel	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse	2014 - 2016
8	Mrs. Sheela Durai	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse	2014 - 2016
9	Mr. C. Sampath	B.Sc., BL	Advocate, Vellore	External, Legal Expert	2016 -2018
10	Dr. Anuradha Rose	MBBS, MD, MHSC (Bioethics)	Associate Professor, Community Health, CMC, Vellore	Internal, Clinician	2015 -2016
11	Dr. Ratna Prabha	MBBS, MD (Pharma)	Associate Professor, Clinical	Internal,	2015 – 2017

			Pharmacology, CMC, Vellore	Pharmacologist	
12	Dr. Denise H. Fleming	BSc (Hons), PhD	Honorary Professor, Clinical Pharmacology, CMC, Vellore	Internal, Scientist & Pharmacologist	2016 - 2018

### 2.2.3 Independent consultants

The IRB may call upon independent consultants who may provide special expertise to the IRB on proposed research protocols. These consultants may be specialists in ethical or legal aspects, specific diseases or methodologies, or they may be representatives of communities, patients, or special interest groups. They are required to give their specialized views and may be required to attend convened IRB meetings but do not take part in the decision making process, which is conducted by members of the IRB

### 2.2.4 Education of IRB members

- i. IRB members will be provided a training pack consisting of relevant guidelines regarding the science and ethics of biomedical research.
- ii. All RC members must have attended basic training in research study design and the ethics of human research participants' protection. All members are encouraged to familiarize themselves with the CONSORT, STARD, STROBE and other relevant guidelines for the design, conduct and reporting of various types of research designs.
- iii. All EC members must be conversant with the ICMR guidelines for research involving human participants, Schedule Y of the Drugs and Cosmetics Act, the Declaration of Helsinki and ICH-GCP guidelines.
- iv. IRB members will also be provided with a copy of the Policies and Standard Operating Procedures.
- v. IRB members will be offered ongoing opportunities for enhancing their capacity for ethical review, including participation at the periodic Research Ethics and GCP workshops conducted by the Office of Research.
- vi. A record will be maintained of the training obtained by IRB members and updated annually.

### 2.2.5 Responsibilities of IRB members

- i. Membership of the IRB is a position of responsibility and IRB members are expected to approach this position with the seriousness and professionalism befitting their role in aiding the advancement of science and protection of research participants.
- ii. IRB members are expected to show interest and motivation, commitment and availability, experience with or education regarding the science and ethics of research, respect for divergent opinions and ability to work as a team, integrity, diplomacy and ability to maintain confidentiality.
- iii. IRB members should attend a minimum of 7 of the 11 IRB meetings every year and not miss three consecutive meetings. Information should be provided at the beginning of each month if a member is unable to attend an IRB meeting.
- iv. Members should inform the Office of Research in advance if they anticipate being unavailable for three consecutive IRB meetings.
- v. IRB members should assess in detail the proposals allotted to them as primary or secondary assessors and come to convened meetings with their prepared report. Reports by IRB members should be succinct but sufficiently detailed so as to highlight deficiencies and suggested improvements in design or execution of

the study. IRB members function as facilitators of sound and ethical research, not primarily as regulators of research.

- vi. All IRB members are expected to declare competing conflicts of interest with respect to research proposals or investigators, if any, before commencement of each meeting.
- vii. IRB members are expected to agree to not be present during presentation of proposals in which they are co-investigators, unless requested to answer clarifications; they may present proposals if they are principal investigators, but in both situations should leave the room before IRB discussions and decisions. It is the duty of IRB members to adhere to this without being reminded of this duty.
- viii. IRB members are required to sign a confidentiality agreement on joining and this will be renewed with every extension.
- ix. Members should submit an updated CV on joining the IRB and with each extension.
- x. Members should not make copies of any material provided to them and ensure destruction or return of all materials sent for review (CD containing research proposals and supporting documents) after the IRB meetings.

## 2.3 RESEARCH PROTOCOL SUBMISSION PROCESS

All research proposals to be submitted to the IRB should be on prescribed application forms failing which applications will not be accepted.

### 2.3.1 Application

- i. All research proposals will be submitted to the Office of Research on specific forms according to the design of the study. These forms can be downloaded from the Research Website or obtained from the Office of Research. Applications for interventional studies, studies to determine diagnostic test accuracy and studies for epidemiological research have separate forms and checklists. Study designs that do not conform to the above may be submitted in the general application form (see Section 4 for samples of these forms).
- ii. All applications will be concurrently reviewed for scientific merit by the Research Committee and ethical considerations by the Ethics Committee at the meeting of the IRB, hence the sections in the application forms dealing with the science and ethics of the study should both be filled in and submitted for the proposal to be considered.
- iii. All relevant documents detailed under Documentation should accompany the application.
- iv. Researchers submitting proposals funded by other funding agencies or pharmaceutical agencies that have other kinds of application formats need to submit the agency-specific format *as well as* the IRB application forms relevant to the design of the study. Failure to do this is likely to result in rejection of the application.
- v. Submission procedure
  - Project proposal,
  - Curriculum Vitae
  - Information sheet and informed consent forms
  - The aforesaid in translated versions need to be in **PDF format**.
  - **Signatures by all** investigators and the Guide/Head of the Department/Unit need to be scanned.

All the above mentioned should be submitted both in hard copy and soft copy so as to reach the Office of the Additional Vice-Principal (Research) on or before the due date. **Applications submitted after the due date will not be entertained.**

- vi. At the time of submission the checklist for submission should also be submitted; if this indicates incomplete submissions, the application will be returned.
- vii. All incomplete submissions will have to be completed and returned before the 1st of the month for it to be considered for review at the IRB meeting for that month. This is to ensure that IRB members have sufficient time to review the proposals in detail. Researchers are requested to keep to this deadline and not attempt to place undue pressure on the IRB to accept last minute applications or seek expedited review without justification.
- viii. If the application is complete and accepted, the date and time of the IRB meeting that will review the proposal will be intimated to the Principal Investigator in writing. He/she or one of the co-investigators will be required to be present to offer clarifications. If none of the investigators are able to be present for discussion of the proposal, it will not be taken up for review. **For all student/post-graduate presentations, it is essential that the guide or a co-guide attend the meeting along with the student/post-graduate. If no guide or co-guide is present, the proposal will not be considered for review.**

### 2.3.2. Processing fee for IRB Clearance for industry funded research

- i. A non-refundable processing fee will be levied on all external research proposals that are funded by agencies or organizations with a commercial orientation (pharmaceutical companies, contract research organizations, etc) for IRB approval.
- ii. This fee is not applicable to proposals that are funded by non-commercial sponsors (governmental or non-governmental funding agency).
- iii. This processing fee is independent of the eventual decision to accept, revise or reject the proposal.
- iv. The processing fee applicable will be Rs. 50, 000 (Rs. Fifty thousand only) per proposal for proposals sponsored by overseas organizations or agencies (parent organization is based overseas even if there are significant Indian operations) or Indian agencies with significant overseas operations, and Rs. 20,000 per proposal for Indian organizations or agencies.
- v. This fee is non-negotiable. Under exceptional circumstances, as decided by the Additional Vice-Principal in consultation with the Principal, a reduction or waiver of this fee may be made.
- vi. This fee is to be remitted by crossed demand draft payable to the State Bank of India, Vellore, in the name of the 'CMC Vellore Association.'
- vii. The receipt of payment of this fee will have to accompany the IRB application for the review to take place at the IRB meeting for the month.

### 2.3.3. Documentation

The researcher should submit an application of the study protocol in the prescribed format for the study design (see section 4).

The protocol should include the following: -

1. The title of the project with affiliation and signatures of Principal Investigator (PI) and all co-investigators as attestation for agreement to conduct the study. If co-investigators are not available for signature at the time of submission of the protocol, a signed letter with the title of the study with names of all authors should accompany the proposal and stating that the co-investigator has read the protocol as submitted, approves the submission and the role of all investigators and agrees to the terms of participation.
2. Signature of the Head of the Department or Unit, as applicable. For interdepartmental studies, an agreement letter from concerned departmental heads is desirable, especially if they are not co-investigators.
3. Clear research objectives and rationale for undertaking the investigation in the light of existing knowledge.



4. Recent curriculum vitae of the Investigators indicating qualification and experience.
5. Participant recruitment procedures and brochures, if applicable.
6. Inclusion and exclusion criteria for entry of participants.
7. Precise description of methodology of the proposed research, including sample size (with justification), type of study design, intended intervention, dosages of drugs, route of administration, duration of treatment and details of invasive procedures, as appropriate. A diagrammatic representation of the study participant flow is encouraged for all study designs, where appropriate.
8. Plan to withdraw or withhold standard therapies in the course of research.
9. Plan for statistical analysis of the study.
10. Procedure for seeking and obtaining informed consent with sample of patient information sheet and informed consent forms in English and all local languages of expected participants.
11. Safety of proposed intervention and any drug/device or vaccine to be tested, including results of relevant laboratory, animal and human research.
12. Proposed compensation and reimbursement of incidental expenses and management of research related and unrelated injury/ illness during and after research period.
13. If applicable (in study-related injuries); a description of the arrangements for insurance coverage for research participants and copy of insurance documents from an Indian insurance agency.
14. If applicable; all significant previous decisions (e.g., those leading to a negative decision or modified protocol) by other regulatory authorities for the proposed study (whether in Vellore or elsewhere) and an indication of the modification(s) to the protocol made on that account. The reasons for negative decisions should be provided.
15. An account of storage and maintenance of all data collected during the trial.
16. Plans for publication of results, whether positive or negative, while maintaining the privacy and confidentiality of the study participants, with names of proposed authors and their expected contributions.
17. A statement on probable ethical issues and steps taken to address these, such as the justification for washout of a standard drug, or the use of a placebo control.
18. All other relevant documents related to the study protocol e.g., investigator's brochure for trial on drugs/ devices/ vaccines/ herbal remedies, statement of relevant regulatory clearances.
19. Any material used for advertisement to recruit participants to the study - this may include flyers, posters, radio and TV advertisements.
20. Details of Funding agency/ Sponsors and breakdown of fund allocation.
21. 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); clearance from the Department of Biotechnology (DBT) for recombinant DNA experiments; and from the Bhabha Atomic Energy Commission (BARC) for experiments involving ionizing radiation.
22. For exchange of biological material in international collaborative studies, a MoU/ Material Transfer Agreement between the collaborating partners.
23. A statement on conflict of interest (COI), if any.
24. Agreement to follow the latest version of the ICMR guidelines and the Declaration of Helsinki with amendments, if any.

25. For clinical trials in humans, agreement to prospectively register the trial in the Clinical Trials Register-India (www.ctri.in) and/or other clinical trial registries as required by Indian regulatory authorities.
26. Agreement to report adverse events as required by institutional policy, and/or provides details of the Data Safety and Monitoring Board (DSMB) and to submit to review and audit if required.
27. Agreement to inform the IRB in writing of any deviations to the approved protocol.
28. Agreement to submit progress reports, if applicable or requested, and a final report (for institutionally sponsored as well as externally funded research) within six months of completion of the study, unless an extension is granted by the Additional Vice-Principal.
29. Agreement to write up and submit the results of the research to a peer-reviewed journal within a reasonable time (within two years of completion of submission of the final report).

## 2.4 REVIEW PROCEDURE

- i. All properly submitted applications will normally be reviewed during the month following the submission and according to the review procedure described below.
- ii. Each application will be screened by the Office of Research for their completeness and depending on the risk involved categorise them into three types, namely, *exemption from review*, *expedited review* and *full review* (see below for explanation).
- iii. A study with minimal risk would be defined as one which may be anticipated as harm or discomfort not greater than that encountered in routine daily life activities of general population or during the performance of routine physical or psychological examinations or tests. 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.
- iv. An investigator cannot decide that her/his protocol falls in the exempted category without approval from the IRB. All proposals will be scrutinised to decide under which of the following three categories it will be considered.
- v. It is important to remember that the IRB is constituted both as a Research and an Ethics Committee, and the purpose is to review and improve scientific quality in addition to human subjects' protection, hence even if the study is of less than minimal risk, it may still need to be considered by the full IRB.
- vi. ***For all post-graduates, it is essential that the guide be present for the discussion of the proposal by the IRB.***

### 2.4.1 Exemption from review

Proposals which present less than minimal risk fall under this category as in situations such as research on educational practices such as instructional strategies or effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

#### **Exceptions:**

- a. When research on use of educational tests, survey or interview procedures, or observation of public behaviour 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.
- b. When interviews involve direct approach or access to private papers.



## 2.4.2 Expedited Review

Research activities that present no more than minimal risk to human participants, and involve only procedures listed in one or more of the categories listed below may be reviewed by the Chairperson or Deputy Chairperson of the Research Committee through the expedited review procedure.

### Categories of research considered for expedited review

- i. Minor deviations from originally approved research during the period of approval (usually of one year duration).
- ii. Revised proposal previously approved through full review by the IRB or continuing review of IRB approved proposals where there is no additional risk or activity is limited to data analysis.
- iii. Research activities that involve only procedures listed in one or more of the following categories
  - Clinical studies of drugs and medical devices only when research is on already approved drugs (except when studying drug interaction or conducting trials on vulnerable populations or for new indications)
  - Research involving clinical materials (data, documents, records, or specimens) that have already been collected for non-research (clinical) purposes
  - Collection of blood samples by finger prick, heel prick, ear prick, or venepuncture:
    - ▶ from healthy adults and non-pregnant women of normal weight 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;
    - ▶ 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 in an 8 week period and not more than 2 times per week. From neonates, any blood collection should be considered very carefully and is unlikely to be approved with an expedited clearance.
  - Prospective collection of biological specimens for research purposes by non-invasive means. For instance:
    - ▶ skin appendages like hair and nail clippings in a non-disfiguring manner;
    - ▶ dental 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;
    - ▶ excreta and external secretions (including sweat);
    - ▶ un-cannulised saliva collected either in an un-stimulated fashion or stimulated by chewing gum or by applying a dilute citric solution to the tongue;
    - ▶ placenta removed at delivery;
    - ▶ amniotic fluid obtained at the time of rupture of the membrane prior to or during labour
    - ▶ mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
    - ▶ Sputum collected after saline mist nebulization and bronchial lavages.
  - Collection of data through non-invasive procedures routinely employed in clinical practice. Where medical devices are employed, they must be cleared/ approved for marketing, for instance

- ▶ physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the participant or an invasion of the participant's privacy;
  - ▶ weighing or testing sensory acuity;
  - ▶ magnetic resonance imaging;
  - ▶ electrocardiography, echocardiography; electroencephalography, thermography, detection of naturally occurring radioactivity,
  - ▶ electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow,
  - ▶ Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
- Research involving clinical materials (data, documents, records, or specimens) that will be collected solely for non-research (clinical) purposes.
  - Collection of data from voice, video, digital, or image recordings made for research purposes.
  - Research on individual or group characteristics or behaviour not limited to research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behaviour or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.
- a. Proposals requesting expedited review should provide sufficient detail to enable a decision to be made in this regard. In the case of minor protocol amendments of approved research studies, the application should clearly specify the amendments that need expedited review.
  - b. All projects, whether internally or externally funded, are expected to submit a **report to the IRB annually for monitoring**. In approved and ongoing studies, the report will undergo expedited review by the Deputy Chairpersons of the RC and EC or their nominees from among the IRB members. Currently used informed consent forms must be submitted for ongoing review, along with an update on the study and any relevant new information that may affect the conduct of the study.
  - c. A brief summary and all review decisions will be placed before the IRB members in the next meeting.
  - d. The expedited review procedure may not be used where identification of the participants and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
  - e. The expedited review procedure may not be used for fresh applications with prospective data collection or interventions involving human participants. The Expedited review cannot be given to overseas investigators.
  - f. The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review, expedited or convened, utilized by the IRB.

### 2.4.3 Full Review

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

Previous Studies which have undergone previous IRB clearance in excess of 2 years, need a fresh IRB renewal in case of major proposal changes, novel ideas, major budgetary presentations or new sponsors are involved.

#### **2.4.4 Review of final reports**

All final reports submitted in the prescribed format will be reviewed by one member of the Research Committee assigned to review final reports. If the report is satisfactory, the investigator will not be asked to make a presentation to the IRB. In case of any queries regarding the report, the investigator will be asked to attend the next convened IRB meeting to make a presentation of their work and answer queries.

### **2.5 IRB MEETING**

- i. The IRB Silver & Red will meet every month at 10 a.m. on the 3<sup>rd</sup> Wednesday to enable detailed review of all proposals scheduled for the convened meeting.
- ii. The IRB Blue & Green will meet at 1.00 p.m. on a date to be decided by mutual consent of the members at the previous meeting to enable detailed review of all proposals scheduled for the convened meeting.
- iii. In the event that the timing is unsuitable, the meeting could be rescheduled by the Additional Vice-Principal (Research) in consultation with the Chairpersons of the Research and Ethics committees.
- iv. All decisions will be taken at convened meetings and not solely by circulation of project proposals.

#### **2.5.1 Distribution of proposals to members and preparation for the IRB meeting**

- i. The Office of Research shall prepare an agenda and send this to the members of the IRBs at least two weeks before the meeting.
- ii. Each member of the IRB shall receive a CD with copies of all proposals (or hard copy if preferred) with all submitted documents along with the agenda.
- iii. Each member of the IRBs will be allotted primary or secondary reviewer status for each proposal by the Office of Research. Thus each proposal will be reviewed in detail by two members of the Research Committee for scientific considerations and by two members of the Ethics Committee for ethical review.
- iv. Members are expected to indicate at the earliest their participation at the scheduled IRB meeting.
- v. If there are potential conflicts of interest in reviewing their allotted proposals, they shall inform the Office of Research sufficiently early so that these may be re-allotted or be encouraged to review with the nature of the declared conflict recorded in the minutes of the IRB meeting.
- vi. IRB members are encouraged to seek clarification from researchers directly or via the Office of Research before the IRB meeting so that conclusive decisions can be facilitated.
- vii. IRB members will prepare brief assessment reports for the assigned proposals.
- viii. If expert opinion is thought necessary, members are free to seek this directly from a suitable person but confidentiality of the proposal should be ensured. The name, affiliation and nature of expertise and the opinion of the expert should be submitted with the review report. In case, more than one reviewer is unable to review a proposal, it may be referred to an independent consultant, recommended by an IRB member or chosen from a standing list of consultants in the Office of Research.
- ix. While designated proposals will be the primary responsibility of IRB members, they are encouraged to review all proposals, if possible, and share their views at the meetings.

#### **2.5.2 Combined research and ethics review by IRB**

- i. The IRBs, comprising the Research and Ethics committees, will meet together at a designated venue that will accommodate all members of both committees.

- ii. The meeting is chaired by the Chairperson of the Ethics Committee. In his/her absence, the meeting can be chaired the Chairperson of the Research Committee or the deputy Chairs of either committee. Scientific review of the proposal by the Research Committee will precede the ethical review.
- iii. If the Principal/ Medical Superintendent / Chaplain / Dean, College of Nursing/ Nursing Superintendent are unable to attend, a representative from their offices may attend.

#### 2.5.2.1 Quorum

- i. The quorum for RC review will be 4 members.
- ii. The quorum for EC review will be 5 members and should fulfil the following composition (as prescribed by Schedule Y):
  - ▶ One basic medical scientist (preferably one pharmacologist).
  - ▶ One clinician
  - ▶ One legal expert or retired judge
  - ▶ One social scientist/ representative of non-governmental organisation/ philosopher/ ethicist/ theologian or a similar person
  - ▶ One lay person from the community.
- iii. The quorum should be maintained throughout the meeting and the names of members present during each proposal should be recorded to ensure compliance with Schedule Y of the Drugs and Cosmetics Act.

#### 2.5.2.3 Conduct of Meeting

- i. The members of the Research Committee with responsibility for primary and secondary review shall summarise the proposal and present their reports.
- ii. Researchers will be present during the presentation and will be invited to offer clarifications if required to do so; they may also volunteer clarifications or additional information. For PG trainees and students, the guides or co-guides must be present for the presentation and discussion of the proposal.
- iii. There will be provision for review of proposals on computers for each member of the IRB and projection of proposals and member's reports if needed.
- iv. Once the Research Committee has made their decision about the scientific validity of the study, the same process of review by the Ethics Committee will commence.
- v. Independent consultants/experts will be invited to offer their opinion on specific research proposals, if needed. When invited for consultation, the consultant/expert will be expected to follow the provided IRB SOP and sign a letter stating that they understand the terms of reference and a confidentiality agreement.
- vi. At each meeting, the pharmacologist or the Deputy Chairperson of the RC will present the data obtained from the CMC IRB Safety Monitor on SAEs for ongoing studies at CMC, and the investigator may be requested to be present for discussion if considered necessary by the IRB.

#### 2.5.2.4 Elements of Review

1. The **Research Committee** shall review the scientific aspects of the proposal as follows:
  - the rationale and need for the study in view of existing literature
  - the appropriateness of the study design in relation to the objectives of the study, the statistical methodology (including sample size calculation), and the potential for reaching sound conclusions with the smallest number of research participants.

- the explanation of risks and benefits, the justification for the use of control arms, criteria for withdrawal or study termination.
  - the adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a data safety monitoring board (DSMB).
  - the adequacy of the investigative team, site, available facilities, and procedures.
  - the manner in which the results of the research will be reported and published.
2. The **Ethics Committee** will take into account the process and outcome of the scientific review by the Research Committee, and the requirements of applicable laws and regulations. In addition, the EC will also consider the following:

#### **Care and Protection of Research Participants**

- The suitability of the investigators' qualifications and experience for the proposed study.
- Any plans to withdraw or withhold standard therapies for the purpose of the research, and the justification for such action.
- The medical care to be provided to research participants during and after the course of the research.
- The adequacy of medical supervision and psycho-social support for the research participants.
- Steps to be taken if research participants voluntarily withdraw during the course of the research.
- The criteria for extended access to, the emergency use of, and/or the compassionate use of study products.
- The arrangements, if appropriate, for informing the research participant's general practitioner or consultant, including procedures for seeking the participant's consent to do so.
- A description of any plans to make the study product available to the research participants following the research.
- A description of any financial costs to research participants; the rewards and compensations for research participants (including money, services, and/or gifts);
- The provisions for compensation/treatment in the case of the injury/disability/death of a research participant attributable to participation in the research;
- The insurance and indemnity arrangements;

#### **Protection of Research Participant Confidentiality**

- A description of the persons who will have access to personal data of the research participants, including medical records and biological samples.
- The measures taken to ensure the confidentiality and security of personal information concerning research participants.

#### **Informed Consent Process**

- i. A full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent;
- ii. The adequacy, completeness, and understandability of written and oral information to be given to the research participants, and, when appropriate, their legally acceptable representative(s);



- iii. Clear justification for the intention to include in the research individuals who cannot consent, and a full account of the arrangements for obtaining consent or authorization for the participation of such individuals;
- iv. Assurances that research participants will receive information that becomes available during the course of the research relevant to their participation including their rights, safety, and well-being;
- v. The provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project.

### **Informed consent in emergency protocols**

- i. This section describes responsibilities related to informed consent when research participants are enrolled in emergent circumstances, as when human participants are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
- ii. Obtaining informed consent is not feasible because (i) the participants will not be able to give their informed consent as a result of their medical condition, (ii) the intervention involved in the research must be administered before consent from the participants' legally authorized representatives is feasible, and (iii) there is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.
- iii. Participation in the research holds out the prospect of direct benefit to the participants because (i) participants are facing a life-threatening situation that necessitates intervention, (ii) appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual participants; and (iii) risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of participants, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
- iv. The research could not practicably be carried out without the waiver.
- v. The proposed research protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each participant within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact representatives and make this information available to the IRB at the time of continuing review.
- vi. The IRB has reviewed and approved informed consent procedures and an informed consent document. These procedures and the informed consent document are to be used with participants or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a participant's participation in the research.

In addition, the IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, of the participant's inclusion in the research, the details of the research and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, that he or she may discontinue the participant's participation at any time without penalty or loss of benefits to which the participant is otherwise entitled. If a legally authorized representative or family member is told about the research and the participant's condition improves, the

participant is also to be informed as soon as feasible. If a participant is entered into research with waived consent and the participant dies before a legally authorized representative or family member can be contacted, information about the research is to be provided to the subject's legally authorized representative or family member, if feasible.

### **Community Considerations**

- i. the impact and relevance of the research on the local community and on the concerned communities from which the research participants are drawn;
- ii. the steps taken to consult with the concerned communities during the course of designing the research;
- iii. the influence of the community on the consent of individuals;
- iv. proposed community consultation during the course of the research;
- v. the extent to which the research contributes to capacity building, such as the enhancement of local healthcare, research, and the ability to respond to public health needs;
- vi. a description of the availability and affordability of any successful study product to the concerned communities following the research;
- vii. The manner in which the results of the research will be made available to the research participants and the concerned communities.

### **Recruitment of Research Participants**

- i. The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status, and ethnicity);
- ii. The means by which initial contact and recruitment is to be conducted;
- iii. The means by which full information is to be conveyed to potential research participants or their representatives;
- iv. The inclusion and exclusion criteria for research participants.

#### **2.5.2.5 Decision making**

In making decisions the IRB will take the following into consideration:

- i. A member will withdraw from the meeting during the decision procedure concerning an application where there is a conflict of interest; the conflict of interest should be indicated to the chairperson prior to the review of the application and recorded in the minutes
- ii. Decisions may only be taken when sufficient time has been allowed for review and discussion of an application in the absence of non-members (e.g., the investigator and independent consultants) from the meeting, with the exception of IRB staff.
- iii. Decisions will only be made at meetings where a quorum is present and maintained for each proposal.
- iv. Only members who participate in the review will participate in the decision.
- v. In the interests of sound and ethical research, the members of the RC and EC are encouraged to discuss the proposal in detail before a decision is made.
- vi. Decisions will be arrived at through consensus, where possible; when a consensus is not possible, the IRB will vote.
- vii. In the event of a vote, although the names of members who voted for and against the project may be recorded, this information will not be made public knowledge to avoid coercion and inducements.



- viii. If one of the members has her/his own proposal for review or has any conflict of Interest then s/he should withdraw from the IRB while the project is being discussed.
- ix. The decision must be to recommend / reject / suggest modification for a repeat review or advise appropriate steps.
- x. The record of the discussion will serve as the minutes and will be approved and signed by the Chairperson/ alternate Chairperson/ designated member of the committee. Review reports of primary and secondary IRB members will be filed along with details of the resolution of any concerns raised, outstanding issues and final decisions. Any advice that is non-binding will be appended to the decision.
- xi. In cases of conditional decisions, clear suggestions for revision and the procedure for having the application re-reviewed will be specified.
- xii. A negative decision on an application will be supported by clearly stated reasons.

#### **2.5.2.6 Communicating IRB decisions**

- i. A decision will be communicated in writing to the applicant, preferably within two weeks time of the meeting at which the decision was made.
- ii. The IRB decision, signed by the Chairperson or Deputy Chairperson, will indicate the amount sanctioned from the Fluid Research Fund (if financial support was requested) and will be separate from the IRB clearance.
- iii. The IRB communication of the decision will include, but is not limited to, the following:
  - The exact title of the research proposal reviewed;
  - The clear identification of the protocol of the proposed research or amendment, date and version number (if applicable).
  - The names and specific identification number version numbers/dates of the documents reviewed, including the potential research participant information sheet/material and informed consent form and local translations.
  - If applicable, the following will also be mentioned- Investigator's Brochure, proposed methods for patient accrual including advertisement (s) etc. proposed to be used for the purpose, principal investigator's current CV, insurance policy / compensation for participation and for serious adverse events occurring during the study participation, Investigator's Agreement with the Sponsor, and Investigator's Undertaking.
  - The names and designations of all members present during the presentation and discussion of the proposal.
  - In case of a conditional decision, any requirements by the IRB, including suggestions for revision and the procedure for having the application re-reviewed;
  - in the case of a positive decision, a statement of the responsibilities of the applicant; for example, confirmation of the acceptance of any requirements imposed by the IRB; submission of progress report(s); the need to notify the IRB in cases of protocol amendments (other than amendments involving only logistical or administrative aspects of the study); the need to notify the IRB in the case of amendments to the recruitment material, the potential research participant information, or the informed consent form; the need to report serious and unexpected adverse events related to the conduct of the study; the need to report unforeseen circumstances, the termination of the study, or significant decisions by other IRBs or the Drug Controller General if India; the information the IRB expects to receive in order to perform ongoing review; the final summary or final report; and the need to store documents for at least 5 years after the end of the study

- The schedule/plan of ongoing review by the DSMB;
- In the case of a negative decision, clearly stated reason(s) for the negative decision;

Signature (dated) of the chairperson (or other authorized person) of the IRB.

## 2.6 PROSPECTIVE REGISTRATION OF CLINICAL TRIALS

- i. The ICMR and the WHO require prospective registration of all clinical trials before enrolment of the first participant in a Primary Register of the WHO International Clinical Trials Registry Platform. Further, prior registration is now a condition of publishing clinical trials for many journals. From 1st July 2005 the International Committee of Medical Journal Editors (ICMJE) has declared that their journals will not publish the results of any clinical trials not included on an authorized register.
- ii. The ICMR requires all trials conducted in India to be prospectively registered in the Clinical Trials Registry-India (CTRI; www.ctri.in). Schedule Y requires that all ICMR guidelines be followed for clinical trials. The CTRI is a Primary Register of the WHO International Clinical Trials Registry Platform and trials fully registered here will fulfill the ICMJE criteria of prospective trials registration.
- iii. All interventional clinical trials conducted in India and involving Indian participants need to be registered.
- iv. An interventional clinical trial is any research study that prospectively assigns people to one or more health-related interventions (e.g., preventive care, drugs, surgical procedures, behavioral treatments, etc.) to evaluate their effects on health-related outcomes. Thus, early and late trials, trials of marketed or non-marketed products, randomized or non-randomized trials -- all should be registered.
- v. The CTRI currently is accepting completed and initiated trials, but it is a requirement for CMC investigators to ensure registration prior to recruitment. As of January 2010, the other major web-site for the database registering clinical trials (www.clinicaltrials.gov) offers the following guidance 'Multi-site trials and multi-sponsor trials are susceptible to duplicate registration, thus care must be taken in how the trials are registered. For multi-sponsor trials it is the lead sponsor who should take responsibility for registration. It is critical that investigators and sponsors work together to ensure that a trial is registered once and only once.' Registration in both these registers is free.
- vi. The "Responsible Registrant" for a trial is either the principal investigator (PI) or the primary sponsor, to be decided by an agreement between the parties. The primary sponsor is ultimately accountable for ensuring that the trial is properly registered. For multi-center and multi-sponsor trials, it is the lead PI or lead sponsor who should take responsibility for registration.
- vii. The CTRI requires, in addition to the entry of the WHO 20-item dataset, contact details of IRB and a copy of the IRB approval (and DCGI approval, if applicable).
- viii. The IRB of CMC will only grant provisional approval for clinical trials in humans till the permanent registration number and a copy of the registration document is submitted to the Office of Research. Researchers may not commence recruitment until the final clearance is received.

## 2.7 FOLLOW UP AND MONITORING

- i. The IRB may nominate, when necessary, a subcommittee of one or more persons to oversee the day to day conduct of a trial. This subcommittee will usually consist of members of the faculty of CMC, and operate under the aegis of the CMC Data Monitoring Committee (DMC), chaired by the Head, Department of Biostatistics.
- ii. In addition to possible monitoring by the CMC DMC, the follow-up review intervals will be determined by the nature and the events of research projects, though each protocol will undergo a follow-up review at least once a year.

- iii. Reports should be submitted at prescribed intervals for review. This should be no less frequent than an annual report.
- iv. Final report should be submitted at the end of the study (including externally funded studies).
- v. All SAEs and the interventions undertaken should be intimated to the IRB, in the prescribed format (see section 4) with a copy of the report to the study sponsor, if any.
- vi. Protocol deviations, if any, should be recorded and reported with adequate justifications.
- vii. Any amendment to the protocol should be resubmitted for renewed approval. If these are minor and do not alter the risk-benefit ratio, expedited clearance may be requested.
- viii. Any new information related to the study should be communicated to the IRB and the participants, particularly those that pose additional risks or may warrant premature stopping of the trial.
- ix. Premature termination of study should be notified, with reasons for termination, as well as a summary of the data obtained up to the point of termination.
- x. Change of investigators / sites should be communicated.
- xi. In case of voluntary withdrawal from studies, the reasons for participant withdrawal need to be recorded and submitted to the IRB along with the monitoring and final reports.

## **2.8 CONTINUING REVIEW**

Any research activity involving the use of human participants that has received initial review and approval by the IRB is subject to continuing review and approval. Time intervals for such reviews shall be made at the discretion of the Data Monitoring Committee (if applicable) but shall occur no less than annually.

### **2.8.1 Amendments to protocols**

- Amendments to protocols or consent forms must be requested in writing, and reviewed and approved by the IRB prior to making any changes in study procedures.
- Requests must describe what modifications are desired, why changes are required, and if the changes pose any additional risks to the participants.
- Minor changes (those that do not increase the risk or decrease the potential benefit to participants) may be administratively approved, notified to the IRB at the next convened meeting. Investigators need not be present for this meeting.
- Changes considered to be more than minor must be reviewed at a convened meeting of the IRB and the investigator must be available to answer any queries.
- All amendments are reported to, discussed and approved by the IRB at a convened meeting.

### **2.8.2 Serious Adverse Event Reporting**

- When a participant who is participating in a research study experiences an unexpected or serious adverse event, the PI must promptly report the incident to the CMC IRB Safety Monitor (CISM, a clinical pharmacologist nominated by the Principal to review all SAE data for ongoing trials) and the Data Monitoring Committee (DMC, if applicable).
- In addition, all SAE data from all sites for studies in which CMC is a participating site, must be submitted to the CISM (currently, Dr. Denise Fleming, Department of Clinical Pharmacology) in the CMC format, for inclusion in the CMC SAE database. This will be used to generate the external (non-CMC) SAE report monitored for trends by the CISM and presented each month to the IRB.
- If the adverse event or reaction was anticipated in the protocol and the participant was informed about the possibility of the event in the consent form, there is no need to inform the CISM or DMC unless

the adverse event was unexpectedly serious, life threatening, or fatal.

- If the adverse event or reaction was unanticipated, unexpectedly serious, life-threatening or fatal, the adverse event must be reported to the CISM or DMC and the Office of Research within 24 hours of the investigating team becoming aware of the event. If the adverse event occurs after hours or on a week-end, notification should be sent to the Additional vice Principal (Research). The Medical Superintendent and concerned consultant in charge of clinical care (if applicable) should also be notified at the earliest, if the affected person was a registered patient of CMC.
- If the research study is being supported by an industry sponsor, the PI is also responsible for notifying the sponsor. The sponsor must then notify the regulatory authorities within a designated time period.
- If the PI holds the Investigational New Drug (IND) or Investigational New Device Exemption (IDE) in his/her name, he/she is required to notify the regulatory authorities of the adverse event or reaction within 24 hours, in addition to notifying the DSMB or DMC, as appropriate.
- Notifying the CISM or DMC does not relieve the PI from his/her responsibility to notify the sponsor and regulatory authorities.
- Within 10 working days, the PI must submit a detailed written report of the adverse event or reaction to the CISM/IRB in the specified format.
- For industry sponsored research trials of drugs or devices, sponsors are required to inform investigators of adverse events or reactions that occur at other sites. When PIs are informed of the adverse events in sponsor safety memos and other correspondence, the PI must review the adverse event report and then notify the CISM. This should be done as promptly as possible after receipt of the report from the sponsor.
- Receipt of adverse events reported must be acknowledged in writing and communicated to IRB members at the next convened meeting. The CISM presents a brief summary of all external reports received and a presentation of each SAE at CMC to the IRB each month. If thought necessary, the IRB may request the PI to be present at that meeting or a subsequent meeting to review the risk-benefit ratio in the light of the new information.

## **2.9 RECORD KEEPING AND ARCHIVING**

The following records will be archived and maintained by the Office of Research. Access to this data will only be on a need basis. Care will be taken to maintain confidentiality of this data.

- i. Curriculum Vitae (CVs) of all members of IRB.
- ii. One hard copy and one electronic copy of all study protocols with enclosed documents, progress reports, amendments and SAE reports.
- iii. Minutes of all meetings, duly signed by the Chairperson, or deputed signatory.
- iv. Copies of all existing relevant national and international guidelines on research ethics and all relevant laws, along with amendments.
- v. Copy of all correspondence with members, researchers and other regulatory bodies.
- vi. Interim reports and final report of the approved projects.
- vii. All documents should be archived for 5 years after a study is closed, and will be available for an audit, if required.

## **Section 3**

## **POLICIES TO BE FOLLOWED FOR ALL RESEARCH CONDUCTED AT THE CHRISTIAN MEDICAL COLLEGE**

The following section contains policies that will be followed for all research conducted at CMC Vellore

### **3.1 POLICY ON THE RECRUITMENT OF RESEARCH PARTICIPANTS**

- 3.1.1** In addition to its review for scientific merit and protection of participants from unnecessary research risks, the IRB will evaluate all protocols for participant recruitment especially with respect to women with childbearing potential, minority groups and children. Exclusion of minorities, women or children will be recommended or approved when inclusion is inappropriate with respect to the health of the participants or the purpose of the research.
- 3.1.2** Patients may be identified as potential research participants through direct contact of the PI with his or her patients, collaboration with physicians of other medical specialties, contact with individual consultants, posted written notices, flyers, or other IRB approved methods.
- 3.1.3** Inpatients - May be recruited by the investigator or other member of the research team only after consultation with the patient's consultant/head of the Unit.
- 3.1.4** Outpatients - For minimal risk research which does not bear directly upon a specific continuing therapeutic relationship between the individual and a CMC doctor or unit, outpatients may be recruited without prior notification of their personal physicians. However, when possible, each participant's consultant should be notified of the study and informed that the patient has been entered into a minimal risk study.
- 3.1.5** For more than minimal risk research or any research bearing directly upon a specific diagnosis or treatment, the participant's personal physician/consultant should be notified before enrolling the participant.
- 3.1.6** If the potential research participant is a minor, then contact must be via a parent or legal guardian.

### **3.2 POLICY AND PROCEDURES FOR INFORMED CONSENT FROM RESEARCH PARTICIPANTS**

- 3.2.1** Informed consent is "consent given voluntarily by a competent individual who has received the necessary information, has adequately understood the information and after considering the information, has arrived at a decision without having been subjected to coercion, undue influence or inducement, or intimidation".
- 3.2.2** Informed consent is based on the principle that competent individuals are entitled to choose freely whether to participate in research or not and protects the individual's freedom of choice and respect for the individual's autonomy. It also protects the participants' rights.
- 3.2.3** Taking informed consent is a "process" and does not merely consist of a signature on the consent form. Informed consent is a communication process between the researcher and the participant and starts before the research is initiated and continues throughout the duration of the study. The investigator or his delegate must discuss all pertinent aspects of the study, answer any queries / doubts, request consent and then if freely given, documented. The ultimate responsibility lies with the investigator.
- 3.2.4** Informed consent includes a verbal description and discussion of the details of the study including the process of randomization, the components of the study, and other details mentioned in the checklist below (from Schedule Y 2005). This may be a single document or be structured as two separate documents, a written *information sheet* containing all relevant information in simple, non-technical language in the participant's vernacular and a separate *informed consent form* used to document consent,



both of which are given to the participant to keep. Adequate time must be provided for the participant to decide on participation.

- 3.2.5** In case of illiterate participants, a witness is crucial and thumb impressions are allowed. All signatures should be dated and in case a date is forgotten on the day the consent is taken, it must be retaken on the next visit and dated, with a clear explanation documented in the source document. The investigator **MUST NOT** date the consent at any point in time; this must be done by the witness in the case of illiterate participants.
- 3.2.6** In the case of minors, proxy consent from a parent/responsible guardian is permitted and only the parent/responsible guardian may sign the informed consent form. However, it is mandatory that the minor, if over 7 years of age and considered capable of understanding the study procedures, provides assent (permission) to participate and, if possible, this should be recorded in a separate assent form. If the participant is incompetent to provide valid informed consent and it is deemed ethically justified to include this person in research, then the proxy consent of a responsible family member/legal guardian and a witness must be taken.
- 3.2.7** Each participant (or their representative) must be given a copy of the signed consent form. The original consent form should be filed in such a manner as to insure immediate retrieval when required by auditing entities, IRB, or sponsor monitors.
- 3.2.8** Written documentation of informed consent is required. Therefore, obtaining consent from an authorized third party via the telephone is not acceptable.
- 3.2.9** Obtaining informed consent from participants must be accomplished prior to performing the research activity and using only an IRB approved consent form. Written requests for amendments to an existing consent form must be approved by the IRB prior to implementation.
- 3.2.10** Upon receipt of an IRB approved consent form, all old versions should be discarded to prevent inadvertent use of an outdated consent form. Copies of the most recently approved consent form may be made and should be used until superseded by an amended consent form.
- 3.2.11** The consent form must be reviewed at least annually as part of the continuing review process.
- 3.2.12 Checklist for study Participant's informed consent documents (from Schedule Y). Note that this is designed for clinical trials, where essential elements are not required for other study designs, they need not be included.**

A. Essential Elements:

- Statement that the study involves research and explanation of the purpose of the research
- Expected duration of the Participant's participation
- Description of the procedures to be followed, including all invasive procedures
- Description of any reasonably foreseeable risks or discomforts to the Participant
- Description of any benefits to the Participant or others reasonably expected from research. If no benefit is expected, the Participant should be made aware of this.
- Disclosure of specific appropriate alternative procedures or therapies available to the Participant.
- Statement describing the extent to which confidentiality of records identifying the Participant will be maintained and who will have access to Participant's medical records
- Trial treatment schedule(s) and the probability for random assignment to each treatment (for randomized trials)

- Compensation and/or treatment(s) available to the participant, in the event of a trial-related injury
- An explanation about whom to contact for trial related queries, rights of Participants and in the event of any injury
- The anticipated prorated payment, if any, to the Participant for participating in the trial
- Participant's responsibilities on participation in the trial
- Statement that participation is voluntary, that the participant can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the Participant is otherwise entitled
- Any other pertinent information

**B. Additional elements, which may be required**

- Statement of foreseeable circumstances under which the Participant's participation may be terminated by the Investigator without the Participant's consent.
- Additional costs to the Participant that may result from participation in the study.
- The consequences of a Participant's decision to withdraw from the research and procedures for orderly termination of participation by Participant.
- Statement that the Participant or Participant's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect the Participant's willingness to continue participation will be provided.
- A statement that the particular treatment or procedure may involve risks to the Participant (or to the embryo or fetus, if the Participant is or may become pregnant), which are currently unforeseeable.
- Approximate number of Participants enrolled in the study.

### **3.2.13 Re-consent**

Fresh consent or re-consent is taken for the following conditions:

- Availability of new information which would necessitate deviation of protocol.
- 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.
- When long term follow-up or study extension is planned later.
- When there is change in treatment modality, procedures, site visits.
- Before publication if there is possibility of disclosure of identity through data presentation or photographs (this should be camouflaged adequately).

### **3.2.14 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. If such studies have protections in place for both privacy and confidentiality, and do not violate the rights of the participants then the 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, *eg.*, 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 recognised institutions or qualified investigators, samples or data from repositories or registries *etc.*
- iv. In emergency situations when no surrogate consent can be taken (**see Section 2.5.2.4**)

**The IRB will consider written requests for waiver or alteration of the process when accompanied by sufficient justification along with a copy of the research proposal.**

### **3.2.15 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 authorised 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 document;
- viii. If participant loses consciousness or competence to consent during the research period as in Alzheimer's Disease 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.

*ICMR Guidelines 2006; Schedule Y of the Drugs and Cosmetics Act, 2005*

#### **New Rules**

### **3.2.16 Re: Audiovisual Recording for Informed Consent Clinical Trials- when does it apply?**

As discussed, according to the order of the Honorable Supreme Court, dated 21.10.2013, the Drug Controller General of India (DCGI) has released a communication dated 19.11.2013 that certain clinical trials need to have informed consent audiovisual recorded by the investigator.

Based on the guidelines, the institutional review board of Christian Medical College Vellore (IRB) has implemented the following guidelines:-

All clinical trials wherein a new drug is being used or an old drug for a new clinical indication will require audiovisual recording- whether investigator initiated or industry driven.

The rule will also apply to surgical devices, implants, and stents etc, *which are under the jurisdiction of the Drug controller general of India*, when an old device is being used for a new indication.

In case of situations of ambiguity or when the circumstances so demand, the IRB will make a case by case decision at the time of clearance during the Silver IRB meeting.

The process of audiovisual recording should be done ensuring confidentiality of the subject, and the process itself (of audiovisual recording, itself) should be recorded in the patient information sheet. The investigator will have to read a brief summary of information that is relevant to the clinical trial under visual and audio recording. The subject will then need to give his verbal consent, following which the process of signing the document will need to be recorded.

The audiovisual document should be stored with the investigator on a suitable, but confidential repository and the recordings need to be submitted on monthly basis to the Office of Research at Carmen block with a covering letter. The soft copy of this documentation should immediately be made available to the sponsor or the DCGI, when asked for.

### 3.3. POLICY ON RESEARCH COSTS AND COMPENSATION PAID TO RESEARCH PARTICIPANTS

**3.3.1** If a research participant may have to bear any costs, which would be unnecessary if the participant had declined to participate in the research, all potential participants must be fully informed of the nature and estimated extent of these costs when obtaining consent. Examples of additional research costs include:

- i. Prolongation of treatment or hospitalization.
- ii. Extra diagnostic tests necessary for the research.
- iii. Extra clinical or laboratory assessments to evaluate research treatment outcome.
- iv. A research treatment (whether randomly assigned or not) which may be more costly than a standard treatment.
- v. Other substantial costs associated with extra visits to CMC.

**3.3.2** 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 enrol 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.

### 3.3.3 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.

**3.3.4** 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.

### 3.3.5 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 or provide insurance coverage for an unforeseen injury.

**3.3.6** An Arbitration committee set up by the institution under the Principal's office will decide on the issue of compensation on a case-by-case basis for all institutional funded research. The institution will also establish such a committee to oversee such claims, again on a case-by-case basis, for externally funded research.

**3.3.7** 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.

*ICMR Guidelines 2006*

## 3.4. POLICY ON AUTHORSHIP OF PUBLICATIONS

**3.4.1.** Publishing research is an ethical imperative. Decision regarding authorship should commence at the design stage of each study.

**3.4.2.** The International Committee of Medical Journal Editors has recommended the following criteria for authorship; these criteria are still appropriate for those journals that distinguish authors from other contributors.

- i. Authorship credit should be based on
  - substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data;
  - drafting the article or revising it critically for important intellectual content; and
  - final approval of the version to be published.
  - Authors should meet conditions a, b and c.
- ii. When a large, multi-centre group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript. These individuals should fully meet the criteria for authorship/contributorship defined above and editors will ask these individuals to complete journal-specific author and conflict of interest disclosure forms. When submitting a group author manuscript, the corresponding author should clearly indicate the preferred citation and should clearly identify all individual authors as well as the group name. Journals will generally list other members of the group in the acknowledgements.



- iii. The National Library of Medicine indexes the group name and the names of individuals the group has identified as being directly responsible for the manuscript.
- iv. Acquisition of funding, collection of data, or general supervision of the research group, alone, do not justify authorship.
- v. All persons designated as authors should qualify for authorship, and all those who qualify should be listed.
- vi. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.
- vii. Some journals now also request that one or more authors, referred to as “guarantors,” be identified as the persons who take responsibility for the integrity of the work as a whole, from inception to published article, and publish that information.
- viii. Increasingly, authorship of multi-centre trials is attributed to a group. All members of the group who are named as authors should fully meet the above criteria for authorship/contributorship.
- ix. The group should jointly make decisions about contributors/authors before submitting the manuscript for publication. The corresponding author/guarantor should be prepared to explain the presence and order of these individuals. It is not the role of editors to make authorship/contributorship decisions or to arbitrate conflicts related to authorship.

*International Committee of Journal Editors (<http://www.icmje.org/#author>)*

### **3.5 POLICY ON RESEARCH USING STORED BIOLOGICAL PRODUCTS**

**3.5.1** A bio bank/repository is a collection of resources that can be accessed to retrieve human biological material and data. Human Tissue Repositories collect, store, and distribute human tissue materials for research purposes. As tissue banking concerns research at a later time, the ethical issues pertain to consent requirements for the banking and further uses of tissue and DNA samples, their control and ownership, and the benefit sharing to the individual or community.

**3.5.2 Primary use:** By primary use it is meant that the biological material will be used for the intended purpose as described in the protocol submitted for approval from the IRB. Ownership of the sample lies with the individual, family or community as the case may be.

The IRB should consider following points for approving primary use:

- i. consent should be written, given voluntarily by the donor who has the capacity to do so. The use of the samples shall be reserved for the defined purpose only;
- ii. Participants have the right to withdraw at any time. This does not apply to anonymised samples; Principles for Human Genetics and Genomics arch
- iii. If sample is inadequate or contaminate and, re-contact is likely to be necessary for fresh samples, then this should be incorporated in the consent form, or fresh consent obtained;
- iv. While obtaining data/samples from vulnerable subgroups with reduced autonomy, the IRB should ensure that informed consent be obtained from legally authorized representatives in the presence of an impartial witness. The risks and benefits should be adequately explained;
- v. when samples have to be obtained for specific research from participants belonging to specified communities, permission of the group leader/local leader/authorities must also be obtained. However individual consent should never be compromised even if permission of the gatekeepers/village panchayat has been obtained

- vi. Group consent of the population/community should be obtained through its culturally appropriate authorities before sampling starts, particularly for group specific research like genetic research;
- vii. Samples obtained for archival purposes in a prospective study.

**3.5.3 Secondary Use:** Every request for secondary use shall be examined by the IRB to ensure that:

1. the proposed use does not transgress the original consent given for the earlier study and the validity of the objectives of the new study;
2. provisions for ensuring anonymity of the samples for secondary use are stated;
3. after anonymization of a sample, results are not communicated to the donor;
4. for postmortem uses of samples the permission of the next of kin, legally
5. authorized representative should be obtained; and
6. Waiver of consent is given whenever the donor is not traceable or the sample is anonymised.

**3.5.4** Consent forms for the primary use of biological material should specify the details of what will be done with the material in the future. Sample forms that can be adapted for use are provided in the Appendices.

### **3.6 POLICY ON RESEARCH ON FOETAL TISSUE OR ORGANS FOR TRANSPLANTATION**

**3.6.1 The following policies will be followed for all research on foetal tissues or organ**

#### **Transplantation**

- i. Every transplantation or research project involving the use of embryonic or foetal tissue must be approved by the Institutional Committee for Stem Cell Research and Therapy (IC-SCRT) and ethics committees and referred to National Apex Committee for Stem Cell Research and Therapy (NAC-SCRT) for final approval in case of restrictive research as defined in the Stem Cell Research and Therapy Guidelines.
- ii. All centres doing research on stem cells should be registered with NAC-SCRT.
- iii. All members of the hospital or research staff - medical and paramedical – directly involved in any of the procedures will be fully informed of the purpose and implications of the research project.
- iv. The researcher shall not be a party to deliberate conception and / or subsequent abortion for the sake of obtaining tissue or organ for research or saving the life of a family member or for the purpose of commercialisation.
- v. No research is permitted on the live aborted foetus.
- vi. Tissue for transplantation or research may be obtained from dead embryos or foetuses, their death resulting from legally induced or spontaneous abortion. Death of an intact embryo or foetus is defined as absence of respiration and heart beat.
- vii. Voluntary, informed, written consent will be obtained from the mother in two stages - first for the abortion, next for the donation of tissue from the foetus.
- viii. Termination of pregnancy should not be sought with a view to donate foetal tissue in return for possible financial or therapeutic benefits.
- ix. The mother's decision to donate foetal tissue is sufficient for the use of the tissue unless the father objects in writing. In cases of incest or rape, the father's objection carries no significance.

- x. The mother will not dictate who shall receive the foetal tissue taken for transplantation.
- xi. Anonymity of donor and recipient will be maintained so that neither party is aware of the identity of the other.
- xii. The procedure of abortion, or its timing, will not be influenced by the requirements of the transplantation activity. These should solely be based on concern for the safety of the mother.
- xiii. Those participating in termination of pregnancy will not, in any way, be party to the subsequent usage of embryonic or foetal tissue for commercial purposes.
- xiv. The procurement of embryos, fetuses or their tissue for commercial purposes will not involve profit or remuneration.
- xv. **Intact embryos or fetuses will not be kept alive** artificially for the purpose of removing usable material.
- xvi. **Tissues from aborted fetus can be cultured and banked** for use in research on transplantation. If such stored tissue is to be subsequently used for any purpose other than the original objective, a fresh sanction will be obtained from the ICSCRT and ethical committees.
- xvii. **Cells obtained from fetuses will not be patented** for commercial considerations for their subsequent usage.
- xviii. Use of **umbilical cord blood from a live fetus or neonate** for transplantation: The fundamental principle in any operation on a live fetus or neonate will be to ensure that no harm will occur to the fetus or neonate. Since the exact timing of the clamping of the umbilical cord has a significant impact on the neonate and early clamping may cause an abrupt surge in arterial pressure resulting in cerebral intra-ventricular haemorrhage, particularly in premature neonates, normal clamping protocol will be followed when collecting foetal blood for transplantation. There is a risk that the neonate donor may need his or her own cord blood later in life. If the blood has been used for another, he or she might be without blood when it is needed. Parents will be fully informed of the risks of the donation and written consent obtained from them on behalf of the fetus.
- xix. **Use of tissue or organs from dead anencephalic fetus or neonate** (fetus or neonate lacking brain development above the level of the brainstem) is permitted. Physicians may provide anencephalic neonates with ventilator assistance and other medical therapies that are necessary to sustain organs till such time as the diagnosis of death is made on the basis of cessation of cardiac function.

Retrieval and transplantation of organs of anencephalic fetus are ethically permissible only after such diagnosis of death is made.
- xx. No transplantation of foetal tissue into man will be permitted unless the following criteria have been met:
  - there will be a detailed scientific basis for such transplantation;
  - animal experiments must show successful results - eradication of disease, elimination or amelioration of symptoms and signs or successful substitution of deficient chemicals and restoration of normal physiological function by the transplant. These must be documented in one or more indexed journals with good peer review mechanisms;
  - All records pertaining to animal experiments must be complete and submitted to specialist and general scientific scrutiny. These records must be preserved for a minimum period of 5 years after the completion of the study preferably on a permanent basis as far as possible;

- Success in animal experimentation must be shown on a long-term basis. The studies must include investigations on animals receiving the transplants at periodic intervals after the procedure specially with reference to unequivocal demonstration of absence of any transmission of disease through the transplant.
  - Trials in human patients will commence only on those patients where no other form of treatment is available and where, in the absence of the transplant, the patient is likely to suffer relentless deterioration in his health with fatal termination.
  - After obtaining consent, the mother must be screened for transmissible disease. If possible, the material to be transplanted must also be similarly screened.
  - Trials in human patients will be carried out only at the institutions having clinical and research facilities needed for such trials, including those that may be required to treat complications that may follow such research.
  - The research group and the institution(s) in which they work will undertake to conduct free of charge the research on their human participants and also treat completely any complication that may follow their study even if it appears several years after the conclusion of the study.
  - The research group will provide the human participants a printed document explaining in simple, non-technical language, the purpose of the study, details of the procedures the human participant is to undergo, complications that may follow these procedures, financial implications, interests of the researchers in the conduct of the study, and a commitment to treat completely and free of cost any complication that may ensue. The human participant must certify in writing that he has studied and understood the contents of this document and that s/he is willing to participate in the study.
  - Any adverse effects noted will be immediately discussed with members of the ethics committee and the project grounded if these cannot be explained or reasonably corrected in the course of the study.
- xxi. The local ethics committee must ensure report-back measures at every stage of research and confirm that a detailed report on the procedures, findings and conclusions is submitted to an indexed journal for publication even when the results are of a negative nature. The NAC-SCRT should be kept informed.
- xxii. As with therapeutic transplantation, constantly updated local (metropolitan), regional or national lists of available tissues and organs should be maintained to ensure that optimal use is made of all available donations. These lists should be made freely available to all authorised research workers.

ICMR Guidelines 2006

### 3.7 POLICY ON STEM CELL RESEARCH AND THERAPY

3.7.1 The following policies will be followed for stem cell research and therapy:

#### Permissible Research Areas

- i. *In vitro* studies on established cell lines from any type of stem cell viz. hES, hEG, hSS or fetal/adult stem cells may be carried out with notification to ICSCRT, provided the cell line is registered with the IC-SCRT/NAC-SCRT and GLP is followed.
- ii. *In vivo* studies with established cell lines from any type of stem cells viz., hES, hEG, hSS, including differentiated derivatives of these cells, *on animals other than primates* with prior approval of IC-SCRT, provided such animals are not allowed to breed. This includes pre-clinical evaluation of efficacy and safety of human stem cell lines.

- iii. *In vivo* studies on experimental animals (other than primates) using *fetal/adult somatic stem cells* from Bone marrow, peripheral blood, umbilical cord blood, skin, limbal cells, dental cells, bone cells, cartilage cells or any other organ (including placenta), with prior approval of the IC-SCRT and IEC provided appropriate consent is obtained from the donor as per guidelines provided in this document.
- iv. Establishment of new hES cell lines from spare, supernumerary embryos with prior approval of the IC-SCRT and IEC provided appropriate consent is obtained from the donor as per guidelines given below. Once the cell line is established it shall be registered with the IC-SCRT and NAC-SCRT.
- v. Establishment of fetal/adult hSS cell lines with prior approval of the IC-SCRT and IEC provided appropriate consent is obtained from the donor as per guidelines provided in this document.
- vi. Establishment of Umbilical Cord stem cell bank with prior approval of the ICSCRT and IEC provided guidelines given in this document for collection, processing, and storage etc of the umbilical cord blood are followed. Appropriate SOPs shall be approved by the IC-SCRT and IEC.
- vii. Clinical trial with clinical grade stem cells, following ICMR Guidelines for Biomedical Research and GCP guidelines of the GOI, may be carried out with prior approval of IC-SCRT, IEC and DCGI. Clinical grade stem cells are required to be produced under international GMP/GTP conditions. The cells should be well characterized about their stemness and safety as per guidelines given in Annexure II. The headings under which the clinical trial protocols should be written are given in Annexure III. All clinical trials on stem cells shall be registered with NAC-SCRT through IC-SCRT.

### Restricted Areas of Research

- i. Creation of a zygote by IVF, SCNT or any other method with the specific aim of deriving a *hES* cell line for any purpose.
  - Specific justification would be required to consider the request for approval by the NAC-SCRT through the IRB and IC-SCRT.
  - It would be required to establish that creation of zygote is critical and essential for the proposed research, and no other alternative will serve the purpose.
  - Informed consent procedure for donation of ova, sperm, somatic cell or other as detailed in these guidelines would need to be followed.
- ii. Clinical trials sponsored by multinationals, involving stem cell products imported from abroad. Such collaboration shall require prior approval of the NAC-SCRT through IC-SCRT, the IRB, DCGI and respective funding agency as per its procedure/Health Ministry's Screening Committee (HMSC)
- iii. Research involving introduction of hES / hEG /hSS cells into animals, at embryonic or fetal stage of development for studies on pattern of differentiation and integration of human cells into non- human animal tissues.
 

If there is a possibility that human cells could contribute in a major way to the development of brain or gonads of the recipient animal, the scientific justification for the experiments must be strong. The animals derived from these experiments shall not be allowed to breed.

Such proposals would need approval of the NAC-SCRT through Institutional Animal Ethics Committee (IAEC) and IC-SCRT.
- iv. Studies on chimeras where stem cells from two or more species are mixed and introduced into animals, including primates, at any stage of development viz., embryonic, fetal or postnatal, for studies on pattern of development and differentiation.
- v. Research in which the identity of the donors of blastocysts, gametes, or somatic cells from which the hES cells were derived is readily ascertainable or might become known to the investigator.



## **Prohibited Areas of Research**

- i. Any research related to germ line genetic engineering or reproductive cloning.
- ii. Any in vitro culture of intact human embryo, regardless of the method of its derivation, beyond 14 days or formation of primitive streak, whichever is earlier?
- iii. Transfer of human blastocysts generated by SCNT or parthenogenetic or androgenetic techniques into a human or non-human uterus.
- iv. Any research involving implantation of human embryo into uterus after in vitro manipulation, at any stage of development, in humans or primates.
- v. Animals in which any of human stem cells have been introduced at any stage of development should not be allowed to breed.
- vi. Research involving directed non-autologous donation of any stem cells to a particular individual is also prohibited.

## **Research Using Umbilical Cord Blood Stem Cells**

Cord blood stem cell banking is permissible. All Cord blood banks have to be registered with the Drug Controller General of India (DCGI) as per the guidelines of blood banks. Purpose of banking should be clearly explained to couples interested in storing cord blood. The ethical issues include concern about ownership and risk of transmission of potential genetic disorders, besides other general issues of confidentiality, justice and beneficence. When it comes to registries and banking, the commercial aspects pose additional problems. The advertising involved in getting and collecting samples, conflict of interest, utility of samples, accessibility and affordability should also be carefully looked into. The following points should be considered while collecting umbilical cord blood as specified in "Ethical Guidelines for Biomedical Research in Human Participants" 2000 of ICMR:

- i. No harm should occur to the fetus or the neonate.
- ii. Exact timing of the clamping of the umbilical cord should be defined in the clamping protocol.
- iii. Parents should be informed regarding risks and benefits involved.
- iv. Free informed consent from parents' should be obtained. If there is disagreement between the parents, the mother's wish shall prevail.
- v. ID card should be issued for voluntary donation to enable access/benefit in future in case required for self/relative.
- vi. Standard Operative Procedures for collection, transportation, processing, storage, preservation and clinical use should be laid down with approval of the IC-SCRT and IEC.
- vii. Detailed protocol for isolation and characterization of mesenchymal and/or stem cells should be approved by IC-SCRT and IEC.
- viii. Period of preservation for self- use later in life should be prescribed.
- ix. Detailed protocol for clinical use of stem cells should be in place.
- x. Follow up plans for assessing safety and efficacy of cord blood stem cell therapy should be incorporated.

## **Research Using Fetal Stem Cells/Placenta**

All proposals involving foetuses or foetal tissue, for research or therapy are permissible. However,

- i. Termination of pregnancy should not be sought with a view to donate fetal tissue in return for possible financial or therapeutic benefits.
- ii. Consent to have a termination of pregnancy and the donation of fetal material for purpose of research or therapy should be taken separately.
- iii. The medical person responsible for the care of the pregnant woman planning to undergo termination of pregnancy and the person who will be using the fetal material should not be the same. The woman shall not have the option to specify the use for a particular person or in a particular way.
- iv. The identity of the donor and the recipient should be kept confidential.

### **Approval for Derivation of a New *hESC* Cell Line**

Whether new *hESC* cell lines are derived from spare embryos or embryos created for the purpose, such research shall consider the following:

- i. that the goal of research cannot be achieved in any other way even by research on adult stem cells;
- ii. there is no existing stem cell line that would be suitable for the purpose;
- iii. will increase knowledge about embryo development and causes of miscarriages and birth defects;
- iv. increasing the number of ethnically diverse *hESC* cell lines; 5. advance knowledge, which can be used for infertility treatment or improving contraception techniques;
- v. increase knowledge about serious diseases and use this knowledge to develop treatments including tissue therapies;
- vi. develop methods of therapy for diseased or damaged tissue or organs;
- vii. justification for the minimum number of embryos/ blastocysts required must be clearly defined;
- viii. research teams involved should have appropriate expertise and training in derivation and culture of human/non-human ES cells.

This, however, is not an exhaustive list.

### **Responsibility of Investigators and Institutions**

- i. The investigators and the institutions where the stem cell research is being conducted bear the ultimate responsibility of ensuring that research activities are in accordance with laid down standards and integrity. In particular, scientists whose research involves hES cells should work closely with monitoring/regulatory bodies, demonstrate respect for autonomy and privacy of those who donate gametes, blastocysts, embryos or somatic cells for SCNT, and be sensitive to public concerns about research that involves human embryos.
- ii. Each institution should maintain a registry of its investigators who are conducting hES cell research and ensure that all registered users are kept up to date with changes in guidelines and regulations regarding use of hES cells.
- iii. Each institution shall constitute an IC-SCRT as provided in these guidelines and provide adequate support for its functioning

### **International Collaboration**

- iv. National guidelines of respective countries should be followed.
- v. Collaboration will be permitted as per existing procedures of funding agencies (DBT, ICMR etc) or the HMSC, even if no funding is involved after the joint proposal with appropriate MOU is approved by NACSCRT.

- vi. Export of cell lines will be covered under GOI guidelines for Transfer of Biological materials.
- vii. If there is a conflict between scientific and ethical perspectives of the International collaborator and the domestic side then Indian Ethical guidelines or law will prevail.

### **Commercialization and Patent Issues**

- viii. Research on stem cells/lines and their applications may have considerable commercial value. Appropriate IPR protection may be considered on merits of each case. If the IPR is commercially exploited, a proportion of benefits shall be ploughed in to the community, which has directly or indirectly contributed to the IPR. Community includes all potential beneficiaries such as patient group, research group etc.
- ix. Detailed guidelines have been provided in a separate booklet on 'Stem Cell research and Therapy' as national guidelines.

*ICMR guidelines 2006*

### **Regulatory processes in connection with stem cell related research, laid down by the ICMR**

Regarding Stem Cell Trials:

Autologous stem cell trials may be registered provided minor manipulations (sub-fractionation and amplification only) have been undertaken. Permission may be taken from the Ethics Committee/ Committee specially constituted for clearing trials on stem cells. For other stem cell trials involving major manipulations such as use of Human embryonic stem cells, alteration of gene expression, mesenchymal cells etc., approval from Ethics Committee/Stem Cell Committee, National Apex Committee for Stem Cell Research (NACSCR) as well as DCGI is mandatory, as per ICMR- DBT Stem Cell Guidelines, 2012. These trials may be registered after due advice of the Advisor CTRI.

## **3.8 POLICY REGARDING RESEARCH MISCONDUCT**

### **3.8.1 The Office of Research Integrity**

The Office of Research Integrity was set up in the Office of Research by a Senatus resolution (Senatus Minute no 2478(c) dated 9th April 2007, AC. Minute 110-a:10-07 dated 25.10.2007). The Additional Vice-Principal (Research) will be responsible for its functioning and is designated as the Research Integrity Officer (ROI). The ROI will report to the Principal and to the Director (and the Medical Superintendent when deemed necessary) of CMC Vellore. A committee of three Senatus members nominated by the Principal, will assist the Addl. Vice-Principal (Research). Currently, the members for 2010 to 2012 are Dr. Dolly Daniel (Clinical Pathology), Dr. George John (Medical ICU) and Dr. Sujith Chandy (Pharmacy).

### **3.8.2 Scope:**

This statement of policy and procedures is intended to describe and help carry out this institution's responsibilities in all matters pertaining to the integrity of Research conducted in CMC, irrespective of the source of funding. These policies also satisfy guidance and procedures for all research conducted in CMC that is funded by the US Public Health Service under the US Public Health Service (PHS) Policies on Research Misconduct, 42 CFR Part 93.

The scope of these policies applies only to allegations of research misconduct that occurred within ten years of the date the institution received the allegation.

### **3.8.3 Definitions:**

The role of the Office of Research Integrity is to ensure the integrity of all research conducted in CMC. It is primarily concerned about Research Misconduct.

**Research misconduct** means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

- i. **Fabrication** is the willful making up data or results and recording or reporting them.
- ii. **Falsification** is the willful manipulation of research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research report.
- iii. **Plagiarism** is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.
- iv. Research misconduct does not include honest error or differences of opinion.
- v. Disputes about authorship do not normally come under the scope of research misconduct. In some instances, failure to include a researcher, who contributed significantly to the research, as an author or to acknowledge his/her contribution could amount to plagiarism.
- vi. Matters pertaining primarily to the scientific validity and ethical conduct of research will ordinarily fall under the purview of the Institutional Review Board (IRB), unless they pertain to research misconduct. The ORI will work in conjunction with the IRB in such instances.
- vii. Allegations of research misconduct will be entertained against a person who, at the time of the alleged research misconduct, was employed by, was an agent of, or was affiliated by contract or agreement with this institution.

### 3.8.4 Standard Operating Procedures

The Standard Operating Procedures Document of the Office of Research Integrity contains all policies and procedures pertaining to investigations of allegations of research misconduct are available in the Office of Research.

## 3.9 POLICY REGARDING CONFLICT OF INTEREST

Christian Medical College, Vellore is committed to ensuring its faculty an open and productive environment in which to conduct teaching, patient care, and research. The College's concern with conflict of interest reflects the ever-increasing complexity of our society, our various relations with each other and with outside institutions, along with the heightened national and governmental sensitivity to such matters. Conflicts of interest, in the most conventional sense, arise because faculty members may have the opportunity to influence the institution's business decisions in ways productive of personal gain. Additionally, faculty members' outside relationships may compromise the integrity of decisions they make as teachers, researchers and providers of patient care.

- i. In contrast, a faculty member's more general commitment to the institution requires that the member perform the duties conventionally or specifically associated with the member's position. The nature of these duties, like their compatibility with outside activities, varies. Subject to this general standard of commitment, faculty members appropriately use their own judgment in deciding whether to engage in a variety of extramural activities.
- ii. Questions concerning the definition and resolution of conflicts of interest are frequently matters of degree and judgment. Christian Medical College, Vellore recognizes that members of its faculty are professionals; it expects them to be alert to the possible effect of outside activities on the integrity of their decisions and on their ability to fulfill their obligations to the institution. Likewise, the institution recognizes the value of professional interaction between its faculty and outside entities. It supports and promotes university-industry relationships and, subject to this policy, it maintains an environment in which such relationships may flourish.
- iii. In response to these concerns, Christian Medical College, Vellore has adopted three statements of policy:

- It is the policy of Christian Medical College, Vellore that its faculty have an obligation to avoid unacceptable ethical, legal, financial or other conflicts of interest and to ensure that their activities and interests do not conflict with their obligations to the institution or its welfare.
  - It is the policy of Christian Medical College, Vellore that any faculty member engaging in an outside activity or possessing a personal interest that could lead to a serious conflict of interest must immediately disclose that possibility by informing the Principal and Director in writing. If the Principal, having been provided with all pertinent information, determines that the faculty member's situation presents a serious conflict of interest, that conflict must be resolved. Consultation should be sought when a faculty member is in doubt about whether an interest or activity creates a conflict of interest. Subsequent disputes can be ameliorated more readily if a written record is kept of these consultations. If the faculty member and the Principal disagree, either about the presence of a conflict or about its appropriate resolution, the faculty member may pursue the matter with the Director.
  - It is the policy of Christian Medical College, Vellore that relationships between faculty members and outside institutions must not impede the open communication of research results. This includes sharing, in accordance with applicable legal and ethical principles, of data, samples, physical collections and other supporting materials, unless their dissemination is governed by written proprietary agreements between the institution and a second party. If intellectual property is subject to institutional guidelines (such as those governing technology transfer), a faculty member may not transfer or commit to transfer that property outside the institution without going through approved procedures.
- iv. The requirement of consultation is generally applicable to situations that could lead to serious conflicts of interest. The requirement's relevance to certain specific situations is detailed below.
- Some activities and interests are unlikely to lead to serious conflicts of interest and thus require no consultation. An example is a faculty member's entitlement to examiner fees, consultation fees or honoraria for publications or lectures. These are to be returned to the institution as per institutional rules.
  - Consultation is mandatory if the faculty member has a relationship that might bias a decision the member makes or influences concerning the institution's dealings with an outside organization, leading to personal gain to the member. An example is a faculty member's direct or indirect ownership or control of a financial interest in a business with which CMC has dealings, when the faculty member is in a position to influence the relevant decisions by CMC. The first step to resolve such a conflict is full disclosure by the faculty member to the persons making the relevant decision for CMC; the second is arrangements that clearly exclude the member from participating in the relevant decision.
  - Consultation is mandatory if the faculty member has a financial interest in a business, or has a right to receive, control or benefit from a business, under circumstances that significantly link the fortunes of the business to the member's research. In such situations, it is advisable to couple the formal presentation of research results with disclosure of the interest.

### **3.10 POLICY FOR RETROSPECTIVE STUDIES**

Research studies involving the review, collection and analysis of medical /laboratory record information are descriptive studies. There are several different approaches to the conduct of retrospective medical record research studies that can be approved by the IRB. The general principles to be considered are listed below.



- Data is generated by multiple units and departments in the hospital. No one unit or department has primacy in access to data. This data may consist of medical records, stored images, laboratory online reports or registers.
  - Data cannot be used without informing or obtaining permission from the units or departments that generated the data. Whether the generating department needs to be informed or permission obtained depends on the focus of data usage.
  - There are two ways that hospital data can be used for retrospective studies:
    - 1a. The clinical service unit could use the data; or
    - 1b. The diagnostic service unit could use the data.
  - The retrospective study might be
    - 2a. Mainly focused on the clinical data with minimal use of the diagnostic/lab data;
    - 2b. Mainly focused on the diagnostic/lab data with minimal use of the clinical data; and
    - 2c. Equally focused on both the clinical and diagnostic/lab data.
  - Suggested protocols:
    - I. For 1 a and 2 a: No permission required from anyone. Inform the diagnostic service unit so that they can learn from the study.
    - II. For 1 a and 2 c: Clinical service unit should discuss the study with the diagnostic service unit and request their input. Authorship should ideally include both the groups. .
    - III. For 1 b and 2 b: No permission required from anyone. Inform the clinical service unit so that they can learn from the study.
    - IV. For 1 b and 2 c: The diagnostic service unit should discuss the study with the clinical service unit and ideally both groups should be given authorship.
  - A combination of 1 a and 2 b and 1 b and 2 a is not encouraged and would require specific permission from the IRB. The protocols I to IV need not be discussed by the IRB, unless they are submitted for the purpose of obtaining funding or for research permission for a dissertation.
  - Authorship cannot be given just for providing the data, the author must fulfill the requirements of authorship.
  - Most authorship issues involving retrospective studies should be settled before initiating the study through a process of discussion.
- Not all possible situations are covered in these guidelines. Any disputes will be considered by a committee constituted by the Office of Research. Recommendations of the committee will be implemented by the administration.

### **3.11 POLICY REGARDING BIOSAFETY**

CMC complies with norms instituted by the Department of Biotechnology (DBT), Government of India for researchers working with genetically modified organisms and has constituted an Institutional Biosafety Committee. This committee comprises the Principal, the Addl. Vice-Principal (Research), two scientists engaged in DNA work, a medical expert and a nominee of the Department of Biotechnology. The Institutional Biosafety Committee (IBSC) has an on-site emergency plan according to the manuals/guidelines of the DBT; meets twice annually to review new applications, monitor ongoing studies and prepare reports for submission to DBT. The reports are submitted after approval to the DBT via the DBT website. The IBSC member nominated by DBT is currently Dr. Rajakumar, Adyar Cancer Centre.

## **Section 4**

### **PROCEDURES AND FORMS TO BE USED FOR SUBMISSIONS TO THE**

## IRB (RESEARCH AND ETHICS COMMITTEE)

This section begins with an overview of the process of submitting applications to the IRB and contain forms to be used for submission to the IRBs for Research Grants (for external funding and Fluid Research funding), Ethics approval, Progress reports, Final Reports and for reporting Adverse events.

This section also contains forms that will be used by the IRBs for evaluating proposals.

If you have any doubts regarding the appropriate form to be used or procedures to be followed, please contact [research@cmcvellore.ac.in](mailto:research@cmcvellore.ac.in)

### 4.1 Flowchart for initiating a research study in CMC

(Allow about 3-4 months from first application to recruitment of personnel)

#### Step 1

Read the Policies and Procedures document of the IRB

Read the Declaration of Helsinki, The ICMR Bioethics Guidelines (2006), Schedule Y of the Drugs and Cosmetics Act, The Indian GCP Guidelines

Download the Declaration of Helsinki

Download the ICMR Bioethics Guidelines

Download Schedule Y

Download the Indian GCP Guidelines

Use appropriate format for proposal from IRB applications site on the intranet.  
(This applies to internally and externally funded research)

Download application form for Interventional Trials

Download application form for tests of Diagnostic accuracy

Download application form for Observational Studies

Download application form for any other study design



View Appendices

One soft copy on CD with all supporting documents and checklist and one hard copy signed by all investigators and checklist and all supporting documents with a covering letter (through HOD/HOU) to be sent to the Office of Research (Additional Vice Principal Research).

**Should reach before 1<sup>st</sup> of the month.**



## Step 2

Be present for the IRB meeting at the required time to answer clarifications.  
It is preferable that the guide be also present for PG dissertations



## Step 3

The IRB will provide clearance for studies involving humans  
If any amendments are suggested please send the revised proposal to the IRB at the earliest or re-submit for the next meeting.

If the study involves animals, only research committee approval will be provided and separate clearance is required from the Animal Experimentation Committee



## Step 4

After final approval from the IRB, a letter is needed to the Treasurer to start an account and to activate fluid research funding. For personnel and capital items, AC approval is needed. Write to respective Administrative heads (Principal / MS / GS) depending on category of staff to be employed.

Download application form for Administrative Committee approval (to be obtained from GS Office)

[Click here to see a formal letter to the Treasurer to activate fluid research funding](#)



## Step 5

After AC approval, advertise and recruit through respective Administrator.

Get two or more quotes for capital items and raise a purchase request.

[Click here to see a formal letter to advertise in the CMC Weekly News.](#)

Download application form for Project & Short term appointments (to be obtained from GS Office)



## Step 6

Progress report and final report to be submitted to the committee

(This applies to all proposals)

Download application form for submitting progress report

Download application form for submitting Final Report for Interventional Study

Download application form for submitting Final Report for tests of Diagnostic accuracy

Download Application form for Final Report of Observational studies

Download Application form for Final Report for any other study design

## FORMATS

- 4.2 [Format for Application for IRB clearance for Interventional Studies.doc](#)
- 4.3 [Format for Application to IRB for studies of Test of Diagnostic Accuracy](#)
- 4.4 [Format for Application to IRB for Observational Studies](#)
- 4.5 [Format for Application to IRB for other study designs](#)
- 4.6 [Format for submitting Protocol Amendments](#)
- 4.7 [Format for Reporting Adverse Events](#)
- 4.8 [Format for submitting Progress /Interim Reports to IRB for Studies Approved by IRB](#)
- 4.9 [Format for submitting Final Reports for Interventional Trials approved by the IRB](#)
- 4.10 [Format for submission to IRB of Final Reports of Diagnostic Test Accuracy](#)
- 4.11 [Format for Submission of Final Reports to IRB of Observational \(Case Control, Cohort, Observational\) Studies](#)
  
- 4.12 [Format Submission of Final Report for Other Study Designs](#)
- 4.13 [Indian Council of Medical Research Materials Transfer Agreement](#)
- 4.14 [IRB Reviewer Checklist](#)
- 4.15 [Draft format for Informed Consent](#)
- 4.16 [Draft format for Tissue Banking](#)

## APPENDICES

<a href="#"><u>Appendix I</u></a>	Clinical Trial Registry-India Dataset and Description
<a href="#"><u>Appendix II</u></a>	Instructions for registering trials in the Clinical Trials Registry- India
<a href="#"><u>Appendix III</u></a>	CONSORT Statement ( <a href="http://www.consort-statement.org/">http://www.consort-statement.org/</a> ) for interventional trials and its extensions.
<a href="#"><u>Appendix IV</u></a>	QUADAS (a tool for assessing the quality of tests of diagnostic accuracy)
<a href="#"><u>Appendix V</u></a>	STARD Statement (Standards of Reporting of Diagnostic Accuracy)
<a href="#"><u>Appendix VI</u></a>	STROBE Statement ( <a href="http://www.strobe-statement.org/">http://www.strobe-statement.org/</a> ) Strengthening the Reporting of Observational Studies in Epidemiology
<a href="#"><u>Appendix VII</u></a>	Checklist for Informed Consent
<a href="#"><u>Appendix VIII</u></a>	Guidelines for use of animals
<a href="#"><u>Appendix IX</u></a>	IRB Processing Fee Letter from Principal, CMC Vellore