HUMAN RESEARCH ETHICS COMMITTEE

OF

H.M.PATEL CENTRE FOR MEDICAL CARE & EDUCATION

Standard Operating Procedures (SOP) Revised July, 2011

For Human Research Ethics Committee

1. Objective:-

The objective of this SOP is to contribute to the effective functioning of the Human Research Ethics Committee of H.M.PATEL CENTRE FOR MEDICAL CARE & EDUCATION, Karamsad {HMPCMCE, henceforth referred as "Centre"}so that **a quality and consistent ethical review mechanism** for health and biomedical research is put in place for all proposals dealt by the Committee as prescribed by the Ethical guidelines for biomedical research on human subjects of ICMR (2008).

2. Role of HREC:-

HREC will review and approve all types of research proposals involving human participants with a view to safeguard the dignity, rights, safety and well being of all actual and potential research participants. The goals of research, however important, should never be permitted to override the health and well being of the research subjects. The HREC will take care that all the cardinal principles of research ethics viz. Autonomy, Beneficence, Non - malaficence and Justice are taken care of in planning, conducting and reporting of the proposed research.

For this purpose, it will look into the aspects of

i) Informed consent process,

ii) risk benefit ratio,

iii) distribution of burden

iv) benefit and provisions for appropriate compensations wherever required.

It will (a) review the proposals before start of the study (b) examine compliance with all regulatory requirements, applicable guidelines and laws (c) monitor the research throughout the study until and after completion of the study through appropriate well documented procedures for example annual reports, final reports and site visits etc.

The mandate of the HREC will be to review

i) All research projects involving human participants including postgraduate dissertations / theses; undergraduate and staff members' research proposal to be conducted on site at the Institutions of HMPCMCE,

ii)Research projects undertaken by researchers of HMPCMCE either as principal or co-investigator at sites other than HMPCMCE

iii) Research proposals guided by staff members of HMPCMCE but conducted onsite or outside the

centre.

3. COMPOSITION OF HREC OF H.M.PATEL CENTRE FOR MEDICAL CARE & EDUCATION:-

HREC should be multidisciplinary and multisectorial in composition. Independence and competence are the two hallmarks of HREC of HMPCMCE.

The number of persons in the ethical committee should be kept fairly small (7-9, maximum 12-15 members). A minimum of five persons is required to compose a quorum.

As per ICMR Guidelines, the Chairperson of the Committee will be from outside the institutions to maintain the independence of the Committee. The Member Secretary should conduct the business of the Committee. Other members should be a mix of medical / non-medical scientific and non-scientific persons including lay public to reflect the differed viewpoints.

The composition may be as follows :-

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

The ethical committee at HMPCMCE can have as its members, individuals from other institutions or communities if required. There should be adequate representation of age, gender, community, etc. in the Committee to safeguard the interests and welfare of all sections of the community / society. Members should be aware of local, social and cultural norms, as this is the most important social control mechanism. If required, subject experts could be invited to offer their views, for example for drug trials a pharmacologist, preferably a clinical pharmacologist should be included. Similarly, based on the requirement of research area, for example HIV, genetic disorders etc. specific patient groups may also be represented in the Committee. The membership of HREC will include Epidemiologist(s), Sociologist(s), Lawyer(s), Theologian, Statistician(s), Clinician(s), Basic scientists, Pharmacist(s)/Clinical Pharmacologist(s) etc.

HREC, HMPCMCE should be constituted in the following pattern:

i) A Chairperson
ii) A Deputy Chairman if need be,
iii) A Member Secretary,
iv) 5-15 members from different Departments / Specialties / disciplines or areas etc. (vide Annexure)

4. Authority under which HREC is Constituted:-

The Chief Executive Officer (CEO) of Charutar Arogya Mandal who also heads the H.M. Patel Center for Medical Care & Education and its institutions constitutes the HREC.

Reconstitution of HREC & appointment of members

Purpose: To describe the procedure for the appointment of members to the HREC

i.) The Head of the institution will appoint the members in consultation with the HREC.

ii.) Members are appointed based on their competencies and integrity, and could be drawn from any public or private Institute from anywhere in the country. The members will provide a copy of their Curriculum Vitae to the committee.

iii.) The letter of appointment shall include the date of appointment, length of tenure, assurance that indemnity will be provided in respect of liabilities that may arise in the course of bona fide conduct of their duties as a HREC member.

iv.) Members will be required to sign a confidentiality undertaking upon appointment, stating that all matters of which he/she becomes aware during the course of his/her work on the HREC will be kept confidential; that any conflicts of interest, which exist or may arise during his/her tenure on the HREC will be declared.

v.) Upon appointment, members shall be provided with the following documentation:

- HREC Standard Operating Procedures **(SOP);**
- Up to date list of members' names and contact information
- Any previous reports on the HREC's activities; and
- Any other relevant information

vi.)

a.) The duration of appointment is initially for a period of 3 years

b.) At the end of 3 years, as the case may be, the committee may be reconstituted, and one third of the members may be replaced by a committee constituted by the Head of the institution, the Chairperson, HREC and the Member Secretary, HREC of PSMC.

c.) A member can be replaced in the event of death or discontinued someone who has not attended consecutive 3 meetings or for any action not commensurate with the responsibilities laid down in the guidelines deemed unfit for a member.

d.) A member can tender resignation from the committee with proper reasons to do so.

e.) All members should maintain **absolute confidentiality** of all discussions during the meeting and sign a confidentiality form.

f.) Conflict of interest should be declared by members of the HREC

vii.) New members are expected to attend training sessions as soon as practicable after their appointment. The costs associated with attendance at training and education sessions will be met by center.

viii.) Members may seek a leave of absence from the HREC for extended periods. Steps shall be taken to fill the vacancy.

ix.) Membership will lapse if a member fails to attend three consecutive meetings of the HREC without prior written intimation, unless exceptional circumstances exist. The Chairman will notify the member of such lapse of membership in writing. Steps shall be taken to fill the vacancy, which may arise.

x.) Membership will lapse if a member fails to attend in full at least two thirds of all scheduled HREC

meetings in each year, barring exceptional circumstances.

xi.) A member may resign from the HREC at any time upon giving one months' notice in writing to the Chairman. Steps shall be taken to fill the vacancy of the former member as soon as possible.

Orientation of new members:

Orientation will involve introduction to other HREC members prior to the HREC meeting and informal meeting with Chairman who will explain his/her responsibilities as an HREC member, the HREC processes and procedure.

5. Submission Procedure for New Applications:-

1. All applications for ethical review must be submitted to the member secretary of the HREC, on or before the announced closing date. The closing date for receipt of new applications onto the next HREC agenda shall be readily available to prospective applicants.

2. The closing dates for applications should normally be no earlier than 15 days after the announcement for submission and no later than 14 days prior to each HREC meeting.

3. Applications must be submitted in the appropriate format (Annexure I)as determined by the HREC, and shall include all documentation as required by the HREC as per check list (Annexure II).

4. The procedures for application to the HREC and the application format shall be readily available to applicants.

5. Fee will not be charged for applications submitted by the investigators of the institution for review EXCEPT for Clinical trials wherein fees of Rs 30,000/-will be charged for the review of the new application including initial one amendment followed by Rs. 5000 for each subsequent amendments.

6. Research projects submitted by external investigators but to be conducted within the centre will be charged Rs. 500/- and Rs. 1000/- for non funded projects of students and faculty respectively, where as Rs. 5000/- for funded projects.

7. Conduct of Meetings:-

i.) The HREC shall meet on a regular basis, which will normally be at two monthly intervals. Meeting dates and agenda closing dates shall be publicly available.

ii.) Members will attend HREC meetings in person.

iii.) The Chairman shall cancel a scheduled meeting if a quorum cannot be achieved Should this occur, the HREC will convene within 7 working days of the cancelled meeting to ensure all agenda items are considered.

iv.)Meetings will be scheduled for an allocated time. If the issues have not been completed within the allocated time, then the HREC may either continue the meeting until all agenda items have been considered or schedule an additional meeting. If an additional meeting is called for, then the meeting should be held within 7 working days.

v.) The HREC meeting will be conducted in such a way to ensure confidentiality and open discussion between members and the researcher. Members will be informed of the meeting room details in the meeting agenda.

vi.) Members who are unable to attend a meeting can contribute prior to the meeting through written

submissions to the member secretary. The minutes will record the submission of written comments.

vii.) A quorum must be present in order for the HREC to reach a final decision on any agenda item. A quorum shall exist when at least 5 members are physically present. For clinical trials as per schedule Y of Drugs and Cosmetics Act, 1940 amended in 2005, one member of each of the following categories:

- Basic Medical scientist (preferably pharmacologist)
- Clinician
- Legal expert
- Social scientist/ethics expert
- Lay person

viii.) Any member of the HREC who has any interest, financial or otherwise, in a project or other related matter(s) considered by the HREC. Should declare such interest. This will be dealt with in accordance with SOP 5.

8. Element of review:-

a.) Scientific design and conduct of the study.

b.) Approval of CAM research Society for proposals which have sought funding from same society.

c.) Examination of predictable risks/harms.

d.) Examination of potential benefits.

e.) Procedure for selection of subjects in methodology including inclusion/ exclusion, withdrawal criteria and other issues like advertisement details.

f.) Management of research related injuries, adverse events.

g.) Compensation provisions.

h.) Justification for placebo in control arm, if any.

i.) Availability of products after the study, if applicable.

j.) Patient information sheet and informed consent form in local language.

k.) Protection of privacy and confidentiality.

l.) Involvement of the community, wherever necessary.

m.) Plans for data analysis and reporting

n.) Adherence to all regulatory requirements and applicable guidelines

o.) Competence of investigators, research and supporting staff

p.) Facilities and infrastructure of study sites

q.) Criteria for withdrawal of patients, suspending or terminating the study

9. Conflicts of Interest:-

1. An HREC member shall, as soon as practicable during the HREC meeting, inform the Chairman if he/she has a conflict of interest, financial or otherwise, in a project or other related matter(s) considered by the HREC.

2. The HREC will determine if this results in a conflict of interest for the member and if so, the member will

withdraw from the meeting until the HREC's consideration of the relevant matter has been completed. The member shall not be permitted to adjudicate on the research.

3. All declarations of conflict of interest and the absence of the member concerned will be minuted.

10. Preparation of Minutes:-

1. The HREC member secretary will prepare and maintain minutes of all meetings of the HREC.
2. The format of the minutes will include at least the following items:
   i.) confirmation of quorum
   ii.) attendance reading of minutes of previous meeting
   iii.) conflicts of interest;
   iv.) review of new applications;
   v.) amendments to approved protocols;
   vi.) monitoring reports;
   vii.) any other issue--- expedited reviews , subcommittee minutes etc
3. The minutes should include the recording of decisions taken by the HREC as well as a summary of relevant discussion. This includes reference to views expressed by absent members.
4. In relation to the review of new applications or amendments, the minutes shall record a summary of the main ethical issues considered, including any requests for additional information, clarification or modification of the project.
5. In recording a decision made by the HREC, any significant minority view (i.e 2 or more members) will be noted in the minutes.
6. To encourage free and open discussion and to emphasis the collegiate character of the HREC, particular views should not be attributed to particular individuals in the minutes, except in circumstances where a member seeks to have his/her opinions or objections recorded.
7. Declarations of conflicts of interest by any member of the HREC and the absence of the member concerned during the HREC consideration of the relevant application will be minuted (refer to SOP 5 regarding a members declaration of a conflict of interest).
8. The minutes will be produced as soon as practicable following the relevant meeting and should be checked by either the Chairman and/or the Deputy Chairman, for accuracy.
9. The minutes will be circulated to all members of the HREC before the next meeting. All members will be given the opportunity to seek amendments to the minutes prior to their ratification. The minutes will be formally ratified at the next HREC meeting.
10. The original copy of each meeting's minutes will be retained in a confidential 'Minutes' file.

11. Communication of Decisions of the HREC:-

Purpose: To describe the procedure for the notification of decisions of the HREC concerning the review of new applications

1. The HREC will report in writing to the principal investigator (PI), advising whether the application has

received ethical approval (including any conditions of approval), after the minutes are signed by the chairman.

2. If the HREC determines that further information, clarification or modification is required for the consideration of a project, the correspondence to the PI should clearly articulate the reasons for this determination, and clearly set out the information that is required.

3. If the requested information is not received from the applicant within 3 months, the project may be dismissed and the applicant will be required to resubmit the project at a later date.

5. The HREC will notify the applicant of the ethical approval of a project only when all outstanding requests for further information, clarification or modification have been satisfactorily resolved. Notification of ethical approval will be in writing in a standard format, and will contain the following information:

- Title of project;
- Name of the PI
- HREC project code number;
- Date of HREC meeting at which the project was first considered;
- Date of HREC approval and
- Conditions of HREC approval, if any.

6.If the HREC determines that a project is ethically unacceptable, the notification of the HREC's decision will include the grounds for rejecting the project

7.The status of the project shall be updated on the HREC's register of received and reviewed applications.

12.Exempt review and Expedited Review:-

Purpose: To describe projects that are exempt from review and the procedure for the expedited review of research by the HREC

13. Submission of Amendments:-

Purpose: To describe the procedure for the submission and HREC review of requests for amendments.

1. Proposed changes to approved projects are required to be reported by the PI to the HREC for review.

2. Requests shall outline the nature of the proposed changes, reasons for the request, and an assessment of any ethical implications arising from the request on the conduct of the research. All amended documents must have the changes highlighted and contain revised version numbers and dates.

3. Expedited review of requests for minor amendments, and urgent amendments to approved protocols for safety reasons may be undertaken by the HREC member secretary between scheduled meetings at the discretion of the Chairman which will be ratified at the next HREC meeting.

4. All other requests for amendments shall be reviewed by the HREC at its next available meeting, provided the request has been received by the member secretary by the agenda closing date.

5. The HREC will report in writing to the PI, advising whether the proposed amendment and/or request for extension has been given ethical approval, within 15 working days of the meeting at which the request was considered (this may be the full HREC meeting or the expedited meeting).

6. Notification of the approval of amendments and extensions will be in writing in a standard format.

7. If the HREC determines that further information, clarification or modification is required for the

consideration of the request for amendment or extension, the correspondence to the investigator should clearly articulate the reasons for this determination, and clearly set out the information that is required.

8. All received and approved requests for amendments and extensions shall be recorded, and the status of the project shall be updated on the HREC's register of received and reviewed applications.

14. Concerns and Complaints about the Conduct of a Project:-

Reporting

1. The HREC will require, as a condition of approval of each project, that the researchers immediately report to the HREC any concerns or complaints received.

2. The member secretary of HREC is the person nominated to receive concerns and complaints from participants in research or members of the public about the conduct of projects approved by the HREC.

3. The member secretary of HREC is responsible for obtaining, in writing, the grounds of the concern or complaint. The member secretary of the HREC will notify the Chairman of the HREC of the report as soon as possible.

4. The member secretary of the HREC will send an acknowledgment to the complainant outlining the mechanism for investigating the concern or complaint.

Investigation

5. The Chairman of the HREC will examine the concern or complaint and determine whether the concern or complaint warrants a further investigation. Where there is to be no further investigation the Chairman of the HREC will inform the complainant.

6. Where the Chairman determines that the concern or complaint warrants a further investigation the Chairman will notify the head of the institution who will then convene a Review Committee to investigate and determine the consequences.

7. The membership of the committee will also include the Chairman of the HREC or delegate, and other members with appropriate expertise as required.

8. The member secretary of the HREC will send a letter of notification to the PI of any concern orcomplaint about a project received by the HREC outlining the mechanism for investigating the concern or complaint. Where the complaint concerns the conduct of the any other person the review Committee will also notify that person.

9. The Review Committee will immediately instigate an investigation into the concern or complaint. The investigation will take no longer than 2 weeks from the time of notification for the concern or complaint, unless exceptional circumstances exist.

10.The Committee will give the complainant and the PI an opportunity to make submissions. Where the complaint concerns the conduct of any other person the Incident Review Committee will also provide that person with an opportunity to make submissions.

11. The Review Committee may seek any other information it requires and may access any documents relating to the project, interview other people, and seek internal and external expert advice, as it sees fit.

Consequences

12. If the Review Committee is satisfied that the concern or complaint is justified it will determine the

consequences by considering the following matters:

- The severity of the matter;
- The sensitivity of any information concerned including the amount and type of information and the level of identifiability; and
- Whether any breach of the approved protocol, which may be established, was inadvertent, negligent or intentional.

13 The possible consequences include the following:

- Notation on the file of the occurrence of the matter;
- Increased monitoring of the project;
- Counselling on security practices;
- Amendments to the approved protocol;
- Suspension or cancellation of DOHWA approval of the project (with the immediate return or destruction of all data file);
- Reporting the individuals responsible for any breach to the head of the instiute, with a complaint of misconduct in the conduct of the project;

14 The Chairman of the Review Committee will notify the institution, the PI and any other person for whom there is an individual consequence of the outcome of the investigation and the consequences in writing.

15 The Chairman of the Review Committee will notify the HREC and any other institutional HRECs concerned with the project of the outcome of the investigation and the consequences.

16. The HREC may review the ethical approval of any project in the light of the outcome of the investigation of any breach or complaint and will notify the responsible institution and the PI if ethical approval for the project is withdrawn.

17. The Chair of the Incident Review Committee will send a written report of the outcome of the investigation and the consequences to the complainant.

15. Reporting and Handling of Adverse Events:-

Purpose: To describe the process for reporting and handling of adverse events in clinical trials

Introduction

An adverse event refers to undesirable clinical responses to an intervention including a treatment or diagnostic procedure.

Reporting of Adverse Events

1. Principal Investigators should immediately report all adverse events in clinical trials to the HREC the research in accordance with the reporting conditions required by Schedule Y

2. Principal Investigators should report all adverse events and the response to those events in the periodic and final reports for the project.

16. Record Keeping:-

1. The member secretary will prepare and maintain written records of the HREC's activities, including agenda and minutes of all meetings of the HREC.

2. The member secretary will prepare and maintain a confidential electronic and/or paper record for each application received and reviewed and shall record the following information:

- code number;
- names of PI;
- title of the project;
- ethical approval or recommendations for modifications or rejections with date, ;
- approval or otherwise of any changes to the project proposed by the researcher;
- the terms and conditions if any, with approval of the project;
- whether approval was by scheduled full committee review or expedited review or review by subcommittee;
- action taken by the HREC while monitoring the conduct of the research.

The physical records shall contain a hard copy of the application, any relevant correspondence between the applicant, other stake holders and the HREC, other material used to inform potential research participants and all approved documents.

3. All documents of the HREC, including applications, membership, minutes and correspondence will be kept confidential and in accordance with schedule Y and ICMR guidelines

4. To ensure confidentiality, all documents provided to HREC members, which are no longer required, are to be disposed of in a secure manner, such as shredding or placed in confidential bins.

5. All relevant records pertaining to research projects shall be held for sufficient time to allow for future reference. Retention periods shall comply with the schedule Y and ICMR guidelines.

Exempt Review : ICMR GUIDELINES PAGE 11

1. Projects will be exempt from ethical review where they:

- Involve only negligible risk or
- Involve the use of existing collections of data or records that contain only non-identifiable data about human beings.

2. The HREC will decide whether a project is exempt from ethical review.

Expedited review: This can be done for the following reasons:

- Re-examination of a proposal already examined by HREC,
- Research study of minor nature e.g. examination of case records,
- Urgent proposal of national interest.

All revised proposals, unless specifically required to go to the main committee, will be examined in a meeting of identified members convened by the Chairman to expedite decision making. However, decisions taken should be brought to the notice of the main committee.

Expedited review of research projects may be undertaken between scheduled meetings at the discretion of the Chairman. The member secretary may seek advice from other HREC members or suitably qualified experts, as appropriate, before reaching a decision. The decision of this review must be tabled for ratification at the next HREC meeting.

Research with the potential for physical or psychological harm should generally not be considered for expedited review. This includes clinical trials, research involving invasive physical procedures and research

exploring sensitive personal or cultural issues.

17. Monitoring of Approved Projects:-

Purpose: To describe the procedure for monitoring projects approved by the HREC to ensure compliance with ethical approval

1. The HREC will monitor approved projects to ensure compliance with the approved protocol. In doing so it may request and discuss information on any relevant aspects of the project with the investigators at any time. In particular, the HREC will require applicants to provide interim reports on stipulated dates and a final report at completion of the study. Continuing approval of the research will be subject to the PI submitting an interim report by the stipulated date.

2. The HREC shall require the following information in the report:

- Progress to date, publications or outcome in the case of completed research;
- Maintenance and security of records and data;
- Compliance with the approved protocol;
- Compliance with any conditions of approval;
- Changes to the protocol or conduct of the research;
- Changes to the personnel of the PI /other investigators; and
- Adverse events or complaints relating to the project.

3. The HREC may adopt any additional appropriate mechanism/s for monitoring, as deemed necessary, such as: random inspections of research sites, data and signed consent forms; interview, with their prior consent, of research participants.

4. The HREC shall require, as a condition of approval of each project, that investigators immediately report anything which might warrant review of ethical approval of the protocol, including:

- proposed changes in the protocol;
- any unforeseen events that might affect continued ethical acceptability of the project; and
- new information from other published or unpublished studies which may have an impact on the continued ethical acceptability of the trial, or which may indicate the need for amendments to the trial protocol.

5. The HREC shall require, as a condition of approval of each project, that investigators inform the HREC, giving reasons, if the research project is discontinued before the expected date of completion, and that the investigators comply with the approved Retention and Disposal Plan.

6. Where the HREC is satisfied that circumstances have arisen such that a research project is not being or cannot be conducted in accordance with the approved protocol, the HREC may withdraw approval. In such circumstances, the HREC shall inform the PI and the head of the institute, the research project be discontinued, suspended, or that other necessary steps be taken.

7. In determining the frequency and type of monitoring required for approved projects, the HREC will give consideration to the degree of risk to participants in the research project.

8. The HREC will monitor projects approved by the CHIC and will apply the provisions of this Standard Operating Procedure to those projects.

18. Review of Standard Operating Procedures:-

1.The Standard Operating Procedures shall be reviewed based on changed requirements.

2. The Standard Operating Procedures may be amended by following the procedure below:

For those proposals made by a HREC member:

- The proposal must be in writing and circulated to all HREC members for their consideration.
- The views of the members should be discussed at the next scheduled meeting of the HREC, and a vote take at that meeting. Any member unable to attend such a meeting may register his or her views in writing.
- The amendment will be incorporated after the consensus approval by the full committee.

prescribed format duly signed by the Principal Investigator (PI) and Co-investigators / Collaborators should be forwarded by the Head of the Departments / Institution to the ethics committee.

3. The date of meeting will be intimated to the researcher, to be present, if necessary to offer clarifications.

4. The decision will be communicated in writing. If revision is to be made, the revised document in required number of copies should be submitted within a stipulated period: 2 weeks from the date of receiving the copy as specified in the communication or before the next meeting.

19. HREC Annual Report Requirements

1. The HREC shall provide an annual report on its progress for the financial year to the head of the institution, including:

- membership/membership changes;
- number of meetings;
- number of projects reviewed, approved, pending review, pending approval (non compliance by researcher to modifications suggested) and rejected;
- general issues raised.