Standard Operating Procedure (SOP) version 6.1 dtd.8/07/13

| Complete Name of the Ethics Committee | : | Institutional Ethics Committee, Smt. NHL Municipal Medical College, Ahmedabad (NHLIEC) |
| Complete address of the office of the Ethics Committee | : | Department of Pharmacology, First floor, Smt. NHL Municipal Medical College, Ellisbridge, Ahmedabad-380006 |
| Hospitals attached to the Institution and the Institutional Ethics Committee | : | Sheth V.S. General Hospital, Ellisbridge, Ahmedabad SCL General Hospital, Saraspur Ahmedabad Shri C.H. Nagari Municipal Eye Hospital, Ellisbridge, Ahmedabad |
| Frequency of Ethics Committee Meeting | : | As per the requirement, [usually 6-8 in a year] |
| Date of Next/ immediate Ethics Committee meeting | : | As decided by the Member secretary after consultation with Chairperson & Institutional Head. |
| Lead time required by the Ethics Committee before which they discuss documents submitted to them | : | 15-20 days |
| Complete home and contact number of Ethics Committee member whose details will appear on the informed consent form | : | Dr. Falguni Majmudar Dept. of Pharmacology, Smt. NHL Municipal Medical College, Ellisbridge, Ahmedabad-380006 (M): +919925170216 |
| Date from which SOP is effective | : | 08-July-2013 |

Purpose

The purpose of this Standard Operating Procedure (SOP) is to outline the

a) Composition, roles and responsibilities of Members of NHLIEC

b) Application process for review of submitted clinical trials by NHLIEC
e) Review guidelines for NHLIEC members
f) Decision-making by the NHLIEC and notification to the applicant
g) Ongoing review of the conduct, progress, efficacy and safety of a clinical trial.
h) Special consideration for vulnerable population

The SOPs provide clear, unambiguous instructions so that the related activities of the committee are conducted in accordance with Indian laws and relevant, National and International Guidelines

Objective

The NHL Institutional Ethics Committee (NHLIEC) of the Smt. NHL Municipal Medical College, Ellisbridge, Ahmedabad-380006, India in the western zone of Ahmedabad, is established with an objective that all clinical trials/studies on patients of all affiliated hospitals are being conducted as per ICH and GCP guidelines and the safety & well being of the patients are properly maintained.

The NHLIEC essentially targets patient care and ethical aspects of research & education, being undertaken in the affiliated hospitals and college departments. It safeguards the rights, safety and well being of all trial subjects. Special attention will be paid to trials that may include vulnerable subjects. The Committee will ensure that clinical trials are conducted in accordance with the ethical principles laid down in the Declaration of Helsinki, ICMR guidelines, Schedule Y of Drugs & Cosmetics Act and ICH & GCP guidelines.

Scope

Each trial, under the GCP principle, should be conducted in compliance with the protocol that has received prior EC approval/favorable opinion. This SOP covers all clinical trials from Phase I to Phase IV. This includes the investigator initiated research as well as organization or pharmaceutical company sponsored trials that are submitted to NHLIEC.

Role :

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

The NHLIEC will take care that all the cardinal principles of research viz. Autonomy, Beneficence, Non-malafide and justice are taken care of in planning, conduct and reporting of the proposed research. For their purpose, the NHLIEC will look into the aspects of informed consent process, risk benefit ratio whenever required.

The NHLIEC will review the proposals before start of the study as well as monitor the research throughout the study until and after completion of the study. The NHLIEC will also examine compliance with all regulatory requirement, applicable guidelines and laws.

Composition:

a. The NHLIEC has been constituted under the authority of the ex officio Dean & Institutional Head, Smt. NHL Municipal Medical College, Ellisbridge, Ahmedabad-380006 and shall comprise of 10-15 members (to allow a quorum of at least 5 members at each review meeting in order to provide collective expertise ensuring a comprehensive review (scientific and ethical) of the projects submitted to it.

b. The Dean & Institutional Head in office shall be a part of the committee.

c. The composition may be as follows:-
   1. Chairperson
   2. 1-2 basic medical/non medical scientist
   3. 1-2 clinicians from each specialty
   4. One legal expert or retired judge
   5. One social scientist / representative of non-governmental voluntary agency/ philosopher / ethicist
   6. One lay person from the community
   7. Member Secretary

d. Dean & Institutional Head in office should appoint, from among its members, a Chairperson (who is from outside the institution) and nominate a Member Secretary.

e. The member secretary would generally, belong to the same institution and would conduct the business of the committee.

f. There will be adequate representation of age, gender, community, etc. in the NHLIEC to safeguard the interests and welfare of all sections of the community/society.
g. Members should be aware of local, social and cultural norms, as this is the most important social control mechanism.

h. The committee will comprise a diverse working group without any gender bias.

i. The following qualities are sought in the NHLIEC members:
   ✓ interest and motivation,
   ✓ commitment and availability,
   ✓ experience or education,
   ✓ respect for divergent opinions,
   ✓ interest in committee work,
   ✓ integrity, and
   ✓ diplomacy.

For review of each protocol the quorum of NHLIEC should be at least 5 members with the following representations:
(a) basic medical scientists (preferably one pharmacologist).
(b) clinicians
(c) legal expert
(d) social scientist/ representation of non-governmental voluntary agency / philosopher / ethicist / theologian or similar person
(e) lay person from the community.

In any case, for the appropriate quorum, the NHLIEC must include at least one member whose primary area of interest/ specialization is nonscientific and at least one member who is independent of the institution / trial site preferably, the Chairperson.

If required, Subject experts may be invited to offer their views.

Further, based on the requirement of research area, e.g. HIV AIDS, genetic disorders etc. specific patient groups may also be represented in the NHLIEC as far as possible.

Only those NHLIEC members who are independent of the clinical trial and the Sponsor of the trial should vote / provide opinion in matters related to the study.

**Terms of Appointment**

a. The members including the member secretary will be nominated & appointed by the Dean & Institutional Head in office, who would be a mix of medical, non-medical scientific and non-scientific persons including lay public to reflect differed view points.

b. The members will be selected to have an equitable representation of all specialties. It includes scientists, clinicians, members of the community, a lawyer /expert in ethics, a social worker.
c. Duration: The members will be appointed for duration of 5 years.
d. Renewal: The membership may be renewed after the stated term for a period of 3 years.

Replacement/Removal procedure

The members may be replaced/ removed at the discretion of the Dean & Institutional Head in office or committee members when a majority vote is obtained.
A member may be relieved of his/her membership when he/she remains absent from the meeting frequently without prior information to the member secretary.
A member may also be relieved of his/her membership in case of a conduct unbecoming for a member of the Ethics Committee.

Resignation procedure

The member can resign from the committee after discussion and advance notice to the Dean & Institutional Head in office

Updating IEC members

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

Archiving/Record keeping

a. Curriculum Vitae (CV) of all members of NHLIEC.
b. Copy of all study protocols with enclosed documents, annual reports, side-effects/ADRS etc.
c. Minutes of all meetings with due signature of Chairperson.
d. Copy of all existing national and international guidelines on research ethics.
e. Copy of all correspondence with members, researchers and other regulatory bodies.
f. Final report of the approved projects.

Follow up procedures

a. Reports should be submitted for regular review.
b. Final report to be submitted at the end of study.
c. Any serious side effects, adverse drug reactions and the interventions undertaken are to be intimated as per the latest amendments in The Drugs &
Cosmetics Rules vide GSR no. 53(E) dated 30-01-2013 inserting a rule 122DAB, and a new Appendix in Schedule ‘Y’ along with other amendments
d. Protocol deviation, if any, to be informed with adequate justifications.
e. Any new information related to the study should be communicated.
f. Premature termination of study should be notified with reasons and summary of the studies done so far.

Quorum

The quorum consists of at least five members who must be present at each meeting as per ICMR guidelines and schedule ‘Y’:
1. Basic Medical Scientist/ Pharmacologist
2. Clinician
3. Legal Expert
4. Social Scientist /representative of an NGO
5. Lay person from Community

At least one female member should remain present.
As per Schedule-Y, it is preferable that at least one of the NHLIEC members who are not affiliated to the Institute be present during each review meeting.

Voting status

In matters where unanimity is not possible voting can be done. All members including the member secretary have the right to vote. Chairman will cast a deciding vote in case of a tie.

Institutional Ethics Committee membership list would be as per Appendix 1

Conflict of Interest:
Definition: A situation in which a person, such as a public official, an employee, or a professional, has a private or personal interest sufficient to appear to influence the objective exercise of his or her official duties.
There are three key elements in this definition: financial interest, official duties, and professional interest.

A conflict of interest occurs when:
• An individual’s private interest differs from his or her professional obligations to the institute.
• Professional actions or decisions occur that an independent observer might reasonably question.
• A conflict depends upon situation and not on the character or actions of the individual.
• Potential conflicts of interest must be disclosed and managed as per policy.

Measures to monitor or prevent Conflict of Interest for NHLIEC Members:
1. At the beginning of the tenure and before he/she commences to review research projects submitted to NHLIEC and before he/she starts to function as an NHLIEC member and before he/she starts attending NHLIEC meetings will read the Confidentiality and Conflict of Interest Agreement Form carefully and thoroughly and will sign and date the document before the Member Secretary. The signed form shall remain with the office of the Committee and a photocopy shall be handed over to each member. [The appropriate Confidentiality and Conflict of Interest Agreement Form will be provided to the NHLIEC members annexed as Annexure 2.0]

2. Whenever such situation arises e.g. any NHLIEC member being one of the investigators in the proposed research, he/she would not participate in the proceedings of the meeting related to the referred proposal. His/her participation if needed will be only limited to the clarifications sought by the other members related to the referred research proposal in which he/she is one of the investigators.

In other situations decision will be jointly taken by all the members.

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

It is the policy of the NHLIEC is that no member may participate in the review, comment or approval of any activity in which he/she has a conflict of interest except to provide information as requested by the NHLIEC.

The Member Secretary will immediately disclose to the Chairperson of the NHLIEC any actual or potential conflict of interest that he/she may have in relation to any particular proposal submitted for review by the Committee, and to abstain from any participation in discussions or recommendations or decision making in respect of such proposals.

If an applicant submitting a protocol believes that an NHLIEC member has a potential conflict, the investigator may request that the member be excluded from the review of the protocol. The request must be in writing and addressed
to the Chairperson. The request must contain evidence that substantiates the claim that a conflict exists with the NHLIEC member(s) in question. The Committee may elect to investigate the applicant’s claim of the potential conflict.

When a member has a conflict of interest, the member should notify the Chairperson and may not participate in the NHLIEC review or approval except to provide information requested by the Committee.

**Training of the NHLIEC Members in Research Ethics**

- An individual selected as a new member of the NHLIEC will be required to attend one meeting as an ‘Observer’ before being inducted as a member.
- Member-secretary or an NHLIEC member will provide an introductory training to the new member.
- The NHLIEC Member Secretary, member, Chairperson will be encouraged to receive continued training by participating in a workshop, conference and/or retraining program related to research ethics, as a delegate, faculty, facilitator, etc. at least once every year.
- The NHLIEC will conduct workshops on Ethics in Clinical Research and Good Clinical Research practices from time to time to impart training to the NHLIEC Members to the Institutional faculty members.
- The NHLIEC may sponsor or reimburse the expenses of an NHLIEC member or prospective members for attending conference, continuing education session workshop and/or training program etc.

**Responsibility**

The Institutional Ethics Committee (NHLIEC) is setup to ensure that the clinical research studies carried out at Smt. NHL Municipal Medical College:

- are sound in scientific design, have statistical validity and are conducted according to the parameters of ICH-GCP as well as local regulatory requirements.
- do not compromise the safety, rights and well being of the patients participating in the research study.
- are conducted under the supervision of medical persons with the required experience / expertise
- include safely, patients who, through their legally acceptable representative have given informed consent for participation in the research study.
All members should maintain in absolute confidentiality of all discussions during the meeting. They have no rights to participate if they are principal investigator.

The member secretary / designee / Institutional Ethics Committee (NHLIEC) coordinator will record the minutes during each meeting

Correspondence between the Institutional Ethics Committee (NHLIEC) and the principal investigator / study team and other relevant records (response letter, minutes of meetings, membership list composition etc) will be retained for minimum period of 5 years after completion of the trial.

The Institutional Ethics Committee (NHLIEC) will review all research projects and also the ongoing research projects at intervals appropriate to the degree of risk to the study subjects.

The committee will maintain a list of projects submitted, approved / disapproved and the outcome of each project, relevant correspondence and all study related documents.

In one academic year, beginning from July of each year, any principal investigator shall be allowed to handle between 2-3 clinical/research trials in his field of work in the institution.

**The NHLIEC expects from the principal investigator to be informed about:**

- a) The randomization of the first patient,
- b) The progress of the study at interval of every month,
- c) Any Serious Adverse Events occurring in the course of the study within 24 hrs. of their occurring [Report directly to Chairperson]
- d) Any changes in the protocol and patient information /informed consent documents, prior to their implementation.
- e) Amendments/revisions to any study-related document as well as patient safety related information
- f) Study completion and discontinuation with reasons
- g) Justification for approval to restart studies discontinued earlier
- h) The final report of the study shall be submitted to the NHLIEC in all cases, even when the study abandoned for any reason(s).

**Procedure**

The applicant of the proposal generally the principal investigator is required to submit his/her application letter and 12 copies of a dossier comprising of following documents, at least 15 days before a scheduled meeting:
The PI will submit the application for the proposed Clinical Trial in a particular format. [1 copy only]

- Research protocol.
- Protocol Amendment, if any.
- Investigator’s Brochure.

**Case Report Form**

- Informed consent form, [English]
- Informed consent form, [English to Gujarati translation].
- Informed consent form, [Gujarati to English back translation].
  - including translation certificate [1 copy]
- Informed consent form, [English to Hindi translation].
- Informed consent form, [Hindi to English back translation].
  - including translation certificate [1 copy]

- Patient/ volunteer information Leaflet [English]
- Patient/ volunteer information Leaflet [English to Gujarati translation].
- Patient/ volunteer information Leaflet [Gujarati to English back translation].
  - including translation certificate [1 copy]
- Patient/ volunteer information Leaflet [English to Hindi translation].
- Patient/ volunteer information Leaflet [Hindi to English back translation].
  - including translation certificate [1 copy]

**Safety Reports**

- DCGI Approval Letter [1 copy]
- Insurance Policy [1 copy]
- Import license, where applicable[1 copy]
- Investigator’s undertaking[1 copy]
- Registration number with Clinical Trial Registry of India (CTRI)
- Clinical trial Agreement (CTA) as given below

- The NHLIEC is to be notified of any payments proposed to be made to study patients towards reimbursement of incidental expenses.

- The fees for the consideration of the protocol/clinical study in question will be Rs.15,000(INR). The fees for any protocol &/or other amendment/s in the study shall also be Rs.15,000 (INR) and should be in the form of a cheque addressed to “AMC Medical Education Trust”

- Ethics Committee Members Conveyance Allowance has to be given by sponsor/Investigator as per the existing rules as on the date of submission of the protocol/amendment. The member secretary will be aware of the amount decided by the Institutional Head.

- The Principal investigator (PI)/Sponsor/CRO/SMO will pay administrative charges in the form of a cheque addressed to “AMC Medical Education Trust” to the institute before initiating the clinical trial. The amount of administrative charges will be 15% of the budget allocated for the clinical
trial for that site. If the 15% of the budget allocated for the clinical trial for that site is amounting less than Rs.50,000 (INR), the PI/Sponsor/CRO/SMO will pay minimum Rs.50,000 (INR) before initiating the clinical trial.

- A tri-partite or four-party clinical trial agreement will be done according to the parties involved, including “Institutional Head/ Dean, Smt NHL Municipal Medical College” as one of the party.

- The PI will also sign a “Financial Disclosure Statement”.

- It will be a responsibility of the PI & SPONSOR/CRO/SMO (Whatever applicable) to acknowledge the Institute Head & NHLIEC regarding any changes in the Financial Transactions from the SPONSOR/CRO/SMO (Whatever applicable) within 15 workings days.

Committee Meetings

- The committee shall meet in an academic year beginning from July as and when required. The dates for the meeting shall be decided by the member secretary after due consultation with the Chairperson and the Dean & Institutional Head in office.

- Advance notice, 07-15 days before each meeting will be sent out to the NHLIEC members, along with the agenda.

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

- Decisions will be made only in meetings where quorum is complete.

- All nominated members including the member secretary have the right to vote.

- Only those NHLIEC members who are independent of the clinical trial and the Sponsor of the trial should vote / provide opinion in matters related to the study.

- The Investigator/Co-investigator is called to the meeting to present the study or answer specific queries. However, he / she will not participate in the decision making / voting process of that study even if he / she is a regular member of the NHLIEC.
A Study Team member including the Principal Investigator will be deemed an interested party with regard to the review.

The Study Team Member's non participation in the decision making / voting process will be recorded in the response letter from the NHLIEC.

The decision of the committee will be taken by a majority vote after the quorum requirements are fulfilled to recommend / reject / suggest modifications for a repeat review or advise appropriate steps.

In case NHLIEC revokes its approval accorded to a trial protocol, it must record the reasons for doing so and at once communicate such a decision to the Investigator.

In all cases, the study will be unambiguously identified using a code number accorded by name of sponsor, name of Principal Investigator, short form of molecule studied/protocol title and the year of approval.

Should an amendment to a study related document be administrative in nature and not involving study design or safety criteria, it may be provisionally approved in writing, by the Chairperson/member-secretary of the NHLIEC without calling a full meeting.

The Chairperson/member-secretary will inform other members of the NHLIEC of amendment and his / her decision during the subsequent regular meeting of the committee and the decision will be ratified. After the review meeting, the member-secretary will convey the decision of the committee to the Principal Investigator in writing by a response letter.

The NHLIEC shall also carry out ongoing review of the trials at appropriate intervals as per regulatory requirements for safeguarding the rights, safety and well being of the trial subjects.

The response/decision letter must contain following information:

- Date, place and time of NHLIEC meeting.
- Names and designation of the Chairperson and members who attend the meeting.
- Title of the Research proposal
- Name of the Principal investigator
- List of documents (with date and version number wherever possible) reviewed by the Institutional Ethics Committee (NHLIEC)
- A clear Statement of the Decision Reached.
- Any advice (non-binding) by the Institutional Ethics Committee (NHLIEC)
- In the case of Negative decision, reasons for not approving the proposal must be mentioned
In the case of "approval" decision, the responsibilities of the Principal investigator must be communicated
The response letter will also include the signatures with dates of the NHLIEC chair person and member-secretary.

(Dr. Falguni Majmudar)  (Dr. Mahendra Joshi)  (Dr. Pankaj R. Patel)
Member Secretary      Chair person            Institutional Head
Date:                  Date:                   Date:
### Appendix 1
Institutional Ethics Committee membership list

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Name of the NHLIEC Member/Qualifications</th>
<th>Designation with Gender Specification</th>
<th>Affiliation (Institutional/Non-Institutional)</th>
<th>Role in NHLIEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dr. Mahendra Joshi</td>
<td>Retired Judge, (M)</td>
<td>Consumer Forum (Non Institutional)</td>
<td>Chairperson Member –Legal expert</td>
</tr>
<tr>
<td>2</td>
<td>Dr. Pankaj R. Patel M.S. (Ortho)</td>
<td>Dean, Smt. NHL Muni. Med. College, Prof of Orthopedics(M)</td>
<td>Smt. NHL Mun. Med. College</td>
<td>Institutional Head-Member</td>
</tr>
<tr>
<td>3</td>
<td>Dr. Asha N. Shah M.D. (Medicine)</td>
<td>Prof of Medicine (F)</td>
<td>B.J. Medical College (Non Institutional)</td>
<td>Member-Clinician</td>
</tr>
<tr>
<td>4</td>
<td>Dr. Falguni Majmudar M.Pharm., PhD.</td>
<td>Asst.Prof., Dept. of Pharmacology (F)</td>
<td>Smt. NHL Mun. Med. College</td>
<td>Member Secretary</td>
</tr>
<tr>
<td>5</td>
<td>Dr. Varsha Patel M.D. (Pharmacology)</td>
<td>Prof. &amp; Head, Dept. of Pharmacology (F)</td>
<td>Smt. NHL Mun. Med. College</td>
<td>Member-Pharmacologist Basic medical scientist</td>
</tr>
<tr>
<td>6</td>
<td>Dr. Parul D. Shah M.D. (Microbiology)</td>
<td>Prof. &amp; Head, Dept. of Microbiology (F)</td>
<td>Smt. NHL Mun. Med. College</td>
<td>Member Basic medical scientist</td>
</tr>
<tr>
<td>7</td>
<td>Dr. Pratik Patel</td>
<td>Prof. &amp; Head, Dept. of Forensic Medicine (M)</td>
<td>Smt. NHL Mun. Med. College</td>
<td>Member Basic medical scientist</td>
</tr>
<tr>
<td>8</td>
<td>Dr. Sharad Thaker</td>
<td>Philosopher-writer (M)</td>
<td>Freelance (Non Institutional)</td>
<td>Member-Philosopher</td>
</tr>
<tr>
<td>9</td>
<td>Dr Mahadev Desai M.D. (Medicine)</td>
<td>Physician (M)</td>
<td>Practicing Physician (Non Institutional)</td>
<td>Member-Clinician</td>
</tr>
<tr>
<td>10</td>
<td>Dr. Shefali Desai</td>
<td>Laproscopic surgeon, Sanved Hospital (F)</td>
<td>Sanved Hospital (Non Institutional)</td>
<td>Member-Clinician</td>
</tr>
<tr>
<td>11</td>
<td>Dr. Nilay Suthar</td>
<td>Assoc.Prof., Dept. of Medicine (M)</td>
<td>Smt. NHL Mun. Med. College</td>
<td>Member-Clinician</td>
</tr>
</tbody>
</table>
Appendix 2
Confidentiality Agreement Form for NHLIEC Members

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

It is the policy of the NHLIEC that no member may participate in the review, comment or approval of any activity in which he/she has a conflict of interest except to provide information as requested by the NHLIEC.

The Undersigned should protect the secrecy and respect the Confidentiality of the data submitted by the sponsors, and will not divulge the contents to any party.

The Undersigned will immediately disclose to the Chairperson of the NHLIEC any actual or potential conflict of interest that he/she may have in relation to any particular proposal submitted for review by the Committee, and to abstain from any participation in discussions or recommendations or decision making in respect of such proposals.

If an applicant submitting a protocol believes that an NHLIEC member has a potential conflict, the investigator may request that the member be excluded from the review of the protocol.

The request must be in writing and addressed to the Chairperson. The request must contain evidence that substantiates the claim that a conflict exists with the EC member(s) in question. The Committee may elect to investigate the applicant’s claim of the potential conflict.

When a member has a conflict of interest, the member should notify the Chairperson and may not participate in the NHLIEC review or approval except to provide information requested by the Committee.
Agreement on Conflict of Interest

Please sign and date this Agreement, if the Undersigned agrees with the terms and conditions set forth above. The original (signed and dated Agreement) will be kept on file in the custody of the NHLIEC. A copy will be given to you for your records.

Whenever I have a conflict of interest, I shall immediately inform the Chairperson not to count me for discussion or decision making in respect of such proposal.

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

________________________________________________________
Signature Date

________________________________________________________
Chairperson’s Signature Date

I acknowledge that I have received a copy of this Agreement signed by the NHLIEC Chairperson and me.

________________________________________________________
Signature Date