Annexure 5

AX 05/SOP 05/V5

Guidelines for Investigators

1. All the studies qualifying as 'clinical research' need to be submitted for the Institutional Ethics Committees review.
2. An Investigator planning to conduct a research study involving human participants; **funded by Government agencies and Pharmaceutical companies** at Seth G.S. Medical College & K.E.M. Hospital will need an approval by the **Institutional Ethics Committee (IEC)** before commencing a study..

   Research studies which are undertaken as **dissertation projects** (postgraduate students :MD, MS, MCh, DM, DNB, PhD, MSc, MPTh, MOTh, Nursing), **research projects of undergraduate students** (Indian Council for Medical research studentship) and **investigator initiated** research studies which are **self funded** and those funded by Research Society of KEM Hospital, Diamond jubilee Society trust will need an approval by the **Institutional Ethics Committee (IEC)** before commencing a study.
3. Location and Office Address (current):

   Institutional Ethics Committee (IEC),

   New UG/PG Hostel, 20 Storey hostel building, ground floor, KEM Hospital Campus, near main boy's hostel, Parel, Mumbai 400 012. Telephone no. (GSMC and KEMH): 91 22 410 7000 Ext. 7515, 24107515, 24122188, Email: iec-1@kem.edu and iec-2@kem.edu

   The IEC office hours for submission of documents, enquiries and telephonic communication with the IEC staff are as follows:

   Monday to Friday - 1.30 p.m. to 4.00 p.m.
   Saturday - 10.30 a.m. to 12.00 noon.

   The office will remain closed on Sundays, all public holidays and last working day of every month.
4. There will be no meetings held in the month of May and November (during college vacations). In case a meeting is to be held during vacation due to unavoidable reasons, the decision will be taken by the Member Secretary in consultation with Chairperson.
5. The clinical trial (Any investigation in human research participants intended to discover or verify the clinical, pharmacological, and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy [ICH-GCP]) must be registered with the Clinical Trial Registry of India (CTRI) or any other WHO platform registry and a copy of the documentation of registration must be provided at the time of submission of a new study proposal for review.
6. General responsibilities of PI and Co-PI .

- **MRC :**

Investigators involved in the trial are competent having a valid medical degree registered with the Medical Council of India (MCI) / State Medical Council or a dental degree registered with the Dental Council of India / State Dental Councils.

- **Updated CVs:**

Investigators responsible for conduct of clinical trials are adequately qualified, experience.

- **GCP:**

Investigators are knowledgeable in trial process, ethical issue and applicable rules and regulation ensuring data integrity and protection of subject rights, safety and wellbeing.

Investigators should be GCP trained regularly at the interval of three years and GCP training certificate should be provided to the IEC at the time of submission of a new study proposal / prior to initiation as applicable.

- **SOPs of IECs:**

Investigators should follow documented procedure i.e. Standard Operating Procedures (SOPs) of IEC in compliance with the regulation and the approved protocol or informed consent, safety reporting management, delegation of responsibilities and training, investigational product, clinical trial documentation, record retention, archival and destruction.

- **Investigators site specific SOPs for regulatory studies:**

Investigator should prepare the site specific SOPs which should be approved by the IEC and one copy should be handed over to the IEC for IEC records. Site specific SOPs should also cover the following elements related to the conduct of the clinical trial.

a. Updated investigators Brochure and clinical trial oversight plan
b. Work delegation log signed by the PI
c. SOP/Policy document to ensure continuity of trial in case of staff and investigator attrition
d. Clinical trial site shall have a policy of investigators handling over the trial case he /she to leave investigator will continue to be responsible for the trial until such time another investigator takes over the trial. Authorized person from the site shall communicate with the sponsor and ethics

committee if needed. There should be back up research staff to ensure that the recruited subjects rights safety and wellbeing is not compromised.

6. The IEC is currently following the version 5 dated 26th July 2017 of the Standard Operating Procedures (SOPs), which are individual activity based and are 20 in number. The SOPs are available at our website www.kem.edu .
7. The following steps need to be followed by investigators while **submission of a New study proposal to** the IEC:

I Prior to approval of a research study

a) **e-EC software registration for the Principal Investigator:**

- **PI should keep ready following information and documents (in PDF versions) at the time of registration:**

1. Employee / Student ID Numbers of study team
2. Current Medical Council Registration certificate
3. Passport size photo
4. Biodata
5. GCP training Certificate (within the preceding ~~five~~ three years)

- **Follow the link as http://iecmanager.org**

1. Select institution as **Seth GS Medical College and KEM Hospital, Mumbai**.
2. Register
3. Submit the required information (registration) to get associated with institution for the project submission under following heads.
    a. Basic information
    b. Professional information
    c. Certifications
    d. Trainings
    e. Submit (Request)
    - Principal Investigator registration request will ~~set~~ for IEC Admin verification. After IEC admin approval, user will get the account activation link to his/her email. Through this he/she can set their own password to login to system as Principal Investigator(PI).

Note: Only PI can forward the Project to IEC Admin.
Project proposals submitted via e-EC **on or before 20th of every month till 24.00 am will** usually be taken up for discussion at the next month's IEC meeting.

b) The investigator should ensure that there is an 'Ethics Section' in the protocol which is in compliance with the ICMR 2006 Guidelines. The section should include the following aspects which may be stated in the Ethics Section or elsewhere in the protocol:

- A statement saying that the study will be conducted in adherence to relevant national/international laws.

- Policy regarding autonomy (voluntariness, right to withdraw).
- Confidentiality
- Recruitment policy ensuring equitable enrollment.
- Protection of vulnerable participants.
- Process of obtaining informed consent.
- Policy regarding treatment of study related injury, compensation for study related injury and compensation for participation.
- Policy regarding dissemination of data, presentation of data, publication.

c) Incompletely filled forms / forms without signatures / proposals will not be accepted and same will be conveyed to the PI.

d) Decision on type of review:

Member secretary will review the protocol and related documents and will take the decision regarding the type of the review required for the particular protocol as follows:

a) Full Board Review (refer SOP XXXX)
b) Expedited Review (refer SOP XXXX)
c) Exempt from Review (refer SOP XXXX)

e) An investigator may refer to the SOP. No. 23 for 'Request for Waiver of Written Informed Consent' whenever necessary.

f) An investigator is required to refer to the format of an Informed Consent Document for genetic study whenever applicable AX 07/SOP 05/V5

For all projects sponsored by pharmaceuticals, the processing fees will be total of Rs. 60,000/ project + Taxes, for the Government sponsored projects, the processing fees will be Rs. 7,000 /project and for all academic (non- sponsored) projects the processing fees will be Rs. 1,500/-project (in hard cash). The processing fees shall be collected only once at the time of submission of the project. The sponsored projects fees will be accepted by cheque / demand draft which will include the tax , drawn in the name of 'Diamond Jubilee Society Trust, Seth G. S. Medical College'. The funds of the IEC are maintained in the Diamond Jubilee Society Trust (DJST) account, PAN no. AABTS5336G.

Duplicate copy of any document (for e. g. Permission letter, certificate, query letter) will be charged Rs. 200/-).

g) An investigator may be invited (telephonically/ through written communication) to the IEC meeting to discuss issues related to the study proposal.

h) Investigator will be able to track the status of the submitted project and respective meetings dates on PI's dashboard of e-EC software.

i) For clinical study planned on an "alternative system of medicine" (Ayurveda, Homeopathy, Siddha, Unani), a Co-Investigator/ Collaborator from that system should be included in the study team. The

co-investigator appointed should be independent and he/she should not have a conflict of interest with the study, investigator or sponsor. This is in accordance with the ICMR 2006 guidelines.

j) An investigator is expected to submit reply to the letter of recommendations/ queries sent by the IEC within 180 days of date of receipt of the letter. In the absence of any response, the project will be declared closed for the IEC office records. The documents for these projects will be shredded by IEC staff and same will be recorded in the log book for shredded documents.

II Once approval for a study is granted

a) An approval will be granted for the entire duration of the study.

b) It is the responsibility of the principle investigator that for studies which will continue for more than a year, a continuing review report needs to be submitted (within 1 month of the due date i.e. 11 months from the date of approval)

For all projects sponsored by pharmaceuticals, the annual continuing review fees will be Rs. 10,000/ project (approved in 3rd September 2014 minutes), for the Government sponsored projects, the processing fees will be Rs. 1,000 /project (approved in 3rd September 2014 minutes). For academic (non- sponsored) projects (in hard cash) no continuing review fee will be charged (approved in 3rd September 2014 minutes). The continuing review fees shall be collected every 11 months from the date of approval (unless specified otherwise). The sponsored continuing review fees will be accepted by cheque / demand draft which will include the tax,drawn in the name of 'Diamond Jubilee Society Trust, Seth G. S. Medical College'. The funds of the IEC are maintained in the Diamond Jubilee Society Trust (DJST) account, PAN no. AABTS5336G.

c) Submission of Study Related Documents for IEC review

Study related documents (protocol amendments, SAE reports, status reports, study completion reports, protocol deviations/ violations) will be accepted during the office hours specified above. Only one set of the above stated study related documents need to be submitted for the IEC review.

Agenda for the IEC meeting is prepared 3 days in advance before the date of meeting and is sent to the IEC members at least 2 days in advance. Hence the study related documents like answers to the IEC queries and amended study related documents (Protocol, ICD, CRF and IB) received within seven days and other types of documents within 3 days preceding the date of meeting will not be considered for the meeting. It will be deferred to the next month's meeting for discussion (**Exception -** any matter which in the opinion of the IEC secretariat has direct bearing on the safety of the research participants such as SAE report, major protocol violation).

d) Submission of Amended Protocol and Protocol Related Documents

All amendments to the approved research proposal (only one set) should be submitted to the committee for its review no later than 7 seven days prior to the date of forthcoming meeting.

No changes in the protocol, case record form and /or Informed Consent Document shall be initiated without prior written approval from the committee, except when necessary to eliminate immediate hazards to the research participants, or when the change(s) involve only logistical or administrative aspects of the trial (e.g. change of monitor(s), telephone number(s).

A covering letter should be submitted mentioning reason/s for amendments and summary of changes and the amended text must be highlighted in the revised Protocol and Protocol Related Documents.

e) Submission of Report of Protocol Deviations/ Violations in the study protocol Please use 1- Deviation / Non-Compliance / Violation Record AX 01/SOP 12/V5 for submitting report of Protocol Deviations/ Non-Compliance / Violations.

f) Submission of Report of Serious Adverse Events (SAEs)

The Principal Investigator should submit within 24 hours on site SAE report or the unexpected adverse event report as per the format specified in *AX 01/SOP 14/V5* (Appendix XI of Schedule Y) and *AX 02/SOP 14/V5 to* the IEC or by email. The report of SAE of death after due analysis shall be forwarded by the Investigator to chairman of the IEC and Chairman of the Expert Committee constituted by the Licensing Authority under Appendix XII with a copy of the report to the Licensing Authority and the head of the institution where the trial is been conducted within 10 calendar days of SAE of death. The report of the SAE other than death after due analysis shall be forwarded by the Investigator to Licensing Authority, chairman of the IEC and the head of the institution where the trial is been conducted within 10 calendar days of occurrence of SAE.

The SAE report should be accompanied by detailed narrative of the SAE and CIOMS form.

It should be submitted as per checklist detailed by Licensing Authority in (Annexure A) and given in ***AX*** *01/SOP 14/V5.*

The sponsor or his representative shall pay the compensation in case of clinical trial related injury or death within 30 days of the receipt of such an order from Licensing Authority.

g) Any new information that may adversely affect the safety of the research participants or conduct of the trial should be informed to the IEC.

h) If an investigator wishes to appeal against the decision about rejection of a research proposal by the IEC, please contact the IEC and submit your appeal in writing, addressed to the IEC Chairperson with justification relevant to the issues/ objections raised by the committee within twelve (12) weeks of the receipt of the committee's decision. In absence of appeal, the project will be declared closed for the IEC office records.

i) Submission of continuing review report in case of studies which continues for more than a year.

- For studies which will continue for more than a year, a continuing review report as per the format *AX 02/SOP 10/V5* will need to be submitted for review
- If the Principal Investigator fails to submit the continuing review report within one month of the due date (i.e. 11th months from the date of approval, unless specified otherwise), the IEC secretariat will send a reminder as per the format *AX 01/SOP 10/V5* within 7 working days of this due date. If there is no response within 15 days after the date of reminder, the IEC secretariat will put up the matter for discussion at the forthcoming full board meeting for appropriate action which may consist of but not limited to

a) A letter of reprimanding the Investigator

b) Not reviewing future projects from the PI for a specified period of time

c) A letter asking the Investigator to put recruitment of new participants on hold

III Once a study is over

Submission of Study Completion Report

For studies which are completed within the IEC approval period, a study completion report as per the format given in *AX 01/SOP 11/V5* should be submitted to the IEC, by the investigator. The study completion report is expected for review within 1 month of completion of the study at the site. A brief study report containing data analysis from all centres should be submitted once available from the sponsor.

IV In case a study is not initiated or terminated, the same should be communicated to the IEC stating reasons for the same. The format for submission of report of premature termination of the study is as per *AX 01/SOP 13/V5* should be used

1.The IEC archives all the study related documents for a period of 5 years after the study is completed / terminated/ reported as not initiated at our site. In case, an investigator needs a copy of any document submitted to the IEC, a written request can be made for retrieval of the same using the form1- Document Request Form *AX 01/SOP 19/V5*

Sponsor responsibilities

Any report of serious adverse event or death occurring in clinical trial after due analysis shall be forwarded by the sponsor to the chairman of the IEC and the head of the institution where the trial is been conducted within ten calendar days of occurrence of the SAE or death. The report of the SAE other than death after due analysis shall be forwarded to chairman of the IEC and the head of the institution.

In case of injury or death occurring trial subject the sponsor (whether a pharmaceutical company or an institution) or his representative, whosever had obtained permission from the Licensing Authority for conduct of the clinical trial shall make payments for medical management of the subject and also provide financial compensation for the clinical trial related injury or death in the manner as prescribed in SOP 5 Annexure 6.

Appendix I: Regulatory permissions

- **DCG(I) approval**

  Studies which plan to use a new drug (as defined in 122-E of the Drugs and Cosmetics Act, 1945) require DCG (I) permission. For such studies, a copy of the permission letter issued by the DCG (I) to the pharmaceutical company/investigator also needs to be submitted to the IEC. If the DCG (I) permission is awaited, a letter of provisional 'approval will be issued by the IEC and the final IEC approval will be given after a copy of DCG(I) permission is submitted to the IEC. No study should be initiated until the final letter of permission is issued by the IEC.

- FDA marketing/manufacturing license for Ayurvedic/ herbal formulations/ nutraceutics
- Health Ministry Screening Committee (HMSC) approval in case a study involves collaboration with any foreign laboratory/clinic/institution

- Bhabha Atomic Research Centre (BARC) approval in case a study involves use of radioisotopes/ ionizing radiations
- Genetic Engineering Advisory Committee (GEAC) approval in case a study involves use of gene therapy
- **Administrative sanction** from the head of the Institution should be sought by investigators for studies involving collaboration with other Indian or foreign Laboratory/ Clinic/Institution.
- **Administration sanction** from the head of the Institution for sending the samples to laboratories outside KEM Hospital.
- It is mandatory as per the directive by the DCGI (w.e.f.15th June 2009, which is applicable for clinical trials initiated after 15th June 2009) to register clinical trial at ICMR clinical trial registry at www.ctri.in before enrolling first patient in the study. (Registration is mandatory for interventional clinical trials)

Appendix II: List of forms required for submission of study related documents

The following forms are available in the IEC office and should be used for submission of study protocol and other study related documents as per revised SOPs of the IEC:

- Project Submission Application Form for Initial Review ***AX 1-A/SOP 05/V5 / AX 1-B/SOP 05/V5***
- Checklist of Protocol submission ***AX 02/SOP 05/V5***
- Serious Adverse Event Report Assessment Form for SAE at our site *AX 01/SOP 11/V5*
- Deviation / Non-Compliance / Violation Record *AX 01/SOP 10/V5*
- Continuing Review Report Form *AX 01/SOP 07/V5*
- Study Completion Report *AX 01/SOP 08/V5*
- Premature Termination Report *AX 01/SOP 09/V5*
- Document Request Form *AX 01/SOP 16/V5*
- Guidance document for Department Review Boards (*AX 08/SOP 05/V5)*
- AV consent checklist for participants (SOP 12, AX02/SOP12/V5)

Submission of Projects for IEC Review

Submission of project proposal by Investigator [as per checklist –*AX 02/SOP 05/V5*]
(Sponsored by Pharmaceutical companies and Government Organizations)
[Till 20th of every month eg. 20th June]

↓

Documents checked by the Administrative officer

Complete ↓ | Incomplete ↓

Received by IEC → **1st Review** → Returned

Review by the IEC members by circulation of projects [about 4 weeks] and Discussion at full board meeting [3rd/ 4th week of the next month eg. 3rd week of July]

Decision communicated to investigator [within 14 days of meeting eg. 1st week of August] (Approval/Disapproval with reasons/ Modifications in the proposal)

Submission of response to IEC queries/modified project documents [to be submitted within 180 days after the IEC query letter is sent]

2nd Review

Member Secretary/ Chairperson, informed to members at full board meeting

Full Board discussion

two/more designated members, informed to members at full board meeting

Decision communicated to investigator [within 14 days of meeting eg. 1st week of August] (Approval/Disapproval with reasons/ Modifications in the proposal)

3rd / Subsequent Review Procedures- Similar to **2nd** Review