Version : 06
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DCGI Registration No. - ECR/108/Indt/MH/2013

INTERSYSTEM BIOMEDICA ETHICS COMMITTEE

ISBEC
Ethics • Safety • Human Research

STANDARD OPERATING PROCEDURES

For

INTER SYSTEM BIOMEDICA ETHICS COMMITTEE(ISBEC)

Version 6 Dated 1st June, 2018

(Registered under Section 25 of the Companies Act, 1956)

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INTRODUCTION

Ethics is a science of moral values, human conduct and Medical ethics refers to moral principles to guide the members of the Medical Profession. The code refers to the accepted norms for the Practitioners in dealing amongst values or principles with each other, with the state and with subjects.

Ethics in Medicine has been recognized and documented, as early as 2000 BC in early days of Sushrut, Charak and Vagbhat:

"Anyone who treats is a physician, but one who treats scientifically, after practical experience, with ready well prepared medicines, isintelligent, hardworking, well-mannered and truthful and ethical is a superior physician" – (SushrutSutrasthan 34, 1500-2000 B.C.).

Guidelines for behaviour for Doctors are in the form of Oaths, Codes, and Caution etc. The Hippocratic Oath which is recommended from 600 A.D is known for its edict: "to do no harm to the patient" and all physicians have accepted it at the time of graduation.

Scientific query and application of new methods to the health care and intervention is responsible for much of the progress in Medicine. There is a big surge in clinical research on new molecules as well as interventions in the last few decades. Thereby it became abundantly clear that no scientific query should knowingly or unknowingly ultimately harm the subject, who may be the subject of research enquiry. Hence the ethical and scientific standards for carrying out Medical Research on human subjects have been developed and established as International Guidelines over last 60 years. It started in 1947 with the Nuremberg Code, and progressively got modified with other International recommendations as 1) Code of Medical Ethics – MCI 1956, 2) Declaration of Helsinki 1964, 2000, 3) WHO/CIOMS International Guidelines 1984, 1993and1994,4) ICH Guidelines for GCP 1996, 5) Indian Council of Medical Research (ICMR) Guidelines 2002, 2006 , 2008, and 2017 along with the Schedule Y by the DCGI under the Drugs & Cosmetics Act and US OHRP Guidelines, 2018. Compliance with these Guidelines helps to ensure that the dignity, rights, safety and well-being of research participants are safeguarded and the results of scientific investigations are credible. The responsibility of the Ethics Committee is to provide independent, timely and competent review of the ethics of a proposed study.The SOPs are updated as per the International and National Guidelines. Version 6 includes relevant aspects of ICMR guidelines 2007.

While the ethical guidelines in allopathy research are well updated from time to time, enough has not been done in the area of Alternative or Traditional Complementary Systems of Medicine (TCM). The systems consist of Ayurveda, Unani, Siddha, Homeopathy, and Herbal Medicines. Majority of thepopulations in Asia, South East Asia, China, Africaetc have access to only the

Traditional/ Complementary Systems. Increasingly, even in countries like USA, UK, Canada and Europe, there is a substantial number of patients who resort to TCM for relief. In 2002, WHO recognizing the importance of TCM has issued a policy statement - "Global Strategy for TCM". The aims of this policy are: To Review current worldwide use and status of TCM, To Integrate TCM in national policies, To Promote data generation for its safety and efficacy, and To Help establish Regulatory/Technical Guidelines.

National effort in India has been very positive in this respect. Government of India has established under the Ministry of Health- Dept of AYUSH (Ayurveda, Yoga, Unani, Siddha, Homeopathy), to encourage scientific evaluation of TCM to establish safety and efficacy of these systems. The interaction of AYUSH with ICMR and CSIR (The Golden Triangle) further imparts a scientific cutting edge to TCM. Since TCM has been used for decades/centuries in this part of the world there is a wide experiential base. Hence there is a scope for exploratory and experimental studies, a process aptly termed as "Reverse Pharmacology" (RP).

The Council of Scientific & Industrial Research (CSIR) has also initiated various projects under NMITLI (New Millennium Indian Technology Leadership Initiative). It encourages well -equipped research centers to take products of these systems and establish the safety/efficacy through the path of Reverse Pharmacology. Recognised Research Centers involved are Banaras Hindu University (BHU), Medical Research Center of Kasturba Health Society (MRC-KHS), Mumbai, Dept of Ayurveda under Pharmacology Division of Seth G.S. Medical College and KEMHospital.

In order to address the ethics in research projects related to allopathic as well as alternative systems of medicine, the Inter System Biomedica Ethics Committee**(ISBEC)** was first formed as part of BharatiyaVidyaBhavan's Ancient Indian Modern Discoveries project in 2003. The projects approved by the committee have been accepted by the Drug Controller of India (DCGI), Ministry of Health, Indian Council of Medical Research (ICMR), Department of Biotechnology (DBT), Council of Scientific and Industrial Research (CSIR) and Central Council of Research in Ayurveda &Siddha (CCRAS). In April 2008, ISBEC has been registered under Section 25 of the Companies Act, 1956 as an independent, non-profit organization.

The composition and functioning of ISBEC is as per ICMR & WHO Ethical Guidelines for Biomedical Research on Human subjects – 2006 including special requirements of research of other systems, including Good Ayurvedic Research Practices & Homeopathy, a document prepared by ISBEC members.

The Committee consists of Consultants from allopathic system who have considerable scientific research experience. In addition it also has Specialists from other systems of Medicine, like

Ayurveda, Unani and Homeopathy, Lay person, Social scientist, Nutritionist and Legal experts as per the ICMR and Schedule Y requirement.

ISBEC functions as an Independent Ethics Committee. It reviews ethics of the clinical and biomedical research proposals submitted by research institutions, academic institutions, pharmaceutical industries and Clinical Research Organizations (CROs). It ensures the rights, safety and well-being of subjects participating in research. In addition ISBEC makes it a point to ascertain the scientific quality of the research proposals by suggesting improvisation on the protocols. ISBEC endeavours to add value and quality to the proposals through the expertise of its experienced members.

ISBEC was registered in 2008 with the Government of India as an Independent Ethics Committee and as a non –profit organization under the Company Act 1964. It was accredited by DCGI in 2013 (Registration No. ECR/108/Indt/MH/2013 issued under Rule 122DD of the Drugs & Cosmetic Rules 1945). It has been re-registered by DCGI as an Independent Ethics Committee in 2018.

STANDARD OPERATING PROCEDURES:

ISBEC Committee members declare this document to be the Standard Operating Procedures and record their agreement to abide by these.

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Organization and operations of ISBEC are in compliance with the Indian GCP, ICH-GCP and applicable Regulatory requirements.

I.Name:

This committee is known as the Inter System-Biomedica Ethics Committee (ISBEC). Thename will remain unchanged until the members choose to change it by a vote of three-fourths of the current strength. It will also be called BahuVaidyakShastra – Sadvritta – Samiti.

Inter System Biomedica Ethics Committee (ISBEC) is registered with Drug Controller General India for approval and review of BA/BE studies. ISBEC has Ethics Committee Registration No. ECR/108/Indt/MH/2013 issued under Rule 122DD of the Drugs & Cosmetic Rules 1945 wef September 2013 for a period of 3 years.It has been re-registered with DCGI in 2018.

II.Purpose:

The primary purpose of this Committee is:

(i) To ensure the protection of the rights, safety and well-being of human subjects involved in clinical and biomedical research projects.

(ii) The secondary aims of the committee are to uphold the basic principles of ICMR and ICH guidelines on research in human subjects.

(iii) To guide and assist the investigators to conduct research according to the Good Clinical Practice (GCP) laid down in ICH and in CharakSamhita and SushrutSamhita.

(iv) To conduct training programmes to educate its committee members, and members ofmedical community in Clinical Research.

III. Membership:

The membership consists of 15 regular members from different systems of medicine who collectively have the expertise and the experience to review and evaluate the scientific, medical and ethical aspects of a proposed research project. A list of Committee members, their qualifications and affiliations (e.g. hospitals, universities, clinics, social,legal work, etc) is maintained in the Committee's records.

There will be a panel of experts (scientific advisory committee) and an expert may be invited to attend the meeting as per the needs of the project.

ISBEC functions as an Independent Ethics Committee. It reviews ethics of the clinical and biomedical Research proposals submitted by research institutions, teaching,institutions,

pharmaceutical industries and Clinical Research Organizations (CROs)as well as independent researchers/research scholars. It ensures the rights, safety and well-being of subjects participating in research.

The Chairperson in consultation with the other ethics committee members is responsible for appointing a new member for the ethics committee after evaluating the technical expertise, skills and abilities towards their respective. The performance is evaluated by the chairperson every year in annual general meeting of ISBEC.

1. **Members and their tenure:**

a) The tenure of membership is for a continuous period of up to 5 years.
b) Extension of membership is determined by a vote of two thirds or more of the members present in a quorum at a regular committee meeting.
c) There is no limit to the number of times that membership can be extended.
d) New members will be elected to replace members who have resigned or whose tenures of membership have expired, according to the process described in this document.

2. **Regular Membership:**

"A person who studies only one branch of science cannot arrive at proper conclusions. (Sushruta)"

The committee shall have specialists and essential members from different Systems of Medicine recognized in India.

a) The regular members of the Committee will ideally include at least 7 and a maximum of 15 individuals as follows:
    - A majority of members from the medical profession with expertise and experience in diverse health specialitieseg. a physician, pharmacologist, gynecologist, pediatrician.
    - Anexpert from each of the traditional systems of medicine like Ayurveda, Homeopathy, Unani and Siddha medicine.
    - A lay person
    - A person with legal background
    - A basic scientist/ pharmacologist
    - A social scientist

b) The Committee shall have representation from both men and women.

c) At least 3 of the members and the Chairman for that project meeting will be independent of the institution which has submitted the research proposal. If an institution in which the Chairman is working in any capacity submits a project, another independent member will be requested to chair the ISBEC meeting related to that particular project.

d) Additional members from special areas like journalism, consumer protection activity or any specialty of bio-medical field may be included in the committee for a particular project if considered appropriate by the committee members.

3. **Chairperson :**

The Committee members will elect a Chairperson from amongst themselves.

a) The Chairperson is responsible for conducting all committee meetings and all discussions and deliberations pertinent to the review of research proposals.

b) The Chairperson presides over all elections and administrative matters pertinent to the Committee's functions.

c) The Committee will also appoint oneVice Chairperson. He/ she will officiate in absence of the Chairperson, and will have all the powers of the Chairperson for the meeting. The Committee can also request any other member to be the Acting Chairperson to conduct a meeting.

4. **Member Secretary:**

(a) The Committee members will elect 2 Member Secretaries from amongst themselves.

(b) In consultation with the Chairperson, both the Member Secretaries will be responsible for the following functions.However one Secretary may look mainly after the project committee, minutes, approval letters, DCGI correspondence etc and the other may mainly look after the accounts, auditing, liaison with the GOI etc.The responsibilities of Member Secretary include:

- Receiving all research proposals.
- Maintaining all related documents-list of EC members, their bio-data, guidelines and SOPs, minutes of all meetings and accounts.
- Establishing time limits for receipt of reviewers' comments.
- Preparation and dissemination of agenda for all Committee meetings.
- Dissemination of related project materials to the EC members as required.
- Inviting special attendees from relevant therapeutic areas to the scheduledmeetings as decided by Committee members.

- Notification of review outcome to investigators of research proposals.
- Retention and safekeeping of all records and documents.
- Any other duties assigned by the Chairperson.
- Preparation of minutes (within 7 days of meeting), and circulation of same to members, after approval of Chairperson.

c) The Committee shall also elect 1 or 2 Joint Secretaries from amongst the members who shall assist the Secretaries in day to day function of the committee including writing of minutes and reports.

The Chairperson, Acting Chairperson, Vice Chairperson, and both Member-Secretaries are authorized to sign letters on behalf of ISBEC.

5. **Election of New Members:**

New Members are elected under the following circumstances.

a. When a regular member completes the tenure and does not wish to continue membership

b. If a regular member resigns

c. If a regular member is unable to continue working in the committee

d. If a regular member fails to perform the duties described in this document or on specific grounds as judged by the chairperson.

e. If a regular member retires from the position which he/she was working i.e. the biodata is , the member, if approved by the Committee , continues to remain a member.

f. A new member will be from the same category / area as that of the member being replaced.

IV. Responsibilities of the Committee:

1. The primary responsibility is the protection of rights and confidentiality of research subjects.

2. The Committee will also uphold the investigator's right to the confidentiality of proprietary information. The Committee Members will be required to sign the Conflict of Interest & Confidentiality Agreement (as per Appendix A)

3. The Committee will review all research proposals submitted to it within specified time limits.

4. The Committee will review the qualifications of all investigators participating in the proposed research study. In projects related to traditional systems of medicine at least one investigator or co-investigator shall belong to that system of medicine.

The committee will maintain concise and clear document of its views on the research proposals.

3. The committee will review the progress of each ongoing research study at appropriate and specified intervals, usually at one year.
4. The committee will review the background information or review of literature, the method of preparation of the study drug as claimed by the investigators, the subject selection criteria, proposed investigations including quality controls and liabilities of the budgeting authorities so that the interests of the research subjects are protected. In case of traditional medicines the procedures shall satisfy the requirements of the WHO, ICMR and the methods specified for biological standardization for preparation of Traditional Systems of Medicine in India.
5. If part of the study involves animal experimentation, the EC will review and apply guidelines for animal experimentation. A veterinary expert or an expert in animal experimentation may be invited as a special member.
6. Scientific Advisory Committee(Panel of Experts): The Chairman in consultation with Committee members can form separate panel of expert/experts, based on their special expertise to be member of Scientific Committee. They will be invited to review a research proposal only, and cannot participate in voting on the research proposal. The opinion of these special expertise will be minuted.

V. STATEMENT OF GENERAL PRINCIPLES

Any biomedical research or experimentation shall be as per the details given in the Statement of General Principles (as per Appendix B).These are based on

a. Respect for persons (autonomy)
b. Beneficence
c. Non-maleficence and
d. Justice

The highlights of Appendix B are as follows (based on ICMR Guidelines, 2017):

1. Principles of essentiality whereby, the research entailing the use of human subjects is considered to be absolutely essential.

2. Principles of voluntariness, informed consent and community agreement whereby, research subjects are fully apprised of the research and the impact and risk of such research on the research subject amid others, and freedom to withdraw anytime.
3. Principles of non-exploitationand protection of vulnerable population.

4. Social responsibility- harmony should not be disturbed.
5. Privacy and confidentiality-Any publication arising out of research should uphold the privacy of the individuals by ensuring that photographs or other information that may reveal the individual's identity are not published. A specific re-consent would be required for publication, if this was not previously obtained. Data access only to persons identified, unless legally required . Some information may be sensitive and should be protected to avoid stigmatization and/or discrimination (for example, HIV status; sexual orientation such as lesbian, gay, bisexual, and transgender (LGBT); genetic information.

While conducting research with stored biological samples or medical records/data,coding or anonymization of personal information is important and access to both samplesand records should be limited.Data of individual participants/community may be disclosed in certain circumstances with the permission of the EC such as specific orders of a court of law, threat to a person's or community's life, public health risk that would supersede personal rights to privacy, serious adverse events (SAEs).
6. Risk minimization- at all levels, appropriate safety measures, compensation methods: Researcher, sponsor and EC should maximize benefit to the participant.EC assesses Risk/Benefit ratio before approving the project.EC will assess new risks or benefits during the course of the study and take necessary action.
7. Professional competence- Plan, Conduct, Evaluate and Monitor by professionally competent individualswho act with total integrity and impartiality.
8. Maximization of benefit- design research in such a way so as to maximally benefit participants and society.
9. Principles of institutional arrangements whereby, there shall be infrastructure availability and commitment to the 4 principles.
10. Transparency and accountability- Research plan, and outcomes are brought into public domain through registries, reports and publications.
11. All stake holders have responsibilities and these are identified at the beginning of the project.
12. Environmental protection- This is assured at each stage of the project.

These 12 principles laid down under Statement on General Principles are common to all areas of biomedical research.

VI. FUNCTIONS AND OPERATIONS:

1. Meetings:

a) The Committee will hold meetings once every 8 weeks and morefrequently if required.Meetings will be held on the anySaturday of every month as far as possible.

b) All regular members will receive notification of the scheduled meetings at least1-2weeks in advance. Only in exceptional instances the time schedule for informing the members and circulation of projects can be reduced at the discretion of the Chairperson / Member secretaries.

c) All projects will be submitted to the members at least 2 weeks prior to the meetings.

The projects will be previewed by at least 5 the essential members. The preview will be for both scientific content and ethical principles. The primary reviewer will be the chairperson and the secondary reviewer will be the member secretary. If required the chairperson will nominate another primary reviewer depending on the projects to be reviewed. In special cases an expert outside the committee may also be invited if required. He/ She will not have voting rights.The regular members, who are not able to attend the meeting for some reason, can submit written comments to the Chairperson. If no objections or queries are raised by any of the members, the project will be approved by a minimum quorum of five members present- (i) Chairperson or acting chairperson (ii) Member secretary (iii) Lay person iv) Legal expert v) Social scientist. More members or special invitees will attend if the chairperson deems it necessary.Meetings are valid provided there is a minimum quorum of 5 persons as mentioned above.

2. **Hierarchy:**

a)There will be 1 Chairperson, 1 Vice-chairperson, 2 Member-Secretaries and 2 Joint Member-Secretaries

b) The Chairperson is the head of the Committee and all the minutes of the meetings and approvals of projects will be submitted to him / her. The decision to approve, postpone or disapprove any project will be a joint decision of the Committee.If due to some reason the Chairperson is unable to attend the meeting the Acting Chairperson or Vice Chairman or any member approved by the chairperson will chair the meeting.

c) The Member-Secretaries are the guardians of all the documents and funds in the committee's possession.

d) The proceedings of all meetings will be in English and recorded in the form of minutes.

e) The Secretariesand Joint Secretaries are responsible for the co-ordination and recording of the minutes.

f) Majority vote: A majority vote for approval, request for modifications or information, suspension or termination of the research proposal or ongoing study is defined as one half of the members in attendance at the review meeting. The number of votes in favour and against will be recorded. If the number is uneven one person more than half will determine the majority. Absent members will not have a vote unless they have read the project and communicated their opinion in writing or by e-mail.

All voting members present at the review meeting will vote on the research proposal. Absent members will not have a vote.

If any member(s) of the committee is/are participating in the research project under discussion, they will opt out from all deliberations on voting for the project.

Any persons listed as an investigator/co-investigator or may have a conflict of interest will refrain from voting. This is to be recorded in the minutes of the meeting.However, the investigator/co-investigator may be called upon to provide clarifications on the study protocol.

If quorum is lost during a meeting voting cannot take place until it is restored.

3. PROCEDURES:

All communications with ISBEC will be in writing.

The completed applications and proforma will be accepted in the office of ISBEC and circulated to all the Ethics Committee members nominated by the chairperson. At the meeting of all the members held, each project or trial is discussed and decisions arrived at. If necessary, the concerned investigator is invited to attend the meeting to provide clarifications on the queries raised.

A. Review of proposed study:

For initial review of research projects all EC members willreview the following materials in depth:

- ♣ The protocol and IEC application.
- ♣ Proposed patient information sheet, informed consent process and the consent document.
- ♣ Recruitment procedures and materials related to recruitment if any.
- ♣ One primaryreviewer (usually the chairperson) for the individual projects will review the proposal,in addition to the secondary reviewer (usually the secretary) in depth as follows:
- ♣ The complete protocol.
- ♣ The investigator's brochure.
- ♣ The sample consent document.
- ♣ Statement on confidentiality and volunteer compensation when applicable.

B. Outcome of review:

The committee documents its views in the following manner:

a) Permission of commencement Passed in principle but clarification required for technical queries (The Chairman in consultation with member –secretary and or an expert member or the joint secretary is authorized to recommend the approval of the proposal, after appropriate clarifications are received).

b) Project passed in principle but permission of commencement is withheld till approval of Drug Controller General of India is obtained to conduct clinical studies with new drugs.

c) Clear disapproval giving reasons.

C. Review of On-going Studies:

The Committee conducts a review of each on-going study by obtaining the status report (Appendix-E) from the investigator at intervals appropriate to the degree or risk to the human subjects, but at least once a year. The investigator must promptly report the following to the committee:

a) Deviations from or changes in the protocol made to avoid immediate hazards to the trial subjects or for valid administrative reasons.

b) Changes increasing the risk to subjects and/or affecting significantly the conduct of the trial.

c)All adverse events as well as adverse drug reactions (ADRs) both serious and unexpected are reported on the CIOMS forms to the EC within a specified time (1 week). Minor ADRs will be also be reported with each final report or annual report. A copy of the forwarding letter for the report to the DCGI should also be submitted to ISBEC along with the CIOMS forms.

d)New information that may affect adversely the safety of the subjects or the conduct of the trial.

e)The Committee can recommend termination of ongoing trials for reasons like patient safety, or non-compliance on part of Investigator.

The approval of any research project will remain valid for a period of one year fromthe date of letter of approval: A status report of the project should be submitted to ISBEC before the date of expiry of the approval.

During the meeting of ISBEC for a follow up review all members will review the following:

- The protocol - At least two members will review in depth the complete protocol including any protocol modifications previously approved by the ISBEC.
- The consent document, and any modifications.
- A status report on the progress of the research.

D. Follow up review will continue until:

- The research is permanently closed to the enrollment of new subjects;
- All subjects have completed all research-related interventions; and
- Collection and analysis of private identifiable information has been completed.

- If an investigator does not provide continuing review information to the ISBEC or if ISBEC has not approved a protocol before the expiry of date of approval:
- All activities will have to stop, including recruitment, advertisement, screening, enrollment, consent, interventions, and collection of private identifiable information.
- Interventions and interactions on ongoingsubjects may continue only if ISBEC finds an overriding safety concern / ethical issue in the best interests of individual subjects.
- New enrollment of subjects will not take place.

ISBEC may require certain protocols be reviewed more frequently than annually because of any of the following:
1. Noncompliance history
2. Marginal Risk / Benefit Ratio
3. As necessitated by protocol

E. SAE Review, DSMB and SAE handling:
E1. Any SAE will be reviewed immediately by the chairperson of ISBEC and action will be taken as per the DCGI guidelines.
E2. Data Safety Monitoring committee for ISBEC can be constituted withat least3 members:

i) Chairperson ii) Vice Chairman iii) Member Secretary.

External experts can also be invited.
The functions and charges for the utilization of DSMB by projects investigators or sponsors will be independent of Project evaluation and monitoring charges. Projects approved by another Ethics Committee may also be taken up by DSMB.
E3. Flow chart

The researcher is responsible for reporting all SAEs to the EC within 24 hours ofknowledge. Reporting of SAE may be done through email or fax communication(including on non-working

days). A report on how the SAE was related to the researchmust also be submitted within 14 days.

The EC is responsible for reviewing the relatedness of the SAE to the research, as reported by the researcher, and determining the quantum and type of assistance to be provided to the participants. Medical management should be free if the harm is related to the research. All AEs should be recorded and reported to the EC according to a pre-planned timetable, depending on the level of risk and as recommended by the EC.

F. Reports required from investigators:

ISBEC will evaluate the follow up reviewto determine:

• The criteria for approval of research are maintained.
• The protocol verification from sources other than investigators.
• The current consent document is still accurate and complete.
• Any significant new findings that have arisen from the review process and that may be related to subjects' willingness to continue participation are informed to the subjects

The investigators should submit the following reports to the Committee:

i) Annual Progress Report: The first report should be submitted within thirty (30) days of completion of the year following the date of first approval. Subsequent reports will be submitted at one yearly intervals following the first report. In case of short term studies eg bioequivalence, the report may be submitted earlier (within 6 months).

ii) All proposed changes in a research activity.

iii) The premature completion of a study.

iv)Deviations from, or changes of the protocol to eliminate immediate hazards to the trial subjects, changes increasing the risk to subjects and/or affecting significantly the conduct of the trial.

v)All adverse events and adverse drug reactions (ADRs) thatare both serious and unexpected.

vi) New information that may affect adversely the safety of the subjects or the conduct of the trial.

G. Publication Policy:

The public's trust in published research is an essential component of ethical andresponsible research.

Research that is completed, irrespective of results, must be published, since it would beunethical to expose another set of participant/patients/volunteers to the same risks toobtain the same results.

Researchers should provide results of study in the public database of the Clinical Trial Registry-India (CTRI).

VII. GUIDELINES FOR SUBMISSION OF RESEARCH PROPOSAL:

Applicants for evaluation of research projects-
ISBEC will consider the applications from the following:

- **Principal Investigators**
- **Sponsors**
- **Clinical Research Organisation (CRO)**
- **Individual researchers or postgraduate students**

1. A recognized institution/center wanting to conduct any prospective, retrospective studies (on drugs, investigational techniques, behavioral or dietary interventions, surgical techniques or use of biomedical devices) involving human subjects or patients can submit the proposed research protocol (RP) along with the case record form (CRF) drawn as per the GCP / ICMR guidelines.

2. The protocol should be typed in English. It should have the names, designations and dated signatures of the principal investigator (PI) and Co- investigators (CI). It should be submitted through the head of the institution or appropriate authority. If the study involves collaboration with another department or outside center, the collaborators' signatures should also be included. The proforma should include details of the clinical phase of drug trial, type of patients, place of study, duration of study, investigations to be carried out, the names of the sponsoring agencies, the cost of the trial to the sponsors and the cost to each of the participating centers in terms of manpower, man hours and actual costs, the permissions from Drugs Controller General of India (DCGI), ICMR or any other appropriate authorities,import permissions if the drug is imported and theexisting facilities and infrastructure of the institutes / centers conducting the studies.

3. All studies on drugs not marketed in India or a new combination or ingredients marketed separately, or plan to use any drug (from India or from outside) require permission from DCGI. A copy of the permissions should be submitted. If the DCGI permission is not available, the copy of the application to the DCGI can be submitted to ISBEC which may give a provisional approval subject to DCGI permission. The study cannot begin until copy of the DCGI approval is received, by ISBEC.

For drugs investigated or marketed internationally the investigational status and marketing status in all different countries should be mentioned. For multicentric studies the names of all centres and

investigators should be made available to the Ethics Committee and appropriate permissions from DCGI (when required), ICMR , Health Ministry and HMSC should be submitted to ISBEC.

For Ayurvedic, Homeopathic, Unani or herbal drugs, a copy of the manufacturing license issued by FDA, to the company or institute concerned, will facilitate clearance from the Committee.

Alternatively data of the ingredients as mentioned in Standard Reference Text of the Alternative Systems of Medicine will be required.

In addition, the product under investigation should have identifiable biological markers (Passport data) as well as SOP for its manufacture, to ensure Standardization.

For Ayurvedic, Homeopathic, Unani or herbal drugs, a copy of the manufacturing license issued by FDA, to the company or institute concerned, will facilitate clearance from the Committee.

Good Ayurvedic Research Practices (GARP): Testing ofAyurvedic products will be consistent with Modern Standard of Ethics in Medicine,as per the practices mentioned in Good Ayurvedic Research Practices (as per Appendix C).

In a study involving Traditional Systems of Medicine , an investigator, who is a specialist in that system, has to be included as a co-investigator.

Similarly, an expert member from that system should be present in all the proceedings of the ISBEC related to that study.

VIII . DOCUMENTS REQUIRED FOR SUBMISSION:

ISBEC will require the following documents to be submitted by the applicant for evaluation of project. All documents including the covering letter should be in the form of word file or PDF attachments.

i) Prescribed form of ISBEC (Appendix D)

ii) Covering letter indicating the title of the study, number of subjects, and names of centers (sites) to be involved.

iii) Investigator's brochure with data on preclinical and clinical studies carried out till date and complete safety data

iv) Study protocol and amendments if any

v) Case Record Form

vi) Patient information sheet alongwith thetranslations in regional languages

vii) Copy of the Informed Consent Form alongwith the translations in regional languages

viii) Subject recruitment procedures and advertisements if any

ix) Details of study sites

x) Copies of permission from DCGI or any appropriate regulatory authorities/ or copy of application to regulatory authority.

xi) Study monitoring procedures if any including Data Safety Monitoring Board (DSMB) ifapplicable

xi) Monitoring procedures if any

xii) Copy of permission from any other Ethics Committee for the same study at another centre, copy of Health Ministry Screening Committee (HMSC) for International Collaboration

xiii) CTRI registration number

xiv) Copy of registration certificate or Quality Control certificate of the laboratories which will participate in laboratory procedures

xv) Biodata and copy of recent GCP certificate of the Principal Investigatorand Co-Investigator

xvi) Package insert and label of the IP

xvii) Publication Policy

IX. FEES FOR EVALUATIONS:

Auser fee as determined is chargeable for all sponsored projects. The amount is to be paid in advance along with the above documents.

Academic Institutions or Charitable trusts also will be charged a nominal processing fee to be paid in advance.The fee will be rendered as a cheque or demand draft in the name of "Inter System Biomedica Ethics Committee (ISBEC). Separate fees will be charged for Site approval visit, project monitoring visit and a DSMB if required. Direct online Bank transfer to ISBEC account may also be possible.

The expenses of running ISBEC office and various meetings as well as the honorarium to the members is incurred from the user fees. The amounts of user fee as well as the honorarium are approved by all members at each Annual General Meeting.

X. Criteria for approval for research projects:

1. **Risk to the vulnerable populations:**ISBEC shall specifically look into the details of the category of subjects to be recruited in a research study. All members assigned for a project by the Chairperson will evaluate the protocol the Chairperson in consultation with the other ISBEC members will assign a primary reviewer with appropriate scientific expertise to conduct in depth review of the protocol. The chairperson will ensure that at least one person

knowledgeable about or experienced in working with such subject and one lay person (member) will be present at each meeting. The Chairperson in consultation with the other ISBEC members decides whether to obtain consultation from another appropriate scientific and representational expertise.

The vulnerable populations are in the following category:

i) Children and young persons below 18 years of age
ii) Older persons above 75 years of age
iii) Mentally challenged
iv) Students
v) Employees
vi) Prisoners
vii) Military personnel
viii) Physically handicapped
ix) Seriously ill, terminally ill, bed-ridden
x) Pregnant women
xi) Lactating mothers
xii) Extremely poor
xiii) Subjects likely to be vulnerable to coercion or unduly influenced e.g. in transit camps in floods.

These subjects are not independently capable of determining the risk/ benefit ratios and these subjects are normally not included in the usual clinical trials. Research on these subjects cannot be undertaken unless it is of definite benefit to the mental and or physical health of the subjects. Care will be taken that such studies are undertaken only by authorized institutions and by expert investigators. The social component may have to be fulfilled by the investigative agencies when required and additional safeguards must be included to protect their rights and welfare.

2. Minimisation of risk to research participants:

ISBEC will take into consideration, the following requirements, in order to approve the research project:

i) Risks to subjects is minimized by using protocol methodology withsound research design.
i) Risks to subjects is minimized when appropriate by using procedures being performed in the study for diagnostic or treatment purposes.

ii) Risks to subjects is reasonable in relation to the potential benefits if any and the importance of knowledge that might benefit medical research
iii) Selection of subjects is equitable
iv) In making this assessment ISBEC will take into account the purpose of the research and the setting in which the research will be conducted and will particularly cognizant of the special problems involving the vulnerable populations such as children, pregnant women, mentally disabled persons, prisoners, and economically or educationally disadvantaged persons.
v) ISBEC will review the inclusion and exclusion criteria for research subjects to ensure equitable selection of subjects.

4. **Privacy:** ISBEC will determine whether the activities in the research project constitute any violation of privacy. For this purpose ISBEC will look into sources for recruitment of subjects, information on storage of data on subjects, and subjects' expectation of privacy. The investigators must have access to the subjects and the information.

5. **Confidentiality**: ISBEC distinguishes between confidentiality and anonymity. If anyone including the investigator can readily ascertain the identity of the subjects from the data then the research is not anonymous. ISBEC will determine if appropriate protection is in place to minimize the likelihood of the information being inappropriately divulged. The level of confidentiality protections should be commensurate with the potential of harm from inappropriate disclosure.

6. A project that is not scientifically sound cannot be ethical. ISBEC will look into the scientific aspect and approve projects which are scientifically valid.

7. ISBEC will approve projects with the identified Principal Investigator provided the biodata is available and is satisfied that the person is qualified and preferably has undergone GCP (Good Clinical Practice) training. He/ She will have to give an undertaking as required for Schedule Y.

8. The centre or site and laboratory intended for conducting the study will also have to be approved by ISBEC.

9. A trial monitoring visit may be conducted by ISBEC member (s) during the study period for continued approval of the project.

XI. REPORTING OF NONCOMPLIANCE:

All projects and status reports will be reviewed periodically by the chairperson. Any noncompliance by the PI, sponsor or CRO with respect to the conduct of the trial and the reason for the same will be reported by the applicant to the chairperson who will decide the action to be taken as per the seriousness of noncompliance. Noncompliance will be reported as per Appendix I.

Termination or suspension of the Research Project/ongoing study

The validity of approval of research protocol will be 1 year from the date of issuance of approval letter by ISBEC

1.**Validity of approval**: ISBEC will issue a letter of approval after a project has been presented, or circulated, and the modifications, if any, have been examined by the members assigned by the chairman. Once the approval is given it shall remain valid for a period of one year. The Principal Investigator or the applying agency shall inform ISBEC as soon as the project starts and will give 6 monthly or yearly progress reports. They will also inform any adverse events as per the schedule depending on the severity.

Notification of Review Outcome

The outcome of committee review is recorded in writing within a week of the date of review and conveyed to the investigator within a further week.

The IEC's notifications to investigators include:

- Its decision to approve, disapprove, or require modifications to secure approval of research.
- Any modifications or clarifications required by the IEC as a condition for IEC approval.
- When the IEC does not approve or approves with modifications, a statement of the reasons for its decision and an opportunity for the investigator to respond in person or in writing.

Procedures for Appeal

For research proposals rejected by the Committee, the applicant may appeal for a repeat review within four to eight weeks of the receipt of the Committee's decision. While doing so, the applicant shall give justification relevant to the issues/objections raised by the committee. In such appeal cases, the committee considers inviting independent experts in the relevant field as invitees who may give additional assessment of the research proposal.

2. Expedited review

The Committee uses expedited review procedure in case of minor changes in the previously approved research. The expedited review is also used when the amendment appears to involve no more than minimal risk to the study subjects.

Under an expedited review procedure, the review is carried out by the Chairperson of the Committee, or by one or more experienced reviewers designated by the chairperson from among the members of the Committee who reviewed the proposal. The reviewers may exercise all of the authorities of the Committee except that the reviewers may not disapprove the research.

The Committee adopts a method of keeping all members of the Committee informed of these approvals under the expedited review procedure.

Only the Chairperson makes the decision to allow an expedited review and this should be recorded as such.

An experienced reviewer is an expert on the subject and must have served on the ISBEC for six months with experience in reviewing of research protocols.

An expedited procedure may be used to conduct initial review and continuing review includes the proposals presenting no more than minimal risk to research participants.

Minor changes are defined as changes that involve minimal risk procedures and/or do not increase the risk or decrease the potential benefit to subjects, do not involve one or moreof the regulatory criteria, eg. changes in key personnel, non-significant changes in sample size, an addition of a site, etcas given below:

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

Clinical studies of drugs and medical devices only when -

i. research is already approved drugs except when studying drug interaction or conducting trial on vulnerable population or

ii. Adverse Event (AE) or unexpected Adverse Drug Reaction (ADR) of minor nature is reported.

4. Research involving clinical materials (data, documents, records, or specimens) that have been collected for non-research (clinical) purposes.
5. When in emergency situations like serious outbreaks or disasters a full review of the research is not possible, prior written permission of Chairperson may be taken before use of the test

intervention. Such research can only be approved for pilot study or preliminary work to study the safety and efficacy of the intervention and the same participants should not be included in the clinical trial that may be initiated later based on the findings of the pilot study.
The reviewers evaluate whether research undergoing initial or continuing review using the expedited procedure meets all applicability criteria.

3. Expedited Review Procedures
When submitting applications for initial or continuing review using the expedited procedure, investigators must submit all applicable materials
A. Initial and Continuing Review and Minor Changes (Amendments) to Previously Approved Research
1. ISBEC will initially review the materials submitted to confirm that the research meets the applicability criteria and one or more categories of research eligible for expedited review.
2. For all review, the complete protocol file and relevant minutes from previous ISBEC review(s), as applicable, will also be available.
3. The expedited reviewer(s) will perform an in-depth review of all submitted materials,
4. For continuing review, ISBEC will also determine the following

- Whether the protocol needs verification from sources other than the investigators that no material changes occurred since previous IRB review,
- That the current consent document is still accurate and complete.
- Any significant new findings that arise from the review process and that may relate to participants' willingness to continue participation will be provided to participants.

When reviewing proposed research activities using expedited procedures, IRB reviewers may take one of the following actions:

- Approved
- Modifications Required (to secure approval)

When an expedited reviewer cannot take one of the actions above, the research will be referred for review by the convened IRB. Reviewers may not disapprove research by expedited review.

In conducting initial or continuing review, the reviewer must determine that all applicability criteria are met and that all research activities fall into one or more categories of research allowing review by the expedited procedure.

In conducting review of modifications to a previously approved protocol, the reviewer must make sure that the modification is a minor change as defined by policies and procedures.
When the convened IEC requests substantive modifications or clarifications that are directly relevant to the criteria for approval of research and require more than simple concurrence, the response goes back to the convened IEC.
When contingent modifications of the convened IEC not directly relevant to the determinations required by the IEC, they are reviewed by the IEC chair or IEC member designated by the IEC chair.
The reviewer is provided and reviews the investigator's current curriculum vitae or other documentation evidencing qualifications.

4. Review of Amendments to the Approved Research Proposal.

1. All amendments to the approved research proposal shall be submitted to the committee Chairperson immediately before its review.
2. No changes in the protocol, case record form and/or ICF can be initiated without prior written approval from the committee, except when necessary to eliminate immediate hazards to the subject, or when the change(s) involve only logistical or administrative aspects of the trial (e.g. change of monitor/s, telephone number(s).However these changes should be communicated by the investigators to the EC at the earliest.
3. All ISBEC members are informed of all modified documents in enough depth to discuss the information when they are present at the next meeting. For review of modifications to previously approved research by ISBEC, at least one member reviews all modified documents in-depth.
4.ISBEC requires the status report from investigators to determine whether:

- The criteria for approval of research are met when the modification affects one or more criteria for approval of research.
- Any significant new findings that arise from the review process and that might relate to subjects' willingness to continue participation are provided to subjects.

5.When amendments, modifications, or changes are reviewed by the ISBEC, all members will have access to a copy of all documents submitted by the investigator. Minor changes to the protocol or consent forms may be administratively approved.
6.Any changes in approved research initiated without ISBEC approval to eliminate apparent immediate hazards to the subject have to be:

- Promptly reported to the ISBEC.

- Reviewed by the ISBEC to determine whether the change is consistent with ensuring the subjects' continued welfare.

5. Review of Advertisements for patient Recruitment.

All advertisements are reviewed and must be approved by the ISBEC prior to their implementation in the study.

A. The ISBEC will review:

• The information contained in advertisements.
• The mode of their communication.
• The final copy of printed advertisements.
• The final audio/video taped advertisements

The ISBEC reviews advertising to ensure that advertisements:

- Do not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.
- Do not include language that makes or appears to make research subjects waive any of their rights.
- Do not emphasize the payment or the amount to be paid, by such means as larger or bold type.
- Do not promise "free treatment" when the intent is only to say subjects will not be charged for taking part in the investigation.
- Are limited to the information prospective subjects need to determine their eligibility and interest, such as:

• The name and address of the investigator and research facility.
• The purpose of the research or the condition under study.
• In summary form, the criteria that will be used to determine eligibility for the study.
• A brief list of participation benefits, if any.
• The time or other commitment required of the subjects.
• The location of the research and the person or office to contact for further information.
• Do not make claims, either explicitly or implicitly, about the drug, biologic or device under investigation that are inconsistent with labeling.
• Do not use terms, such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational
• Do not include compensation for participation in a trial offered by a sponsor to involve a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

B Payments to participants / subjects in research:

The ISBEC reviews payments to determine that:

- The amount of payment and the proposed method and timing of disbursement is neither coercive nor presented undue influence.
- Credit for payment accrues as the study progressed and is not contingent upon the subject completing the entire study.
- Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn.

The ISBEC prohibits:

- Payments to professionals in exchange for referrals of prospective subjects("finder's fees").
- Payments to subjects in exchange for referrals of prospective subjects ("finder'sfees") unless they are judged not to increase the possibility of coercion or undue influence on subjects by using unreasonable compensation or unreasonable conditions for distribution of compensation.
- Payments designed to accelerate recruitment that are tied to the rate or timing of enrollment ("bonus payments") unless they are judged not to interfere with providing prospective subjects with sufficient opportunity to consider whether to participate and do not increase the possibility of coercion or undue influence on investigators or subjects.

6. Suspension or Termination of IEC Approval.

A. **Suspension & Termination Policy**

a) Suspension means a temporary withdrawal of approval of some or all research, or a permanent withdrawal of approval of some research activities. A suspended protocol requires continuing review.

b) Termination means a permanent withdrawal of approval of all research activities. A terminated protocol does not require continuing review

The ISBEC could suspend or terminate approval of research that:

- Is not being conducted in accordance with the ISBEC's requirements.
- Has been associated with unexpected serious harm to subjects.

The principal investigator,sponsor and regulatory bodies are authorized to suspend or terminate research on an urgent basis, which should be reported to ISBEC immediately.

When IEC approval is suspended or terminated, the IEC or the person ordering the suspension or termination:

- Considers actions to protect the rights and welfare of currently enrolled subjects.
- Considers whether procedures for withdrawal of enrolled subject take into account their rights and welfare [e.g., making arrangements for medical care in a research

study, transfer to another investigator, and continuation in the research under independent monitoring].

- Considers informing current subjects of the termination or suspension.
- Has any adverse events or outcomes reported to the ISBEC.
- Considers violation of any regulatory procedures.

B. **Reportingof suspensions or terminations**

ISBEC will report all suspensions or terminations of ISBEC approval, all serious or continuing non-compliance and all unanticipated problems involving risks to subjects or others.

Reports are made to:

- Organizational officials of Research sites
- Organizational officials of the specific sites that submitted the report leading to the IEC action
- The local regulatory authority.
- Other regulatory agencies when the research is overseen by those agencies, and they require reporting.
- The notification of suspensions or terminations of IEC approval, serious or continuing non-compliance and unanticipated problems involving risks to subjects

XII.Policy for On-going Training of Ethics Committee Members& New Members/Investigators.

a) All members will be required to know latest ICMR and DCGI guidelines, schedule Y of Drugs & Cosmetics Act and ICH/GCP guidelines.

b) The Chairperson identifies the training requirements of the committee members/ investigators.

c) The Chairperson and Member Secretary will update all the members with any new guidelines or modifications in the existing Regulations by national or international organizations.

d) The Chairperson with Committee members will finalize areas for training, and topics for workshop and hold one such meeting per year

e) The Chairperson in consultation with the Committee members may plan a training programme on Clinical Research for the benefit of all personnel of various specialities involved in Clinical research

f) New ISBEC members will be required to read the SOPs, sign the "agreement for confidentiality and conflict of interest" and attend a GCP workshop or update organized by ISBEC or any other competent agency.

XIII. Provisions for Monitoring Data

The investigator should provide periodic status reports at appropriate intervalsbased on the safety concerns.

Site visits can be made especially in the event of reporting of adverse events or violations of human rights.

SAE reports from the site as well as other sites are reviewed by ISBEC and appropriate action taken when required.

In case the ISBEC desires so, reports of monitoring done by the sponsor and the recommendations of the DSMB may also be sought.

The ISBEC requires the establishment of a DSMB in cases in which the risk level is more than minimal.

The following elements of the DSMB will be reviewed by the ISBEC to determine whether the DSMB has adequate potential for qualified, timely review of useful information regarding participant information:

a. Reporting mechanisms
b. Frequency of monitoring and reporting; such as subject accrual number, or length of time after study has begun
c. Qualifications and number of people serving on the DSMB and whether they have any perceived conflict of interest with the investigator or sponsor.
d. A specific list of the data to be reviewed.
e. Procedures for reviewing, analyzing and interpreting the participant data.
f. If specific end-points are anticipated in a study under scrutiny of a DSMB, a list of the actions the DSMB might take when such end-points are reached.
g. Methods of communication betweenthe DSMB and the IEC/ISBEC, and if the studyisa multi-site study
h. Methods of communication between the sites, DSMB and the ISBEC /IEC

XIV."Minutes." The ISBEC minutes must document:

1.Date, time and venue for the meeting

2. List of members attending the meeting

3. Chairperson

4. Minutes of last meeting and actions taken by the ISBEC.

5. Votes for each protocol as numbers for, against, or abstaining.

6. Attendance at the meeting.

7. Titles of projects discussed and comments and suggestions by ISBEC committee on each project

8. When an alternate member replaced a primary member.

9. Approval or disapproval of the project or suggestions for resubmission.

10. For initial and continuing review, the approval period.

11. The names of ISBEC members who left the meeting because of a conflicting interest along with the fact that a conflict of interest is the reason for the absence.

Unless documented in the ISBEC minutes, required determinations and protocol-specific findings supporting those determinations for:

- Waiver or alteration of the consent process.
- Research involving children.

12. The rationale for significant risk/non-significant risk device determinations.
13. Report on site approval visits and project monitoring visits
14. Adverse Event Reporting if any and discussion
15. Future training of members, conferences , workshops if any
16. Any other matters with the permission of the Chairperson

Circulation of Protocols, Agenda and Minutes to members:

Protocols and Agenda will be circulated only to those members who have been invited for the meeting. Minutes will be written within 1 week and approved by the Chairperson and Member Secretary. These will be circulated to all members after this approval to keep all members informed of the projects discussed and any other matters which may be discussed in the meeting eg planning of GCP training, Conferences , Monitoring visits, action taken for archival project copies, DCGI reports etc. Parts of the minutes relevant to a project will be communicated to the PI in writing (e-mail) so that appropriate action is taken and project may be resubmitted with revision. Final approval will be issued only after the original or revised protocol is approved.

XV. Records Retention&Retrieval of Documents

The Committee retains the following records for a period of at least five (5) years after the completion / termination of a study. The final report of the study including microfilms, CDs and videorecordings, if submitted, will be retained. After 5 years the hard copies of old projects will be destroyed by shredding under the supervision of the member –Secretaryor Joint secretary.
The soft copy or "back up" of all documents including agendas, minutes, SOPs, projects, monitoring reports, audits etc will be preserved in the ISBEC laptop and a separate hard disk.
The documents and soft copies will be kept in a locked cupboard which can be accessed only by the member- secretaries, joint secretaries and office staff. A fire extinguisher will be available in the same room.

The following documents will be retained:

1. Standard operating procedures (SOPs) – all versions
2. Membership listsand Biodata of all members with their signatures
3. Occupation/affiliations of the members at the time of review.
4. All documents pertinent to the research proposal.
    - Protocols.
    - ISBEC applications.
    - Scientific evaluations.
    - Reports of injuries to subjects.
    - Records of continuing review activities.
    - Correspondence between the IEC and investigator.
    - Statements of significant new findings provided to subjects.
5. Minutes of meetings.
6. Hard copies of all correspondence with the research investigator.Correspondence by e-mail will be available on-line.
7. If a protocol is cancelled without subject enrollment, IEC records are maintained for at least three years after cancellation. These records are made available to relevant statutory authorities upon request.

For initial and continuing review of research by the expedited procedure:

- The specific permissible category.
- Description of action taken by the reviewer.
- Any findings required under the regulations.

XVI.Reports to the Relevant Regulatory Authorities

The committee makes a yearly activity report for, which includes the following elements

- A quantitative evaluation of the activities of the committee in a year
- The list of the proposals reviewed in a year.
- Status of each study proposal.
- Auditor's report

An annual / 6 monthly status report of ISBEC will be submitted to the CDSCO / DCGI and concerned zonal office. The DCGI requires a quarterly report to be submitted to CDSCO headquarters and concerned zonal office by ISBEC as it is registered with the DCGI since 20th September, 2013.

XVII.Location and Business Address:

The location and business addressof the committee is as follows:
Inter System Biomedica Ethics Committee
C/o Kasturba Health Centre,
Sthanakwasi Jain AradhanaDham,
Khandubhai Desai Road, Vile Parle (West) Mumbai-400056
Tel. No. 022-2615147. E. Mail: isbec.india@gmail.com

XVIII.Amendments to the Standard Operating Procedures

1. Amendments to the Standard Operating Procedures of the Ethics Committee will be proposed in writing.
2. The proposal for amendment is submitted to the Member-Secretary.
3. The proposal for amendment is presented to the regular members at a scheduled committee meeting.
4. Only regular members vote to accept or reject the proposal amendment.
5. A proposal amendment is approved by a vote of three-fourths of the members present in a quorum at a scheduled committee meeting, rounded to the next whole number.

XIX.Conflict of interest.

Definitions:

- "Immediate Family" means spouse and dependent children.
- "Financial Interest Related to the Research" means financial interest in the sponsor, product or service being tested, or competitor of the sponsor or product or service being tested.

Involvement of the IEC member, consultant, or their immediate family in the design, conduct, or reporting of the research.

Financial interests of the IEC member, consultant, or their immediate family as follows:

Ownership interest, stock options, or other financial interest related to the research unless it meets four tests:

- Does not exceed $50,000 (more thanRs 35,00,000/-) when aggregated for the immediate family.
- Publicly traded on a stock exchange.
- No arrangement has been entered into where the value of the ownership interests will be affected by the outcome of the research.
- Does not exceed 5% interest in any one single entity when aggregated for the immediate family.

Compensation related to the research unless it meets two tests:

- Does not exceed $50,000 in the past year when aggregated for the immediate family.
- No arrangement has been entered into where the amount of compensation will be affected by the outcome of the research.

Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.

All ISBEC members will sign agreement for confidentiality and conflict of interest for all future meetings until they remain members of ISBEC (Appendix A).

At the start of each convened meeting, any member with a conflict of interest must excuse himself/herself before the discussion of the research begins, unless asked to be present to answer questions or provide information to the ISBEC.

ISBEC members are asked to self-identify research in which they have a conflicting interest, inform the ISBEC Chair (or acting Chair), and excuse themselves before convened discussion begins. Although ISBEC members are asked to self-identify conflicts, the Chair has the final authority to determine when there is a conflict and to ask a member to leave the room as necessary.

IEC members/consultants with a conflict of interest:

- Are excluded from voting.
- Are not counted towards quorum.

APPENDIX A

CONFIDENTIALITY AGREEMENT & CONFLICT OF INTEREST DECLARATION (ON LETTERHEAD OF ISBEC)

Inter System Biomedica Ethics Committee

Confidentiality and Conflict of Interest Agreement form/Financial Disclosure for ISBEC Members

In recognition of the fact, that I, Dr/ Ms/ Mr……. herein referred to as the "Undersigned", have been selected as a member of the Inter System Biomedica Ethics Committeeandwould be asked to assess research studies involving human subjects or laboratory studies in order to ensure that they are conducted in a humane, scientific and ethical manner, with the highest standards of care according to the applied national and local regulations;

Whereas, the inclusion of the undersigned as a member of the ISBEC is based on individual merits and not as an advocate or representative of a home province/ territory/ community nor as the delegate of any organization or private interest;

Whereas, the fundamental duty of an ISBEC member is to independently review research protocols involving human subjects or laboratory studies and make a determination and the best possible objective recommendations, based on the merits of the submissions under review;

Whereas, ISBEC must meet the highest ethical standards in order to merit the trust and confidence of the communities with respect to the protection of the rights and well-being of human subjects;

The undersigned, as a member of ISBEC is expected to meet the same high standards of ethical behavior to carry out its mandate.

This Agreement thus encompasses any information deemed Confidential or Proprietary provided to

the Undersigned in conjunction with the duties as a member of ISBEC. Any written information provided to the Undersigned that is of a Confidential, Proprietary, or Privileged nature shall be identified accordingly.

As such, the Undersigned agrees to hold all Confidential or Proprietary trade secrets ("information") in trust or confidence and agrees that it shall be used only for contemplated purposes, shall not be used for any other purpose or disclosed to any third party. Written Confidential information provided for review shall not be copied or retained. All Confidential information (and any copies and notes thereof) shall remain the sole property of ISBEC.

The Undersigned agrees not to disclose or utilize, directly or indirectly, any Confidential or Proprietary information belonging to a third party in fulfilling this agreement. Furthermore, the Undersigned confirms that my performance of this agreement is consistent with ISBEC's policies and any contractual obligations it may have to third parties.

Conflict of Interest

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

In accordance of the policy of ISBEC, I shall not participate in the review, comment or approval of any activity in which I have a conflict of interest, except to provide information as requested by ISBEC.

The Undersigned will immediately disclose to the Chairperson of ISBEC 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 in respect of such proposals.

Version : 06
Supercedes Version. No: 5
Effective from : 01-06-2018
Valid till : 31-05-2021

Agreement on Confidentiality and Conflict of Interest

In the course of my activities as a member of ISBEC, I may be provided with confidential information and documentation (which we will refer to as the "Confidential Information"). I agree to take reasonable measures to protect the Confidential Information; subject to applicable legislation, including the access to it, as per the Right to Information Act (RTI), not to disclose the Confidential Information to any person; not to use the Confidential Information for any purpose outside the ISBEC's mandate, and in particular, in a manner which would result in a benefit to myself or any third party; and to return all Confidential Information (including any minutes or notes I have made as part of my Committee duties) to the Chairperson upon termination of my functions as a Committee member.

Whenever I have a conflict of interest, I shall immediately inform the committee not to count me toward a quorum for consensus or voting.

I, Dr/ Ms/ Mr…….. ……have read and I accept the aforementioned terms and conditions as explained in this Agreement.

Undersigned Signature Date

Signature of Member Secretary Date

APPENDIX B:

STATEMENTS OF GENERAL PRINCIPLES:

1. Principles of essentiality whereby, the research entailing the use of human subjects 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 environment well being of the planer.

2. Principles of voluntariness, informed consent and community agreement whereby, research subjects are fully apprised of the research and the impact and risk of such research on the research subject amid others; and whereby the research subjects 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 subjects or someone on their behalf, subject to only minimal restitutive obligations of any advance consideration received and outstanding. Where any such research entails treating any community or group of persons as a research subject, these principles of voluntariness and informed consent shall apply, mutates mutandis, to the community as whole and to each individual member who is the subject of the research or experiments. Where the human subject is incapable of giving consent and it is considered essential that research or experimentation be conducted on such a person incompetent to give consent, the principle of voluntaries and informed consent shall continue to apply and such consent and voluntariness shall be obtained and exercised on behalf of such research subjects 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 subjects 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 subject involved in any research. The nature and form of the consent and the evidentiary requirements to prove that such consent was taken, shall depend upon the degree and seriousness of the invasiveness into the concerned human subject’s person and privacy, health and life generally, and the overall purpose and the importance of the research.

3. Principles of non-exploitation whereby as a general rule, research subjects 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 subjects kept fully apprised of all the dangers arising in and out of the research so that they can appreciate all the physical risks as well as moral implications of the research whether to themselves or others, including those yet to be born. Such human subjects 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 subjects either through insurance cover or any other appropriate means to cover all foreseeable and unforeseeable risks by providing for remedial action and comprehensive after-care, 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 subject and to ensure that immediate recompense and rehabilitative measures are taken in respect of all affected, if and when necessary.

4. Principles of privacy and confidentiality whereby, the identity and records of the human subjects of the research or experiment are as far as possible kept confidential, and that no details about identity of said human subjects, 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 subject concerned, or someone authorized on their behalf, and after ensuring that the said human subject does not suffer from any form of hardship, discrimination or stigmatization as a consequence of having participated in the research of experiment.

5. Principles of precaution and risk minimization whereby due care and caution is taken at all stages of the research and experiment (from its inception as a research idea, its subsequent research design, the conduct of the research or experiment and its applicative use) to ensure that the research subject and those affected by it are put to the minimum risk, suffer from no 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.

6. 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, the ethical considerations to be become in mind in respect of such 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.

7. 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 purpose 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.

8. Principles of the maximization of the public interest and of distributive justice whereby, the research or experiment and its subsequent applicative use are conducted and used to benefit all human kind and not just those who are socially better off but also the least advantaged, and in particular, the research subject themselves.

9. 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 fully 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.

10. 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 throughscientific and other publications subject to such rights are available to the researcher and those associated with the research under the law in force at that time.

11. 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 to review and remedial action at all stages of the research and experiment and its future use.

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

These 12 principles laid down under Statement on General Principles are common to all areas of biomedical research.

APPENDIX C
GOOD AYURVEDIC RESEARCH PRACTICES

Good Ayurvedic Research Practices (GARP) which are consistent with modern standards of Ethics in Medicine and as given below will be followed.

The history of Good Ayurvedic Practices (GARP) statute traces back to one of the oldest and have traditions in the history of medicine-the Charak-Samhita. The described qualities, ethics and behaviour guiding physicians were primarily meant for doing best for the patient and to do no harm. However, the complexities of modern Ayurveda research necessitate more evolved set of guidelines. An Ayurvedic Physician's ethical and scientific responsibilities besides compassion and care also involve obtaining informed consent or disclosing risk, while involved in bio-Ayurvedic research.

Documentation: All records (including written documents, electronic, magnetic or optical records, scans, x-rays, etc) that describe or record the methods, conduct and results of the study, and the actions taken. The Documents include Protocol, copies of submissions and approvals from the office of the Drugs Controller General of India, ethics committee, investigator(s)' particulars, consent forms, monitor reports, audit certificates, relevant letters, reference ranges, raw data, completed CRFs and the final report.

It is a standard for clinical studies or trials that encompasses the historical use, design, conduct, monitoring, termination, audit, analyses, reporting and documentation of studies. It ensures that the studies are implemented and reported in such a manner that there is public assurance that the data are credible, accurate and that the rights, integrity and confidentiality of the subjects are protected. GARP aims to ensure that the studies are Ayurvedically/scientifically authentic and that the clinical properties of the "Investigational Ayurvedic Product" are properly documented.

Informed Consent

Voluntary written assent of a subject's willingness to participate in a particular study and in its documentation. The confirmation is sought only after information about the trial including an explanation of its status as research, its objectives, potential benefits, risks and inconveniences, alterative treatment that may be available and of the subject's rights and responsibilities has been provided to the potential subject. The consent is not needed when stage 1 experiential documentation is conducted in a therapeutic settings.

An Ayurvedic research project should have all the components of a GCP clinical study – Investigator's brochure protocol, monitor, standardization of Ayurvedic product and quality control, Case Record form, Adverse Drug Event Report, Drug Interaction evaluation and Ethics Committee approval.

Selection of Special Groups as Research Subjects:

Pregnant or nursing women: They 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 or Ayurvedic use has been well documented 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 or pregnant or nursing women or fetuses or nursing infants, and for which women who are not pregnant or nursing would not be suitable subjects.

a) The justification of participation of these women in clinical trials would be that they should not be deprived arbitrarily of the opportunity to benefit from investigations, drugs, vaccines or other agents that promise therapeutic or preventive benefits Example of such trials are, to test the efficacy and safety of a drug for reducing parental transmission of HIV infection from mother to child, trials for detecting fetal 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.

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

c) Clinical trials of Garbha-Raksha remedies, galactogogues or Ayurvedic modalities for better care of pregnant women have to be very carefully scrutinized, both ethically and technically.

d) 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.

Children:

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

b) The purpose of the research is to obtain knowledge relevant to health needs of children. For clinical evaluation of an Ayurvedic drug the study in children should always be carried out if stage I clinicals trials in adults. It can be studied earlier only if the drug has a therapeutic value in a primary disease of the children.

c) A patent or legal guardian of each child has given proxy consent.

d) The assent of the child should be obtained to the extent of the child's capabilities such as in the case of mature minors, adolescents etc.

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

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

g) The child's refusal to participate in research must always be respected unless there is no medically acceptable alternative to the therapy provided/tested, provided the consent has been obtained from parents/guardian.

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

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

Vulnerable groups:

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

a) Research on genetics should not lead to racial inequalities:

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

c) Rights and welfare of mentally challenged and mentally differently able persons who are incapable of giving informed consent or those with behavioral disorders must be protected. The guardians' approval is essential.

d) Adequate justification is required for the involvement of subjects such as prisoners, students, subordinates, employees, service personnel etc. who have reduced autonomy as research subjects.

e) Elderly subjects selected for Rasayana - trials should be declared suitable – physically, mentally and spiritually – for the studies.

Compensation for Accidental Injury:

Research subjects who suffer physical injury as a result of their participation in the Clinical Trial are entitled to financial or other assistance to compensate them equitably for any temporary or permanent impairment or disability subject to confirmation from IEC. In case of death, their dependents are entitled to material compensation.

Obligation of the sponsor to pay:

The sponsor whether a pharmaceutical company, a government, or an institution, should agree, before the research begins, to provide compensation for any serious physical or mental injury for which subjects are entitled to compensation or agree to provide insurance coverage for an unforeseen injury whenever possible.

Communication with Ethics Committee:

Before initiating a study the investigator/institution must ensure that the proposed study has been reviewed and accepted in writing by the relevant ethics committee(s) for the protocol, written informed consent form, subject recruitment procedures (e.g advertisements) and any written/verbal information to be provided to the subjects.

The investigator should promptly report to the ethics committee, the monitor and the sponsor.

(i) Deviations from or changes of, the protocol to eliminate immediate hazards to the subjects.

(ii) Changes that increase the risk to subject(s) and/or affecting significantly the conduct of the study.

(iii) All adverse drug reactions and adverse events which are serious and/or unexpected.

(iv)New information that may adversely affect safety of the subjects or the conduct of the study.

(v) For reported deaths the investigator should supply any additional information e.g. autopsy reports and terminal medical reports.

APPENDIX D

All protocols/projects dealing with human subjects are to be preceded by the following check list irrespective of whether they are for undergraduate or postgraduate study , interventional or non-interventional study or behavioural study, and the Principal Investigator is answerable for any lapses in clinical applications.

Check list for protocol submission:

Serial No	Item	Yes	No	Not Applicable
1	Covering letter signed by the PI /Sponsor as an attachment giving the title and general information and a complete numbered list of all			

	documents submitted as listed below and any additional documents when required			
2	First Page- with Title, address, Names & Signatures of Investigators, Co-Investigators, Centres, Sponsors			
3.	Title- must include type of study, population for study, intervention or observational subject, site of study			
4	Type of Clinical study, address of centres, population to be studied, duration of study			
5	Expected cost of study			
6	Permissions from authorities like departmental or institutional head, DCGI, State authorities, marketing license, Import license when applicable, CTRI registration, HMSC permission for international collaboration			
7	Copy of EC permission from another centre if available			
8	List of project staff & Responsibilities			
9	Infrastructure facilities available, to be acquired			
10	Interventional drugs- Manufacturing batch no, stock received, preservation, shelf life			
11	Instrumental intervention- Manufacturing Licence, Model No, Year of manufacture etc			
12	Nutritional products-preparation, preservation, shelf life			
13	Sample size, study & control subjects when applicable, statistical basis			
14	Period of enrollment, Total duration of study, period for Statistical analysis- Duration of follow up when required			
15	Ayurvedic, Homeopathic, Unani or herbal drugs- manufacturing license, Passport data of plants & extracts, Certificate of analysis, details of types of extracts, formulation			
16	Preclinical data when applicable			
17	Review of Literature and rationale- old as well as recent, summary tables with authors and years of publications			

18	Purpose of the study			
19	Primary Objectives			
20	Secondary Objectives			
21	Investigator's brochure- summary of preclinical and previous clinical trial data			
22	Study Protocol with Amendments if any			
23	Case Record Form, Questionnaire, Food Frequency form, Activity form , QoL Assessment forms etc			
24	Subject information sheet with translations			
25	Informed Consent form with statement on confidentiality, insurance when applicable, translations, Assent forms for children 7 years or more, waiver of consent			
26	Information about ISBEC and Contact information on Consent form			
27	Subject recruitment procedures, advertisements			
28	Study site details, co-investigators			
29	Subject Inclusion /Exclusion criteria			
30	Treatment or Intervention details, package insert, copy of the label			
31	Assessment criteria			
32	Investigations, amount of blood to be collected at each visit and total amount collected during the study, laboratory details, QC certificates, references for methods used			
33	Monitoring Procedures including DSMB when required			
34	Criteria for discontinuation of subject or for the study, Fail Safe procedures, Details of Clinician on project for Student's project when needed, procedures for subjects excluded from study but requiring referralEg Severe anemia, complications			
35	Adverse Event and Adverse Drug Reaction Reporting forms and procedures and plan of management, Data safety, confidentiality procedures			
36	Subject Insurance details when applicable- copy of insurance policy, subject compensation details when applicable			

37	Study site details, co-investigators			
38	Biodata of PI, Co-I, Copy of Recent GCP certificate of PI, Co-I			
39	Signed undertaking by PI			
40	Publication policy			

Principal Investigator:
Signature: Date:

Appropriate fees for the evaluation will be charged depending on the type of Institute/Company submitting the project and the nature of the project.

Applicant will be informed regarding the amount to be paid, and date for the review on receipt of the proposal

A demand draft in favour of "Inter System Biomedica Ethics Committee" should be forwarded before the meeting is scheduled.

Projects on Alternative and Indian System of medicine must include an expert in the system as a co- investigator with the biodata. All collaborations must be mentioned.

APPENDIX E
STATUS REPORT

Status Report should include the following:

1. Number of subjects accrued.
2. A summary since the last IEC review of:
   -Adverse events, untoward events, or outcomes experienced by subjects.)
   -Unanticipated problems involving risks to subjects or others.
   -Subject withdrawals.
   -The reasons for withdrawals.
   -Complaints about the research.
3. Amendments or modifications.
4. Any relevant recent literature.
5. Any interim findings, including data safety monitoring reports
6. Any relevant multi-center trial reports.
7. The investigator's current risk-potential benefit assessment based on study results.

APPENDIX-F
GUIDELINES FOR INFORMED CONSENT

The informed consent document (ICD), which includes patient/participant informationsheet (PIS) and informed consent form (ICF) should have the required elements (see Box).

Item 5.1 of ICMR Guidelines should be referred to for further details and should be reviewed and approved by the EC before enrolment of participants. For all biomedical and health research involving human participants, it is the primary responsibility of the researcher to obtain the written, informed consent of the prospective participant or legally acceptable/authorized representative (LAR). Incase of an individual who is not capable of giving informed consent, the consent of the LAR should be obtained. If a participant or LAR is illiterate, a literate impartial witness should also be present during the informed consent process.

In certain circumstances audio/audio-visual recording of the informed consent processmay be required, for example in certain clinical trials including vulnerable subjects as notified by CDSCO.
Verbal/oral consent/waiver of consent/re-consent may be obtained under certainconditions after due consideration and approval by the EC. See section 5 for furtherdetails.

A. The investigator will obtain the legally effective consent of the subject or the subject's legally authorized representative. Investigators are responsible for ensuring

1. The circumstances of the consent process provide the prospective subject or the legally authorized representative sufficient opportunity to consider whether to participate or not participate.

2. The circumstances of the consent process exclude the possibility of coercion or undue influence.

3. The individuals communicating information to the subject or the legally authorized representative during the consent process provide representative information.

4. The information to be communicated to the subject or the representative during the consent process does not include exculpatory language through which the subject or the legally authorized representative is made to waive or appear to waive any of the subject's legal rights.

5. The information to be communicated to the subject or the legally authorized representative during the consent process does not include exculpatory language through which the subject or the legally authorized representative releases or appears to release the investigator, the sponsor, or its agents from liability for negligence.

B. **Documentation of Informed Consent**

1. The consent document embodies the basic and appropriate additional elements of disclosure as given below.

2. The subject or the subject's legally authorized representative will sign and date the consent document.

3. A copy of the consent document will be given to the person signing the consent document.

4. The investigator will give either the subject or the subject's legally authorized representative adequate opportunity to read the consent document before it is signed.

C. The following are the basic required elements of informed Consent form

1. A statement that the study involves research.
2. An explanation of the purposes of the research.
3. A description of the procedures to be followed.

4. An explanation of the expected duration of the subject's participation
5. Identification of any procedures that are experimental.
6. A description of any reasonably foreseeable risks or discomforts to the subject.
7. A description of any benefits to the subject or to others, which might reasonably be expected from the research.
8. A disclosure of appropriate alternative procedures or courses of treatment, if any, which might be advantageous to the subject.
9. For alternative procedures or treatment that may be available to the subject, include their important potential benefits and risks.
10. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
11. That the monitor, the auditor, the IEC, and the regulatory authority will be granted direct access to the subject's original medical records for verification of clinical trial procedures or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the subject or the subject's legally acceptable representative is authorizing such access.
12. An explanation of whom to contact for answers to pertinent questions about the research before and during the study period.
13. An explanation of whom to contact for answers to pertinent questions about the subjects' rights.
14. An explanation of whom to contact in the event of a research-related injury to the subject.
15. A statement that participation is voluntary.
16. A statement that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.
17. A statement that the subject can discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
18. Benefit sharing in the event of commercialization.
19. Right to prevent use of her/his biological sample (DNA, cell-line, etc) at any time during the conduct of the research.
20. Foreseeable extent of information on possible current and future uses of the biological materials and the data to be generated from the research and if the material is likely to be used for secondary purposes or would be shared with other, clear mention of the same.
21. Risk of discovery of biologically sensitive information and provision to safeguard confidentiality.

22. Publication, if any including photographs and pedigree charts.

Additional elements of informed consent to be applied, as appropriate:

- A statement that the particular treatment or procedure might involve risks to the subject, which are currently unforeseeable.
- A statement that if the subject is or becomes pregnant, the particular treatment or procedure might involve risks to the embryo or fetus, which are currently unforeseeable.
- Anticipated circumstances under which the subject's participation might be terminated by the investigator without regard to the subject's consent.
- Any additional costs to the subject that might result from participation in the research
- The consequences of a subject's decision to withdraw from the research.
- Procedures for the orderly termination of participation by the subject.
- A statement that significant new findings developed during the course of the research which might relate to the subject's willingness to continue participation would be provided to the subject.
- The approximate number of subjects involves in the study.
- The amount and schedule of payments.

D. **For research involving more than minimal risk:**

1. An explanation as to whether compensation is available if injury occurs.
2. If compensation is available when injury occurs, an explanation as to what it consistsof or where further information can be obtained.
3. An explanation as to whether any medical treatments are available if injury occurs.
4. If medical treatments are available when injury occurs, an explanation as to what it consists of or where further information can be obtained.

E. **"Observation of the Consent Process."**

The ISBEC may request to observe the informed consent process to ensure adequate consent

F. 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 minimal risk or when it is necessitated in emergency situations elaborated in the previousChapter. If such studies have protections in place for both privacy andconfidentiality, and do not violate the rights of the participants then IECs may waive off the requirement for informed consent in following instances:

1. When it is impractical to conduct research since confidentiality of personallyidentifiable information has to be maintained throughout research as maybe required by the sensitivity of the research objective, eg., study on diseaseburden of HIV/AIDS.
2. Research on publicly available information, documents, records, works, performances,reviews, quality assurance studies, archival materials or thirdpartyinterviews, service programs for benefit of public having a bearing onpublic health programs, and consumer acceptance studies.
3.Research on anonymised biological samples from deceased individuals, leftover samples after clinical investigation, cell lines or cell free derivatives likeviral isolates, DNA or RNA from recognised institutions or qualifiedinvestigators,samples or data from repositories or registries etc.
4. In emergency situations when no surrogate consent can be taken and the research is essential.
5. The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either that the:

• Only record linking the subject and the research would be the consent document and the Principal risk would be potential harm resulting from a breach of confidentiality.
• Research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. Procedures such as non-sensitive surveys, questionnaires and interviews may not require written consent if deemed not harmful to the participants.
• In cases in which the documentation requirement is waived, the IRB requires the investigator to provide in the application materials a written summary of the information to be communicated to the subject, and the investigator should provide an undertaking that the information collected will be used only for the purpose stated in the protocol and not beyond that. The IRB will consider whether to require the investigator to provide subjects with a written statement regarding the research. If fresh research is to be conducted from same information the project should be reviewed by the IRB.
• The only record linking the subject and the research is the consent document.

APPENDIX G
ADDITIONAL PROTECTIONS FOR CHILDREN

The ISBEC determines whether the criteria for approval of research are met when research involves children.

1. **Category 1:**

No greater than minimal risk to children is presented.

2. **Category 2:**

More than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being.

- The risk is justified by the anticipated benefit to the subjects.
- The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches.

3. **Category 3:**

More than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject.

- The risk represents a minor increase over minimal risk.
- The intervention or procedure involves experiences to subjects that are reasonably commensurate with those inherent in their actual or expected m

The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition.

4**. Category 4:**

The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.

- The regulatory agency, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, determined either:

i) That the research fell into categories 1 through 3; or

ii) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children and the research will be conducted in accordance with sound ethical principles.

APPENDIX H
ADDITIONAL PROTECTIONS: ADULTS UNABLE TO CONSENT

For adults unable to consent, the specific criteria ISBEC considers for approval of such research that provides additional safeguards to protect their rights and welfare.

- A non-therapeutic clinical trial (i.e. a trial in which there is no anticipated direct clinical benefit to the subject) should be conducted in subjects who personally give consent and who sign and date the written consent document.
- Non-therapeutic clinical trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled:

a) The objectives of the trial cannot be met by means of a trial in subjects who can give consent personally.
b) The foreseeable risks to the subjects are low.
c) The negative impact on the subject's well-being is minimized and low.
d) The trial is not prohibited by law.

e) The opinion of the IEC is expressly sought on the inclusion of such subjects, and the written opinion covers this aspect. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed

APPENDIX I
REPORTING OF NONCOMPLIANCE:

a) Non-Compliance

Failure to abide by the policies, requirements, and determination of the ISBEC, when conducting human research activities.

b) Serious Non-Compliance

An act or omission to act that resulted in increased physical, psychological, safety, or privacy risk that compromised the rights and welfare of research participants.

c) Continuing Non-Compliance

That situation in which there has been a pattern of repeated instances of failure to follow regulations, IEC policies and procedures, or determinations or requirements of the IEC

- Investigators and research staff are responsible for promptly reporting possible noncompliance to the ISBEC.
- There are several scenarios that could result in discovery of an event that meets the definition of noncompliance.

For example, complaints from subjects,members of the research team or others could contain allegations of noncompliance.

Reports from the Principal Investigator, study sponsor or study monitor of deviations or violations could contain instances of possible noncompliance.

The ethics committee determines whether the event is serious or of continuing noncompliance, or the event is not serious and not of continuing noncompliance Prompt reporting to appropriate institutional officials and regulations is required .

All ISBEC members are expected to review the information and be prepared to discuss it at the meeting.

• The Protocol or Research Summary;
• The Informed Consent Document;
• The confirmed report of non-compliance;

The ethics committee chairperson assigns a primary reviewer based on scientific expertise to perform an in-depth review of the documents. The primary reviewer will present his/her findings. The primary reviewer and the IEC Chair or IEC Vice-Chair will lead the discussion during the convened IEC meeting.

The IEC votes on whether a confirmed report of non-compliance represents serious non-compliance or continuing non-compliance as defined. IEC staff records the discussion, rationale for any action and vote in the minutes.

If the IEC determines that the confirmed report of non-compliance is neither serious non-compliance nor continuing non-compliance, the IEC considers but is not limited to the following actions:

• Acknowledgement of the problems, requiring no sanctions but with instructions of the necessity to establish procedures and policies to avoid further infractions.
• Require additional education and training applicable to human research participant protections of Investigator and/or staff.
• Request a corrective action plan from the Investigator.
• Approve the submitted corrective action plan.
• No further action.

If the IEC determines the confirmed report of non-compliance represent serious non-compliance or continuing non-compliance, the IEC considers but is not limited to the following actions:

• Verification that participant selection is appropriate.
• Observation of the research and the informed consent process by an IEC administrator.
• Modifications of the protocol.
• Request an increase in monitoring of the research activity via an independent data safety monitor or board.
• Safety intervention as necessary such as visits to the activity site and continuing evaluation of the site by an IEC administrator.

• Request additional Investigator and staff education focused on human research protections from appropriate available sources (e.g. GCP Training,).
• Notify current subjects, if the information about the non-compliance might affect their willingness to continue participation.
• Suspend IEC approval of the respective study pending a written plan for the correction and /or prevention of the non-compliance.
• Remove the Principal Investigator of the research study.
• Suspend or terminate some or all of the research study and possibly other studies being conducted by the Principal Investigator as well .

APPENDIX J
SUGGESTED FORMAT FOR SUBMISSION/PROPOSAL LETTER

Date: XXXXXXXXXXX

To,
The Chairperson,
Inter System Biomedica Ethics Committee (ISBEC),
C/o MRC-Kasturba Health Society,

17, Khandubhai Desai Road,

VileParle (West),Mumbai-400057

Ref: Protocol No: XXXXXXXXX

Study Title: "XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX"

Sub: Submitting documents for Ethics Committee's approval.

Dear Dr. XXXXXXXXXX

Please find enclosed the following documents for the Ethics committee submission.

1. Study Protocol Version <Version No.> dated <Date>.
2. Product literature.
3. Informed Consent Form <Version No.> dated <Date> in English.
4. Informed Consent Form <Version No.> dated <Date> translated from English to <Name of the Language> on <Date of Translation>.
5. Informed Consent Form <Version No.> dated <Date> back translated from <Name of the Language> to English on <Date of Back Translation>.
6. CRF Version XX Dated:
7. Translation certificate for ICD translation
8. Current CV's of PI, Co-I & study directoror co-ordinator
9. Proposed Payment justification form- Volunteer compensation
10. Investigator's Schedule Y undertaking
11. Investigator's GCP certification
11. Details of Clinic/ Centre information.
12. Quality control of laboratory services.
13. Copy of Insurance policy and volunteer compensation

Study details are furnished below for your reference:

- Type of clinical phase- Bioavailability pilot study
- The purpose of research
- The scientific rationale
- A description of the procedures being performed already for diagnostic or treatment purposes.
- The risks and potential benefits of the research.
- Type of patients— XX (+X standby) healthy, adult, human male/Female volunteers
- Provisions for additional safeguards in case of vulnerable populationStudy site: xxxxxxxxxxxxxxxxxxxxxxxxx
- Duration of study: Approximately xx days

- Investigations to be carried out: Demography data, Medical history, General physical examination, hematology, biochemistry, serology, urine analysis, ECG and Chest X-Ray
- Name of the sponsor:xxxxxxxxxxxxxxxxxx.,
- Monitoring provisions
- Import permission for drug (if required)-obtained/not obtained/not required (if obtained please provide copy of it to EC)
  - Marketing status of Investigational product (IP) in India and in other countries
  - Package insert and copy of the label of the IP

- Criteria for withdrawal of subjects
  - Criteria for termination of the trial
  - Copy of permission from regulatory authorities and / or administrative heads

- CTRI registration when applicable

Please fill the details:

- The person who will conduct the consent interview:----------
- The person who will provide consent or permission: ----------
- Waiting period between informing the prospective subject and obtaining consent:----------
- Steps taken to minimize the possibility of coercion or undue influence: ----------
- The language to be used by those obtaining consent: ----------
- The language understood by the prospective subject orthe legally authorized representative: ----------
- The information to be communicated to the prospective subject or the legally authorized representative: ----------

Please revert back for any further clarifications.

Thanks with regards,

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Dr. xxxxxxx

Clinical Investigator

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Dr. xxxxxxxxxxx

Version : 06
Supercedes Version. No: 5
Effective from : 01-06-2018
Valid till : 31-05-2021

Principal Investigator

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Dr. xxxxxxxxxxxx
Study Director

APPENDIX K

LIST OF MEMBERS OF INTERSYSTEM BIOMEDICA ETHICS COMMITTEE

Sr. No	Members Name &Address	Capacity
1	Dr Kiran Marthak, MD (Medicine), F.F.P.M. -D.B.M.	**Member- Chairman** Physician ,ClinicalPharmacologist &Pharmaceutical expert
2	Dr. Deepak Dave M.D (Obst/ Gyn), D.G.O	**Vice- Chairman** Cons. Obst/ Gynaecologist
3	Dr. VanlilaMehta M. B. B. S, D. G. O, DRCOG,	**Member- Secretary** Pharmaceutics expert
4	Dr. Jayashree Joshi MD, DGO, DFP, Ph.D.	**Member,** Clinical Pharmacologist Cons. Obst/ Gynaec
5	Dr. Ashok D. B. Vaidya MD, Ph.D.	**Member** Cons. Pharmacologist
6	Dr. Rama Vaidya MD, DGO, DFP, Ph. D.	**Member** Cons. Obst / Gynaec
7	Dr. Meena Dave M. D. (Pharmacology).	**Member** Clinical Pharmacologist
8	Dr. Pradnya Talawadekar,BAMS, LLM.	**Member** Legal Expert
9	Dr. MrunalMarathe, M.Sc(Psychology), Ph.D(H.S.S)	**Member** Social Scientist
10	Dr. Shobha A. Udipi, M.Sc., PhD	**MemberSecretary** Nutrition Expert
11	Dr. Ashwini Kumar Raut, MD(Ayurved-Kayachikitsa)	Member, Ayurvedic Consultant
12	Dr. Swapnil Patne, MD (Homeopathy)	Member, Homeopathy Expert
13	Dr.Sharique Zafar, MD (Unani), PhD(Ayurveda)	**Member,**Unani Expert
14	Mr Sharad Chitnis , BA, LLM	**Member,** Legal Expert
15	Mrs Manisha Naikdalal,M.Com	**Member,**Lay person

Version : 06
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APPENDIX L

History of the SOP'S

Ver. No.	Reason for Revision/History	Effective Date
00	Ethics Committee was formed as Institutional Committee for Clinical studies of Bhavan's Swami PrakashanandaAyurved Research Center SPARC) with Late DrSatyavatiSirsat, Director, Bhavan's SPARC, as the Chairperson in 1995 when many members were from outside the Institute. It was located in Bhavan's SPARC, Juhu, Mumbai	1995
01	Ethics Committee became an Independent Committee directly under the BharatiyaVidyaBhavan with DrArunSangani as the independent Chairman	2003
02	Ethics Committee became independent of Bhavan, registered as an independent non-profit organization with Dr AS Sangani as the chairman under the company act, Govt of India with the Delhi office in 2008 and relocated in Medical Research Center -Kasturba Health Society, Vile Parle	2008
03	DrArunSangani passed away in 2009. DrMeena Dave was elected as the chairperson. As per the new requirements for international regulations SOPs were revised to include detailed explanations particularly with respect to the vulnerable sections and to include the functions of EC .	2010
04	DrMeena Dave resigned for personal reasons but continued as a member. DrKiranMarthak was elected as the Chairperson in 2011. New SOPs with minor additional features were proposed in 2012 for acceptance in ICMR, US FDA, and European Regulatory System	2012
05	Subsequent to the DCGI accreditation and new guidelines & regulations SOP Version 05 has been formulated	2014
06	Subsequent to re-registration and after ICMR 2017 Guidelines Version 6 was formulated	2018