STANDARD OPERATING PROCEDURE

General Review

(Version No.1, Dated 02-Dec-2019)

Name of the Ethics Commitee

Institutional Ethics Committee, Sibar Institute of Dental Sciences- (IEC-SIDS)

Address of the Ethics Committee:

Institutional Ethics Committee, Sibar Institute of Dental Sciences- (IEC-SIDS)

Sibar Institute of Dental Sciences,
Takkellapadu
Guntur. 522509.
Andhra Pradesh

Chairman

Signature:

Name: DR. MANGALA CHARANA DAS.

Date: 02-DEC-2019

CHAIRMAN
Institutional Ethics Committee
SIBAR INSTITUTE OF DENTAL SCIENCES
GUNTUR

Member Secretary

Signature:

Name: DR. B. VENKAT RAMANA REDDY

Date: 02-DEC-2019.

MEMBER SECRETARY
Institutional Ethics Committee
SIBAR INSTITUTE OF DENTAL SCIENCES
GUNTUR

Authors of SOP:

Name	Designation	Signature	Date
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Approved by:

Name	Designation	Signature	Date
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Accepted by:

Name	Designation	Signature	Date
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Reviewed by:

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Dr. Y. Samatha	Clinician		02-12-19
Mr. B. Srinivasa Rao	Legal Expert		02/12/19
Mrs. P. Padmaja	Social Scientist		02-12-19
Mr. K. Koteswara Rao	Layperson		02/12/19

History of SOP:

Date (DD/MM/YY)	Revision no	Pages	Description of changes	Reason for revision

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Authority for formation of Ethics Committee

- Institutional Ethics Committee, Sibar Institute of Dental Sciences, here after referred as "IEC-SIDS" was constituted under the Director of Sibar Institute of Dental Sciences to protect the dignity, rights, safety and well-being of all research participants in Sibar Institute of Dental Sciences.
- Member secretary is the authorized person for conducting meeting and for recording the minutes of meeting.
- All other EC members are appointed by the Head of the Institution.
- Chairman is the Head of Ethics Committee.
- Chairman will be proposed by the Head of the Institution and elected by the all ethics committee members in earliest meeting.
- The committee will function independently and should not be influenced by the hospital management. And The hospital management should not be interfere in EC decisions or opinions
- The IEC-SIDS will function as per standard operating procedures (SOP), current Indian Guidelines which has been released in 2012 and 2013 (Schedule Y, Requirements and Guidelines for permission to import and/or manufacture of new drugs for sale or to undertake clinical trials, January 5, 2005), and the Good Clinical Practices for clinical research in India, the ICMR ethical guidelines for biomedical research on human subjects (2017) and the ICH-GCP.

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2. Development, Review and Revision of SOP

- This SOP establishes the authority of the IEC-SIDS to review clinical research projects. All clinical trial projects must be submitted to IEC-SIDS for review and approval before commencement of the trial and medical research in the institution.
- SOP shall be developed by member Secretary further to consultation with chairman of Ethics committee
- Every time SOP can be approved by IEC-SIDS (at the time of Initial and whenever amended)
- A copy of the SOP will be circulated to all the members of the IEC-SIDS, Institution Head and Principal Investigators.
- The master copy of the SOP will be kept with the member secretary
- ***This SOP is valid for 3 years from the approval; SOP can be revised at discretion of EC chairman or Member secretary.***

3. Terms of reference for Ethics Committees

- The objective is to contribute to the effective functioning of the Institutional Ethical Committee so that the Quality and consistent ethical review mechanism for health and biomedical research is put in place for all proposals dealt by the committee as prescribed by ICH GCP, Schedule Y and the Ethical Guidelines for Biomedical research on human subjects of ICMR.
- EC will review and approve all types of research proposals involving human participants with a view to safeguard the dignity, rights, safety and well being of all research participants.
- The mandate of the EC will be to review all research projects involving human subjects to be conducted at the Sibar Institute of Dental Sciences. (Industry sponsored trials, Investigator initiated research, ICMR sponsored research and Medical students dissertation)
- The dissertation work of graduates, post graduates, STS projects and project work done by any faculty members for paper presentation or publication, will be evaluated by the EC.
- The Terms of References should include Terms of Appointment with reference to the duration of the term, the policy for removal, replacement, resignation procedure, frequency of meetings, and payment of processing fee to the EC for review, honorarium/ consultancy to the members/ invited experts etc. and these should be specified in the SOP which should be made available to each member.
- EC should have its own written SOPs according to which the Committee should function. The SOPs should be updated periodically based on the changing requirements. .
- It would be preferable to appoint persons trained in bioethics or persons conversant with ethical guidelines and laws of the country. Substitute member may be nominated if meetings have been continuously missed by a member due to illness or other unforeseen circumstances. For this the criteria for number of missed meetings may be defined in the SOP.
- The EC members should be made aware of their role and responsibilities as committee members. Any change in the regulatory requirements should be brought to their attention and they should be kept abreast of all national and international developments in this regard.
- The committee will review all new research projects, human research projects, thesis and the ongoing research projects at intervals appropriate to the degree of risk to the study patients and will maintain a list of projects submitted, approved/ disapproved and the outcome of each project.

The committee expects from the principal investigator

- A report of the research project on an annual basis or more frequently if so desired.
- A report of each serious adverse event with regard to the study.
- To be kept informed of amendments / revisions to any study related documents as well as patient safety related information.
- To be kept informed of study discontinuation with reasons thereof.
- To submit justification for approval to restart studies discontinued earlier
- A copy of the final report

4.0 Ethics Committee Composition

4.1 Composition

- ❖ EC shall be multidisciplinary and multi-sectorial in composition. Independence and competence are the two hallmarks of an EC.
- ❖ The members will be with adequate qualification experience and expertise in their respective fields.
- ❖ The EC consists of upto eleven (11) members. Chairperson from outside the institute and the member secretary from the institute. The members shall be from Medical, Scientific, Non-Medical and Non-Scientific fields including a lay person and appropriate gender representation.
- ❖ The EC shall include at least one member whose primary area of interest or specialization in non-scientific back ground.
- ❖ Members should be conversant with the provisions of clinical trial under the Schedule Y, Indian GCP and the other regulatory requirements to protect the dignity, rights, safety and well-being of the research participants.
- ❖ The Chairperson of the committee should preferably from outside the Institution and not head of the same Institution, to maintain the independence of the Committee. The Member Secretary who generally belongs to the same Institution should conduct the business of the Committee. Other members should be a mix of medical/non-medical, scientific and non-scientific persons including lay public to reflect the differed viewpoints. The composition (As per Indian GCP) may be as follows :-

1. Chairperson
2. 1-2 basic medical scientists (preferably one pharmacologist).
3. 1-2 clinicians
4. One legal expert or retired judge
5. One social scientist / representative of non-governmental voluntary agency
6. One lay person from the community
7. Member Secretary

4.2 Subject Experts and Representatives of vulnerable group

- ❖ If required subject experts could be invited to offer their views.
- ❖ Subject experts and representatives of vulnerable group may be invited to offer their views, but should not take part in the decision making process. However, her/his opinion must be recorded.

4.3 Membership

- The Committee of EC members shall be from varying backgrounds to promote the complete and fair review of human clinical trial and medical research projects to be conducted at the institute.
- The EC can have as its members, individuals from other institutions or communities. There should be adequate representation of age, gender, community; etc. in the Committee to safeguard the interests and welfare of all sections of the community/society.
- Members should be aware of local, social and cultural norms, as this is the most important social control mechanism. If required subject experts could be invited to offer their views.
- The members will be with adequate qualification experience and expertise in their respective fields.
- The maximum total number of members will be eleven (11). All members will be appointed by the Head of the Institution in consultation with member secretary.

4.4 Appointment

- The member secretary will appointed by the head of the institution.
- The members of the ethics committee will be appointed by the head of the institution with consideration of the member of secretary.
- All EC members shall give Biodata or Curriculum Vitae
- Members must apprise themselves of the relevant documents; codes, GCP, ICH guidelines and the ICMR code
- An investigator can be a member of the EC; however, the investigator-as-member cannot participate decision making process for any project in which he/she has presence as a PI, Co-PI or Sub I or potential conflict of interest.
- Members are selected on their personal capacities, based on their interest, ethical and/or scientific knowledge and experience in domain field and profile.
- The members are drawn from different institutes and specialties to give a multisectorial and multidimensional structure.
- A member can tender resignation from the committee with proper reasons to do so.
- Conflict of interest should be declared by all members of the EC.
- Name, gender, profession and affiliation of EC members will be publicized

4.5 Tenure, Reconstitution and Resignation

- Membership can be given for 3 years, after the tenure the member can be continue for another term, atleast minimum one member should be changed for every 3 years.
    - A member can be replaced in the event of death or long-term non availability or for any action not commensurate with the responsibilities laid down in the guidelines deemed unfit for a member.
- A member can submit resignation to chairman of the EC with a minimum notice period of one month, mentioning the valid reason for the resignation. It can be approved by the Head of the Institution in consultation with chairperson / member secretary of EC.
- A member may be relieved or terminated of his/her membership in case of:
    a. Conduct unbecoming for a member of the Institutional Ethics Committee
    b. Inability to participate in the meetings on any grounds

c. Relocate to another city or any such matter.

- In case of resignation of a member, Head of the Institution will appoint a new member falling in the same category of membership. Appointment may be made in consultation with the Chairperson / Member Secretary.
- A member may be removed/ terminated of his/ her membership in case of failure of attending the last 3 consecutive ethics committee meetings.
- In case of resignation of Chairman- IEC-SIDS, Head of the Institution will appoint a new member. Appointment may be made in consultation with member secretary.
- The respective communication shall be maintained at the Ethics Committee records.

4.6 Roles and Responsibilities

- The basic responsibility of an EC is to ensure protection of the dignity, rights, safety and well-being of the research participants.
- Membership of the EC is position of responsibility and the members are expected to approach this position with the seriousness and professionalism befitting their role in aiding the advancement of science and protection of research participants.
- EC members are expected to show interest and motivation, commitment and availability, experience with or education regarding the science and ethics of research.
- EC members should attend a minimum of 70% of the meetings every year and should inform the member secretary at least one week in advance if they are unable to attend an EC meeting.
- EC members should attend the trainings conducted for the members with in EC.
- Every new member will get trained on all of the above-mentioned guidelines (Indian GCP, ICMR, and ICH-GCP) and rules at the time of appointment.
- When a new rule/ guideline / sop revision is happened, all the members would be trained and training record would be maintained for the same.
- Members should inform the secretary in advance if they anticipate being unavailable for three consecutive meetings.
- Will review all the research protocols submitted to them with in specified time limits.
- Are conducted under the supervision of appropriately qualified medical personnel with the required expertise.
- All members should maintain absolute confidentiality of all discussions during the meeting and sign a confidentiality form and expected to declare competing conflicts of interest with respect to research proposals or Investigators if any.
- EC members are requested to sign a confidentially agreement on joining and this will renewed with every extension.
- Members should submit an updated CV on joining the EC and with every extension.
- Members should return all materials (research documents) to the secretary after the meeting and they are not permitted to make copies of any these materials.
- EC ensures the safety, rights and well-being of all trial subjects. Special attention will be paid to trials that may include vulnerable subjects (children, pregnant and nursing mothers, geriatric subjects, disabled subjects and minorities).

- Prime attention and care would be taken to evaluate the safety and well being when the vulnerable category of subjects participating in a clinical trial. The local regulation in the country would be taken as the standard of evaluation.
- Conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution.
- EC will conduct continuing review of each ongoing trial at intervals appropriate to the degree of risk to human subjects.
- EC will ensure that adequate written information is provided in the Inform Consent Form and will ask for additional information to be incorporated in ICF for protection of rights and well-being of the subjects.
- Based on the requirement of research area, for example HIV, genetic disorders etc. specific patient groups may also be represented in the Ethics Committee.
- EC will review both the amount and method of payment to subjects to assure that they neither present problems of coercion nor undue influence on the trial subjects.
- EC will ensure that all the information regarding payment, including amounts and schedule of payments to trial subject to be informed to EC.

4.7 Procedure of Training

- Every EC member trained on "Good Clinical Practice" conducted by THSTI (Transitional Health Science and Technology Institute) during the period of January 31 to February 1, 2019 at NTR University of Health Sciences, Vijayawada, Andhra Pradesh.
- Every EC member refreshed the training on Good Clinical Practice, Local Regulation, Rules & Responsibilities of EC and SOP's of EC at the time of appointment.
- EC members should attend the trainings conducted for the members with in EC for General and Internal SOPs and any updates in SOP's.
- All members are been trained and under continues training with the current and updated rules and regulations.
- Members should be encouraged to attend national and international training programs in research ethics for maintaining quality in ethical review and be aware of the latest development in this area.
- Yearly once every member should get training on updates in Good Clinical Practice, Local Regulation, Rules & Responsibilities of EC and SOP's of EC.

4.8 Confidentiality and Conflict of Interest

- Members are required to sign the confidentiality agreement and conflict of interest at the start of their term.
- The confidentiality agreement protects the privacy and confidentiality of all parties whose information may be disclosed to the EC in the course of its work.

4.9 Quorum

- The number of persons in an ethical committee is kept 7-11 members. It is generally accepted that a minimum of five (5) persons is required to compose a quorum
- For review of each protocol the quorum of EC shall have at least five members with the following,
  1. Basic medical scientist (Preferably Pharmacologist)
  2. Clinician
  3. Legal expert
  4. Social scientist or representative of non-governmental voluntary agency or philosopher or ethicist or theologian or a similar person.

5. Lay person from community.

- ❖ Minimum one non-affiliated member should be part of the quorum.
- ❖ The quorum for reviewing regulatory clinical trials should be in accordance with current CDSCO requirements.
- ❖ No decision is valid without fulfilment of the quorum.

5. Protocol Submission

- ❖ At the time of submission the checklist (**Annexure: 1**) for the submission should be used, the incomplete submission will be returned.
- ❖ Eleven (11) hard copies along with submission letter should be submitted at least 3 weeks before every meeting for the proposal to be considered at that meeting.
- ❖ Failure to submit hard copy with relevant checklist and all supporting documents will result in the proposal not being accepted.
- ❖ If the application is complete and accepted, the date and time of the meeting that will review the proposal will be intimated. The PI or Co/Sub-Investigators will be required to be present the study in meeting and to offer clarifications.

6.Meeting Schedule

- ❖ The meetings will be held once in every 2 months or as and when required. An interim or unscheduled meeting may be convened at the discretion of the chairperson, member secretary and the members of the EC in view of the following
- Projects requiring expedited review (Refer Section on Expedited review).
- Projects already approved but requiring minor changes.

7.Ethical Review

7.1 Review Process

- ❖ All properly submitted applications will normally be reviewed within the specified time and according to the review procedures described below.
- ❖ Each application will be screened by the office for their completeness and depending on their risk involved categorize them Full review and expedited review.
- ❖ An investigator cannot decide that her/his protocol falls in the exempted category without approval from the EC.
- ❖ The Committee will review the project documents and will have the authority to approve, request modifications/changes or to disapprove the project with broad consensus.
- ❖ The Ethics Committee should review every research proposal on human subjects. It should ensure that a scientific evaluation has been completed before ethical review is taken up. The Committee should evaluate the possible risks to the subjects with proper justification, the expected benefits and adequacy of documentation for ensuring privacy, confidentiality and justice issues. The ethical review should be done through formal meetings and should not resort to decisions through circulation of proposals

7.2 Expedited Review:

- Research activities that present no more than minimal risk to human subject and involve only procedures may be reviewed by the member secretary or chairperson and basic medical scientist of EC through the expedited review procedure.

- Proposals requesting expedited review should provide sufficient detail to enable a decision to be made in this regard. In case of minor protocol amendments of approved research studies, the application should clearly specify the amendments that need expedited review.
- A brief summary and review decision of the protocol will be placed before the EC members in the next meeting.
- The expedited review procedure may not be used for fresh applications concerning interventions involving human subjects.
- The standard requirement for Informed Consent (or its wavier or exception) apply regardless of the type of review, expedited or Normal, utilized by the EC

7.3 Full review:

- ❖ All research presenting with more than minimal risk, proposals/ protocols which do not qualify for expedited review and projects that involve vulnerable population and special groups shall be subjected to full review.

7.4 Elements of Review:

- ❖ The appropriateness of the study design in relation to the objective of the study, the statistical methodology (including sample size calculation), and the potential for reaching sound conclusion with the smallest number of research participants;
- ❖ The justification of predictable risks and inconveniencies weighed against the anticipated benefits for the research participants and the concerned communities;
- ❖ The justification for the use of control arms;
- ❖ Criteria for prematurely withdrawing research participants;
- ❖ Criteria for suspending or terminating the research as a whole;
- ❖ The adequacy of provisions made for monitoring and auditing the conduct of the research;
- ❖ The adequacy of the site, including the supporting staff, available facilities,

The IEC-SIDS will take into account the process and the requirements of applicable laws and regulations. In addition, the EC will also consider the following:

Care and Protection of Research Participants

- ❖ The suitability of the investigators' qualification and experience for the proposed study;
- ❖ The medical care to be provide to research participants during and after the course of the research;
- ❖ The adequacy of medical supervision and psycho-social support for the research participants;
- ❖ Steps to be taken if research participants voluntarily withdraw during the course of the research;
- ❖ The criteria for extended access to, the emergency use of, and/or the compassionate use of study products.
- ❖ A description of any financial costs to research participants; the rewards and compensations for research participants (including money services, and/or gifts);
- ❖ The provisions for competitions/treatment in the case of the injury/disability /death of a research participants attributable to participation in the research;
- ❖ The insurance and indemnity arrangement;

Protection of Research Participant Confidentiality

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

- ***Safeguarding confidentiality*** - The investigator must safeguard the confidentiality of research data, which might lead to the identification of the individual subjects. Data of individual subjects can be disclosed only in a court of law under the orders of the presiding judge or in some cases may be required to communicate to drug registration authority or to health authority. Therefore, the limitations in maintaining the confidentiality of data should be anticipated and assessed.

SOP for Vulnerable Population

- A vulnerable category of subjects includes children, prisoners, foetuses / neonates, pregnant women, mentally disabled persons, refugees, displaced persons, who are likely to be vulnerable to coercion or undue influence.
- When a trial is to be carried out in the vulnerable populations like the paediatric, geriatric population, pregnant women, etc., the consent of the trial subject and subject's Legally Acceptable Representative (LAR) is mandatorily taken and the EC will determine that the proposed protocol and/or other document(s) adequately address the relevant ethical concerns and meet applicable regulatory requirements for such trials. Where required consent of the participant will also be taken, and this will be ensured during review and approval of the ICF.
- The EC will not allow the use of trainees/employees working within the organization to be used as trial participants' unless students and staff have the same rights as any other potential subject to participate in the research project, irrespective of the degree of risk.
- Prime attention and care would be taken to evaluate the safety and well being when the vulnerable category of subjects participating in a clinical trial. The local regulation in the country would be taken as the standard of evaluation.
- There are certain specific concerns pertaining to specialised areas of research which require additional safe guards / protection and specific considerations for the EC to take note of. Examples of such instances are research involving children, pregnant and lactating women, vulnerable subjects and those with diminished autonomy besides issues pertaining to commercialisation of research and international collaboration. The observations and suggestions of EC should be given in writing in unambiguous terms in such instances.

Selection of Special Groups as Research Subject

Pregnant or nursing women:

Pregnant or nursing women should in no circumstances be the subject of any research unless the research carries no more than minimal risk to the fetus or nursing infant and the object of the research is to obtain new knowledge about the foetus, pregnancy and lactation. As a general rule, pregnant or nursing women should not be subjects of any clinical trial except such trials as are designed to protect or advance the health of pregnant or nursing women or foetuses or nursing infants, and for which women who are not pregnant or nursing would not be suitable 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 perinatal 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. 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:

Before undertaking trial in children the investigator must ensure that -

α. A parent or legal guardian of each child has given proxy consent;

β. 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;

χ. Research should be conducted in settings in which the child and parent can obtain adequate medical support;

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

ε. 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;

ϕ. 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;

γ. The risk 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.

- Research on genetics should not lead to racial inequalities;
- Rights and welfare of mentally challenged and mentally differently able persons who are incapable of giving informed consent or those with behavioural disorders must be protected.
- Adequate justification is required for the involvement of subjects such as prisoners, students, subordinates, employees, and service personnel etc. who have reduced autonomy as research subjects.

Informed Consent process:

- Prior to the beginning of the Study the Investigator(s) should obtain the Ethics Committee's approval for the written informed consent form and all information being provided to the Subjects and / or their legal representatives or guardians as well as an impartial witness.
- The adequacy, completeness, and understandability of written and oral information to be given to the research participants, and, when appropriate, their legally acceptable representative(s);
- Clear justification for the intention to include in the research individuals who cannot consent, and a full account of the arrangements for obtaining consent or authorization for the participation so such individuals;
- Assurances that research participants will receive information that becomes available during the course of the research relevant to their participation including their dignity, rights, safety and well-being;
- The provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project.
- Site to ensure that the subject document the nominee in the ICF during the ICF documentation.
- As per the Schedule Y, in all trials, a freely given, informed, written consent is to be obtained from each study subject. The investigator must provide information about the study verbally as well as using a patient information sheet, in a language that is non-technical and understandable by the study subject.
- The information should be given to the Subjects and / or their legal representatives or guardians in a language and at a level of complexity that is understandable to the Subject(s) in both written and oral form, whenever possible.
- The Subject's consent must be obtained in writing using as 'Informed Consent Form'. If the subject or his/her legally acceptable representative is unable to read/write – an impartial witness should be present during the entire informed consent process who must append his/her signatures to the consent form.
- The requirement of obtaining written consent, audio-visual recording of the informed consent process of each trial subject, including the procedure of providing information to the subject and his/her understanding on such consent is required to be done while adhering to the principles of confidentiality. Such audio-visual recording and related documentation would be preserved.
- Subjects, their legal representatives or guardians should be given ample opportunity and time to enquire about the details of the Study and all questions answered to their satisfaction.
- Prior to the Subject's participation in the Study the written Informed Consent form should be signed and personally dated by
    1. (i) The Subject *or* (ii) if the Subject is incapable of giving an Informed Consent for example children, unconscious or suffering from severe mental illness or disability, by the Subject's legal representative or guardian *or* (iii) if the Subject and his legal representative or guardian is unable to read / write,
    2. An impartial witness who should be present during the entire informed consent discussion
    3. The Investigator

    By signing the consent form the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the Subject or the Subject's legal representative or the guardian, and that informed consent was freely given by the Subject or the Subject's legal representative or the guardian.

- The Subject's legal representative or guardian (if the subject is incapable of giving an Informed Consent for example children, unconscious or suffering from severe mental illness or disability), the inclusion of such patients in the study may be acceptable if the ethics committee is in principle, in agreement, and if the investigator thinks that the participation will promote the welfare and interest of the Subject. The agreement of a legal representative or the guardian that participation will promote the welfare and interest of the Subject should also be recorded with dated signature. If, however, neither the signed Informed Consent nor the witnessed signed verbal consent are possible – this fact must be documented stating reasons by the Investigator

***Essential information for prospective research on subjects*:**

Before requesting an individual's consent to participate in research, the investigator must provide the individual with the following information in the language he or she is able to understand which should not only be scientifically accurate but should also be sensitive to their social and cultural context:

I. The aims and methods of the research;
II. The expected duration of the subject participation;
III. The benefits that might reasonably be expected as an outcome of research to the subject or to others;
IV. Any alternative procedures or courses of treatment that might be as advantageous to the subject as the procedure or treatment to which she/he is being subjected;
V. Any foreseeable risk or discomfort to the subject resulting from participation in the study;
VI. Right to prevent use of his/her biological sample (DNA, cell-line, etc.) at any time during the conduct of the research;
VII. The extent to which confidentiality of records could be able to safeguard, confidentiality and the anticipated consequences of breach of confidentiality;
VIII. Free treatment for research related injury by the investigator / institution;
IX. Compensation of subjects for disability or death resulting from such injury;
X. Freedom of individual / family to participate and to withdraw from research any time without penalty or loss of benefits which the subject would otherwise be entitled to;
XI. The identity of the research teams and contact persons with address and phone numbers;
XII. Foreseeable extent of information on possible current and future uses of the biological material and of 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 others, clear mention of the same;
XIII. Risk of discovery of biologically sensitive information;
XIV. Publication, if any, including photographs and pedigree charts.

The quality of the consent of certain social groups requires careful consideration as their agreement to volunteer may be unduly influenced by the Investigator.

Informed Consent in Non-Therapeutic Study:

In case of a Non-Therapeutic Study the consent must always be given by the subject. Non-Therapeutic Studies may be conducted in subjects with consent of a legal representative or guardian provided all of the following conditions are fulfilled:

1. The objective of the Study cannot be met by means of a trial in Subject(s) who can personally give the informed consent
2. The foreseeable risks to the Subject(s) are low
3. Ethics Committee's written approval is expressly sought on the inclusion of such Subject(s)

7.5 Safety Review:

- IEC-SIDS will work under the guidelines laid down by the DCGI regarding Compensation, SAE reporting and its procedures etc.
- All Serious and Unexpected Adverse Events (SAE) shall be reported to the IEC-SIDS along with the sponsor and DCGI by the Principal Investigator (or designee) within 24 hours from the day of the occurrence or knowledge of the SAE along with the relevant supporting documents. Investigator/ designee can submit the SAE report to IEC-SIDS via a by-hand/fax/e-mail.

Ethics committee E-mail ID and Fax No. for 24-hr SAE submission	
Ethics committee Email:	drramanabv@yahoo.com
Ethics committee Fax No:	+91 863 2292139

- The Investigator has to submit the initial report of SAE to respective sponsor within 24 hours of SAE occurrence.
- The Investigator has to submit the initial report of SAE to the Health Authority (CDSCO) within 24 hours of SAE occurrence at the below mentioned Email ID/Fax No.

Health Authority E-mail ID and Fax No. for 24-hr SAE submission	
Health Authority Email:	dci@nb.nic.in
Health Authority Fax No:	011-23236973

- The Investigator and Sponsor have to submit the analyzed report of SAE to the EC Chairman, Head of the Institution and Health Authority within 14 calendar days of SAE occurrence. In case of death the analyzed report has to submit to Chairman of Expert Committee (CDSCO) also.
- On receipt of the analyzed report of SAE from the Investigator, the EC will evaluate and give opinion on financial compensation to be paid by the Sponsor/ his representative.
- A detailed report of recommendation of compensation will be submitted to the Health Authority (CDSCO) by EC within 30 calendar days of SAE occurrence.
- If the SAE is death the report should be submitted to the Chairman of Expert Committee (CDSCO) as well within the above mentioned time frame.
- The review of reports could be done through a meeting, teleconference, email or telephonic conversation.
- The Investigator / designee should submit SAE report and its attachments to the IEC-SIDS.
- Prior to submission the Investigator should verify using the SAE review checklist that the SAE report is complete for regulatory acceptance and assessments.
- The filled SAE review checklist signed by the Investigator / designee should be included in the submission.

- The IEC-SIDS would comply with SAE reporting rules mentioned in Appendix XI and XII **(Annexure 2 and 3)** of the amended Schedule Y.
- The IEC-SIDS chairman/ member secretary should sign, date and include the time of receipt of SAE on both the original and photocopy of the cover page of the SAE report with consideration of medical scientist so as to acknowledge the time of receipt of the SAE report.
- The IEC-SIDS should track the SAE reporting timelines by the Investigator and Sponsor as well as the timelines for the IEC-SIDS to send its recommendations to the regulators.
- Research subjects are entitled to get free medical management at Sibar Institute of Dental Sciences, for study related injury in research period.
- The investigator and sponsor should provide the IEC-SIDS a follow up report within 14 calendar days of the initial report with recommendations for the SAE being clinical trial related or clinical trial unrelated as per above listed criteria
- Based on the initial and follow up report the IEC-SIDS to assess the SAE to be clinical trial related or clinical trial unrelated.
- The IEC-SIDS to discuss and decide if the subjects/ nominee are entitled to compensate.
- The IEC-SIDS to use **Annexure 3** (Appendix XII of Schedule Y) to document their recommendation to the Independent Expert Committee appointed by the DCGI
- The chairman/member secretary should sign this recommendation with consideration of medical scientist and forward to the DCGI office within 30 days since the SAE occurred or was known to the Investigator.
- The document should be sent through acknowledgement revert courier.
- The IEC-SIDS should maintain a copy of the air way bill of the courier released and also of the Acknowledgment of receipt at the regulator's office along with the SAE report in the IEC-SIDS files.
- A copy of this recommendation should be provided to the investigator to place on study file and to share a copy with the sponsor.
- The IEC-SIDS to use recommendation for compensation Letter with **Annexure 3** (Appendix XII of Schedule Y) to report document their recommendation to the regulators (and copy to investigator/ sponsor).
- The IEC-SIDS should instruct the investigator to provide an update on the status of compensation paid by sponsor.
- Investigator received any safety information (CIOMS) from the sponsor. He/she should be submitting to EC as early as possible.
- As per the provisions, each SAE including death is required to be examined and decision regarding causality of death and quantum of compensation, if any, is required to be taken by CDSCO in a time bound manner as per the procedure specified in Appendix XII of Schedule Y.
- As per Appendix XII the Investigator shall report all serious and unexpected adverse events to the CDSCO, the Sponsor or his representative whosoever had obtained permission from the CDSCO for conduct of the clinical trial and the Ethics Committee, within twenty four (24) hours of their occurrence.

- In case of serious adverse events of death, the reports shall be examined by an independent Expert Committee constituted by DCG(I) to determine if the cause of death is due to following reasons, which are considered as clinical trial related death and gives its recommendation to CDSCO.
- In case of clinical trial related death the committee shall also recommend the quantum of compensation to be paid by the sponsor or his representative, to CDSCO.
  a. adverse effect of investigational product(s);
  b. violation of the approved protocol, scientific misconduct or negligence by the Sponsor or his representative or the investigator;
  c. failure of investigational product to provide intended therapeutic effect;
  d. use of placebo in a placebo-controlled trial;
  e. adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol;
  f. for injury to a child in–utero because of the participation of parent in clinical trial;
- CDSCO shall consider the recommendations of the Expert Committee and shall determine the cause of death and also the quantum of compensation in case of clinical trial related death within 150 days of receiving the report of SAE of death.
- In cases of serious adverse event other than death, CDSCO shall determine the cause of injury, if any, due to any of the reasons mentioned above as in the case of death, which is considered as clinical trial related injury. However CDSCO has option to constitute an independent Expert Committee, wherever considered necessary, to examine such serious adverse event.
- In case of clinical trial related injury, CDSCO shall also determine the quantum of compensation within 150 days of receiving of the SAE In case of clinical trial related injury or death, the Sponsor or his representative concerned shall pay the compensation as per the order of CDSCO within thirty days of the receipt of such order.
- In order to streamline the submission of reports of SAEs, a system of pre-screening of reports of SAEs at the time of receiving these reports is being introduced in CDSCO.

The pre-screening system will be as under:

- The preliminary scrutiny of the SAE reports will be done by CDSCO officer(s) based on laid down checklist which is attached herewith. During the preliminary examination, the CDSCO officer(s) will scrutinize the SAE reports to ensure that it contains all the required administrative as well as technical information in proper manner as per the checklist. If SAE reports are not submitted in accordance with the format and the checklist, it will not be accepted by CDSCO for further examination.
- Once a report of SAE is accepted, the information in the report will be reviewed by CDSCO as per the specified procedures.

  The sponsor or his representative conducting clinical trials in India are requested to prepare the SAE reports for submission to CDSCO as per appendix-XI of Schedule-Y of D&C Rules and the checklist enclosed.

  The SAE reports must be submitted with proper binding, indexing and page number. Without indexing of page number, no SAE report will be accepted.

(a) The reports of SAEs of deaths should be prepared and submitted in red cover.

(b) The reports of SAE of injury other than deaths should be prepared and submitted in blue cover.

(c) The SAE report other than that mentioned at (a) & (b) above is to be prepared and submitted in white cover.

Clear and unequivocal information should be provided in the SAE report.

Text and tables should be prepared using margins that allow the document to be printed clearly without losing any information and the left-hand margin should be sufficiently large so that information is not obscured by the method of binding. The documents printed on both sides of a page, can be submitted. However, one should take care that the information is not obscured when the page is placed in a binder. While submitting reply to a query, the applicant should always enclose with the reply, a copy of query letter issued by CDSCO.

All items mentioned in the checklist may not be applicable in all the case of SAE's. The items not relevant to a particular SAE should be marked with "Not Applicable (NA)".

Compensation for Participation

Subjects may be paid for the inconvenience and time present, and should be reimbursed for expenses incurred, in connection with their participation in research. They may also receive free medical services. However, payments should not be so large or the medical services so extensive as to induce prospective subjects to consent to participate in research against their better judgement (inducement). All payments, reimbursement and medical services to be provided to research subjects should be approved by the EC. Care should be taken:

When a guardian is asked to give consent on behalf of an incompetent person, no remuneration should be offered except a refund of out of pocket expenses;

When a subject is withdrawn from research for medical reasons related to the study the subject should get the benefit for full participation;

When a subject withdraws for any other reasons he/she should be paid in proportion to the amount of participation.

In cases where the review committee determines that a conflict of interest may damage the scientific integrity of a project or cause harm to research participants, the board should advise accordingly. Institutions need self-regulatory processes to monitor, prevent and resolve such conflicts of interest. Prospective participants in research should also be informed of the sponsorship of research, so that they can be aware of the potential for conflicts of interest and commercial aspects of the research. Undue inducement through compensation for individual participants, families and populations should be prohibited. This prohibition however, does not include agreements with individuals, families, groups, communities or populations that foresee technology transfer, local training, joint ventures, provision of health care reimbursement, costs of travel and loss of wages and the possible use of a percentage of any royalties for humanitarian purposes.7

7.6Quantum of Compensation Formula (Clinical Trial related SAE):

- Formula to determine the Quantum of compensation in the cases of clinical trial related serious adverse events (SAEs) of deaths occurring during clinical trials.
- Independent Expert Committee shall examine the report of serious adverse event of death and give its recommendation to the Licensing Authority within 30 days of receiving the report from the concerned Ethics Committee. The DCG(I) shall, then decide the Quantum of Compensation to be paid by the Sponsor

or his representative and shall pass order as deemed necessary within three months of receiving the report on the Serious Adverse Event of death.

- In case of clinical trial related injury or death, the Sponsor or his representative shall pay the compensation as per the order of the DCG(I) within thirty days of the receipt of such order.
- The Committee after deliberation prepared formula to be followed for the determination of Quantum of Compensation in case of Clinical Trial related death. The details of deliberations held and the formula are as under:

$$\text{Compensation} = \mathbf{B} \times \frac{\mathbf{F} \times \mathbf{R}}{99.37}$$

Where,

B = Base amount (i.e. 8 lacs)

F = Factor depending on the age of the subject as per **Annexure 6** (based on Workmen Compensation Act)

R = Risk Factor depending on the seriousness and severity of the disease, presence of co-morbidity and duration of disease of the subject at the time of enrolment in the clinical trial between a scale of 0.5 to 4 as under:

1. 0.50 terminally ill patient (expected survival not more than (NMT) 6 months)
2. 1.0 Patient with high risk (expected survival between 6 to 24 months)
3. 2.0 Patient with moderate risk
4. 3.0 Patient with mild risk
5. 4.0 Healthy Volunteers or subject of no risk

However, in case of patients whose expected mortality is 90 % or more within 30 days, a fixed amount of Rs. 2 lacs (Basic Amount) should be given

Thus, it will be seen that the compensation amount will vary from a minimum of Rs.4 lacs to a maximum of Rs.73.60 lacs depending on the age of the deceased and the risk factor. However, in case of patients whose expected mortality is 90 % or more within 30 days, a fixed amount of Rs. 2 lacs should be given.

7.7 Decision Making

- The members present will cast their single vote. In case of a tie, the chairperson would use his casting vote to decide the issue one way or the other.
- The special invitees will have no vote.
- No representative of the investigator or sponsor should be present at the time of voting.
- The decision of the committee will be taken by a majority vote after the quorum requirements are fulfilled to recommend/reject/suggest modifications for a repeat review or advise appropriate steps. If subject experts are invited to offer their views they will not take part in voting process. The Member Secretary should communicate the decision in writing.
- A member must voluntarily withdraw from the EC while making a decision on an application which evokes a conflict of interest which should be indicated in writing to the chairperson prior to the review and should be recorded so in the minutes.
- If one of the members has her/his own proposal for review, then the member should not participate in decision making procedure.
- A negative decision should always be supported by clearly defined reasons.
- An EC may decide to reverse its positive decision on a study in the event of receiving information that may adversely affect the benefit/risk ratio.

- The discontinuation of a trial should be ordered if the EC finds that the goals of the trial have already been achieved midway or unequivocal results are obtained.
- In case of premature termination of study, notification should include the reasons for termination along with the summary of results conducted till date.
- The following circumstances require the matter to be brought to the attention of EC :
    - any amendment to the protocol form the originally approved protocol with proper justification;
    - serious and unexpected adverse events and remedial steps taken to tackle them;
    - any new information that may influence the conduct of the study
- The applicant/investigator will be invited to present the protocol or offer clarifications in the meeting. Representative of the patient groups or interest groups can be invited during deliberations to offer their viewpoint.
- Subject experts may be invited to offer their views, but should not take part in the decision making process. However, her/his opinion must be recorded.

7.8 **Minutes of meeting**

- Minutes of meeting shall be prepared by members secretary with the help of Ethics committee coordinator (If appointed)
- Every meeting minutes shall be circulated to all the EC members
- Minutes of meeting records shall be archived along with other EC documents

8.Post Meeting Activities

8.1 Communicating Decisions

- A decision will be communicated in writing to the applicant, preferably within one week time of the meeting at which the decision was made.
- The ***IEC-SIDS*** decision will be signed by the chairperson or members Secretary
- The EC communication of the decision will include, but is not limited to, the following:
    - The exact title of the research proposal reviewed;
    - The clear identification of the protocol proposed research or amendment, date and version number (if applicable).
- In case of non- availability of the chairman, member secretary will communicate the decision.

8.2 Monitoring or Site visits

- The EC can visit the clinical trial site to conduct an on-site review. Such visits can include the review of the following documents at the site:
- Signed informed consent forms and other related source documents.
- Observation of administration of the informed consent process.
- All serious and unexpected and/or related adverse events reports.
- All source documents.
- Completed Case Report Forms.
- Site Contract and Agreements inclusive of financial agreements.
- Amendments of the Protocol or other essential documents.
- Advertisements if any, for the subject recruitment.

8.3 Protocol Deviations and Non compliance

- All the protocol deviations occurred in approved research projects shall be submit to the EC

- The EC can conduct an Audit visit at the site in case of any non-compliance reported to the EC. These reports may follow information to the EC from the study subjects, public, sponsors' progress reports and safety reports.
- The EC will review such allegations of non-compliance and assess whether such allegations/alleged practice would cause injury or other unanticipated harm or risk to subjects or others involved in the trial. In such cases of alleged non-compliance the EC may suspend the trial following a review by the full committee. Such decisions will be intimated to the Investigator and the Sponsor in writing.
- Any complaint of injustice by the study subject will be looked into seriously. The EC is open for Inspections by the Regulatory bodies.

8.4 Interim Reports or Annual report

The Investigator must submit to the EC a progress report on the clinical trial at least once in a year. The report must highlight

- Number of subjects screened, enrolled, completed and withdrawn.
- Current status of enrolment
- Any safety issues.

8.5 Study Completion

- The Investigator must submit a final report to the EC on the successful completion/ termination of the clinical trial at the site (preferably at the time of study close-out visit)9

9. Documentation and Archiving

- All the documents and communications of the EC related to the clinical trial projects will be filed and stored in a safe and secure place. Strict confidentiality will be maintained during access and retrieval procedures.
- Composition of the EC
- C.V. of all EC members
- SOPs (Standing Operating Procedures) of the EC
- Indian Good Clinical Practice Guidelines, ICH Good Clinical Practice Guidelines, Schedule Y and other regulatory documents.
- Copies of the Protocol, Case Record Forms, Investigators Brochure, Informed Consent Form, Data collection forms, Regulatory Approvals and other relevant documents submitted to the EC
- All correspondence with EC members and investigators regarding application, decision and follow ups.
- Agenda of all EC meetings.
- Minutes of all EC meetings signed by the Chairperson
- Copies of decisions communicated to the applicants
- Record of all notification issued for premature termination of a study with a summary of the reasons.
- All Safety reports submitted to the EC
- All the documents should be archived for five (5) years after the study completion / termination and will be available for an audit, if required.

10. EC fees

10.1 For New a submission:

- The EC fees for the review of a clinical research project will be Rs. 75,000/- (Excluding Tax).

  Payee Name: Dr. B. V. Ramana Reddy

10.2 For Amended documents submission:

- If the amendment of documents requires EC approval of clinical research protocol and/or Investigators Brochure. The fee would be Rs. 50,000/- (Excluding Tax) for review and approval.

  Payee Name: Dr. B. V. Ramana Reddy

10.3For Expedited Review:

- The EC fees for such reviews would be Rs 100000/- (Excluding Tax)
- For expedited review of students and faculty research projects the fee would be Rs10000/
- The study documents will be reviewed within two weeks of submission & approval will be granted within a week of review.
- Payee Name: Dr. B. V. Ramana Reddy

11. EC Members

Dr. Mangala Charana Das MBBS MD(Pharmacology) **Chairman & Basic Medical Scientist** **Ph:** 9849439266 **Email**: drmcdas11@gmail.com **Address:** Q.No.1-1-13, Staff Quarters, NRI Medical College Campus, Chinnakakani, Mangalagiri, Guntur, Andhra Pradesh. 522503 Affiliation with Institute: No	Dr. P.Srinivas MDS (Public Health Dentistry) **Clinician** **Ph:** 9849368466 **Email:srinivas_tenali@hotmail.com** **Address:** F No: 304, H.No:48-13-20, Yalamanchali Koteswara Rao Street, Sri Ramachandra Nagar, Near AYUSH Hospitals, Vijayawada – 522008, Andhra Pradesh. Affiliation with Institute: Yes
Dr. B. Venkat Ramana Reddy MDS (Oral Pathology) **Member Secretary & Clinician** **Ph:** 9848885660 **Email**: drramanabv@yahoo.com **Address:** G-2, Sasanka Towers, RamanadhamStreet, Kasturibaipeta, Vijayawada, Andhra Pradesh-522010 Affiliation with Institute: Yes	Dr. Y. Samatha MDS (Oral Medicine and Radiology) **Clinician** **Ph:** 9391307194 **Email**:dra.samatha@gmail.com **Address:** Flat No: 301, The Grand Palace Apartments, 3rd line, 4th cross,VIdya Nagar, Durga Agraharam Guntur – 522007, Andhra Pradesh. Affiliation with Institute: Yes

Dr.V.Siva Prabodh M.D. (Biochemistry) **Basic Medical Sceintist** **Ph**: 9849231126 **Email:** vuddandiprabodh@yahoo.com **Address:** Q No: 1-3-13, Doctor's Quarters, NRI Medica College, Chinakakani, Mangalagiri, Guntur, Andhra Pradesh-522503 Affiliation with Institute: No	Mr. B. Srinivas Rao B Com; BL **Legal Expert** **Ph:** 9866003212 **Email**:srinivasbommanaboyena@gmail.com **Address:** D.No.16-19-165, Near Ankamma Temple, Main Road Old Guntur, Guntur - 522001 Andhra Pradesh. Affiliation with Institute: Yes
Dr. T. Anuroop MS (General Surgery) **Clinician** **Ph:** 7702001230 **Email:** anuroopt@gmail.com **Address:** D.No.29-8-40/A, Chiliku Durgaiah Street,, Suryaraopet, Vijayawada - 522002Andhra Pradesh. Affiliation with Institute: No	Dr. Lalith Prakash Chadra MDS Social Scientist **Ph:** 9848567835 **Email**: drprakash7178@gmail.com **Address:** D.No: 5-54-14/A, Brodipet 4/18-19, Guntur, Andhra Pradesh-522002 Affiliation with Institute: Yes
Dr. L. Krishna Prasad MDS (Oral & Maxillofascial Surgery) Clinician **Ph:** 9848123244 **Email**: dr_lkp@yahoo.com **Address:** D.No.30-5-2, Koka Chalapathi Rao Street, Durga Agraharam Vijayawada – 522002, Andhra Pradesh. Affiliation with Institute: Yes	Mr. K. Koteswara Rao B.Com Lay Person **Ph:** 8142003288 **Email**:kkr31513@gmail.com **Address:** Narakoduru, Chebrolu, Guntur - 522212 Andhra Pradesh. Affiliation with Institute: No

12.0 Annexure

Annexure 1: Project Submission checklist for review by EC

Annexure 2: Serious Adverse Event Review Report for SAE (APPENDIX XI of Schedule Y)

Annexure 3: Checklist of APPENDIX XII of Schedule Y

Annexure 4: Factor (F) for calculating the amount of compensation (Based on Workmen Compensation Act)

Annexure 1:

Project Submission checklist for review by EC

SL. no.	List of documents	Submission		Comments
		Yes	No	
1	Protocol version dated			
2	IB version dated			
3	Amended protocol version dated With the summary of changes highlighted.			
4	ICF English version date			
5	ICF Telugu version date			
6	Translation certificates for ICF			
7	Patient Materials			
8	Study Advertisements			
9	Study insurance			
10	Draft CTA			
11	Regulatory submission & Approval letters			
12	Drug Licenses			
13	Biological Import/export Licenses			
14	CTRI registration			
15	Copy of CRF			
16	Copy of SAE form			
17	CV & MRC of PI			
18	Investigator Undertaking			
19	FDA 1572 (If applicable)			
20	Travel reimbursement (if not included in ICF)			
21	Submission cover letter			

Annexure 2:

Serious Adverse Event Review Report for SAE (APPENDIX XI of Schedule Y)

As per ICH-GCP:

Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (Serious ADR) Any untoward medical occurrence (due to the participation in the concerned trial) that at any dose:

- results in death,
- is life-threatening,
- requires inpatient hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability / incapacity, or
- is a congenital anomaly/birth defect

Investigator(s) shall report all SAE (as above) to the Sponsor within 24 hours and to the Ethics Committee that accorded approval to the study protocol within 24 hours of their occurrence and analyzed report within 14 calendar days of SAE occurrence

Serious Adverse Event Report Form.
Study name:
Study Title:
Study initiated date:
Subject ID:
Event term:
SAE onset date:
SAE reported date to sponsor:
Event related to study drug:
SAE covering letter attached:
Report Information
Initial Report : Final Report:
Demographics
DOB/Age: Sex:
Ht in cm: Wt:
Event Information
Date of Event:
Onset date: End date:
Onset time: End time:
Event Grading and Assessment
Event Grade:
Intensity:
Outcome:
Serious Event Criteria
1) Results in Death:
a. date of death:
b. cause of Death:
2) Impatient hospitalization or Prolonged hospitalization:
a. Date of Admission;
b. Subject hospitalization continued;
c. Treated doctor:
3) Persistent or significant disability;
4) Life threatening:
5) Congenital Anomaly:
6) Medically significant event:
Serious Event Description
Summary of Events:

Relevant and past medical history:

Laboratory Findings:

Therapy Given:

Study Medication

Study treatment start date:

Event related study drug:

Event related study treatment:

Was Study treatment withheld: date of withheld;

Subject discontinued from the treatment: Date of discontinued:

Investigator Signature:

Date:

* Please provide the reason if the PI has not signed the form.

Annexure 3:

Checklist of APPENDIX XII of Schedule Y:

CHECKLIST FOR SUBMISSION OF SERIOUS ADVERSE EVENT REPORT (SAE) OCCURRING IN CLINICAL TRIAL

S.No	Details		
1	**Country (Name of the country should be specified)**		
2	**SAE report of death or other than death, Please tick (✓)**	**Death**	**Other than death**
		Yes/No	**Page No.**
3	**In case of Serious Adverse Event(SAE) ,please specify if there is any injury to the subject (Please specify Yes/No) in the box**		
4	Protocol Title		
5	Protocol Study No./ ID /Code		
6	Copy of Clinical Trial permission obtained from CDSCO		
7	CTRI Registration No. (Mandatory for Clinical Trial Permitted after 15/06/09)		
8	Sponsor(Address with contact no and Email)		
9	CRO (Address with contact no and Email)		
10	Initial / Follow-up (FU)		
11	In case of follow-up: Date & Diary no of initial or recently submitted report information		
12	**Patient Details**		
a)	Initials & other relevant identifier (hospital/OPD record number etc.)		
b)	Gender		
c)	Age and/or date of birth		
d)	Weight		
e)	Height		
13	**Suspected Drug(s)**		
a)	Generic name of the drug		
b)	Indication(s) for which suspect drug was prescribed or tested		
c)	Dosage form and strength		
d)	Daily dose and regimen (specify units - e.g., mg, ml, mg/kg).		

e)	Route of administration		
f)	Starting date and time of day.		
g)	Stopping date and time, or duration of treatment		
14	**Other Treatment(s)**		
	Provide the same information for concomitant drugs (including non prescription/OTC Drugs) and non-drug therapies, as for the suspected drug(s).		
15	**Details of the events**		
a)	Full description of event (s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious. In addition to a description of the reported signs and symptoms, whenever possible, describe a specific diagnosis for the reaction.		
b)	Start date (and time) of onset of reaction.		
c)	Stop date (and time) or duration of reaction		
d)	Dechallenge and rechallenge information.		
e)	Setting (e.g., hospital, out-patient clinic, home, nursing home).		
16	**Outcome**		
a)	Information on recovery and any sequelae; results of specific tests and/or treatment that may have been conducted		
b)	For a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction; any post-mortem findings		
c)	Other information: anything relevant to facilitate assessment of the case, such as medical history including allergy, drug or alcohol abuse; family history; findings from special investigations etc.		
17	**Details about the Investigator**		
a)	CT Site Number, if any		
b)	Name		
c)	Address		
d)	Telephone/Mobile Number & Email		
e)	Profession (Specialty)		
f)	Date of reporting the event to Licensing Authority		
g)	Date of reporting the event to Ethics Committee overseeing the site		
h)	Signature of the Investigator		
18	**Details about the Ethics Committee**		
a)	Name & Address		
b)	Name of Chairman & Address		
c)	Telephone/Mobile Number		
d)	Email		
19	Adverse Event Term / Details of SAE		
20	Causality Assessment (Related/Unrelated) by Investigator		
21	Causality Assessment (Related/Unrelated) by Sponsor/CRO		
22	Details of compensation provided for injury or death. In case no compensation has been paid, reason for the same :		
23 a)	Duly filled SAE Form as per Appendix XI of Schedule Y		
b)	Laboratory investigations report /Discharge summary (if available and applicable)		
c)	Post-mortem report (if applicable)/ Any additional documents)		

Note: Information not relevant to a particular SAE should be marked with NA

Annexure 4:

Factor (F) for calculating the amount of compensation (Based on Workmen Compensation Act)

Age		Factors
1		2
Not More Than	16	228.54
	17	227.49
	18	226.38
	19	225.22
	20	224.00
	21	222.71
	22	221.37
	23	219.95
	24	218.47
	25	216.91
	26	215.28
	27	213.57
	28	211.79
	29	209.92
	30	207.98
	31	205.95
	32	203.85
	33	201.66
	34	199.40
	35	197.06
	36	194.64
	37	192.14
	38	189.56
	39	186.90
	40	184.17
	41	181.37
	42	178.49
	43	175.54
	44	172.52
	45	169.44
	46	166.29
	47	163.07
	48	159.80

49	156.47
50	153.09
51	149.67
52	146.20
53	142.68
54	139.13
55	135.56
56	131.95
57	128.33
58	124.70
59	121.05
60	117.41
61	113.77
62	110.14
63	106.52
64	102.93
65 or More	99.37

13. References

- WHO Operational Guidelines for Ethical Review Committee that Review Biomedical Research (Geneva 2000). Retrieved from - www.who.int/tdr/publications/publications / accessed 24 March 2008
- International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) (1996). Retrieved from - http://www.ich.org/LOB/media/MEDIA482.pdf accessed on 24 March 2008.
- Integrated addendum to ich e6(r1): guideline for good clinical practice e6(r2) dated 11 Jun 2015
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