INSTITUTE ETHICS COMMITTEE

(Human Studies)

Standard Operating Procedures

SEEMA DENTAL COLLEGE AND HOSPITAL, RISHIKESH

UTTARAKHAND

Institutional Ethics Committee

All institutions which carry out any form of biomedical and experimental research or study involving human beings constitutes an appropriate **Institutional Ethics Committee (IEC)** that is consistent with national, international and local guidelines and regulations to protect safety and well-being of all participants and should prevent unethical research.

Basic role of Institutional Ethics Committee of SDCH:

1. IEC constitutes of external and internal members from medical/non-medical, legal, scientific and non-scientific persons, who go through the research protocol/proposal submitted for conducting clinical trial or scientific research or MDS thesis or any other kind of study on human subjects and state whether or not it is ethically acceptable. IEC review all types of research proposals/protocols involving human participants with a view to safeguard the dignity, rights, safety and well being of all actual and potential research participants before approving the research proposals. The goals of research, however important, should never be permitted to override the health and well being of the research subjects.

2. IEC ensures the protection of the rights, dignity, safety and well-being of all actual and potential research participants (human subjects) that are involved in a clinical trial or scientific research or MDS thesis or any other kind of study-

- by preventing the studies that pose an unacceptable risk of harm to participants and
- by ensuring that all participants in research are aware about the pros and cons for their participation and have given appropriate Informed Consent.

3. IEC is also responsible for reviewing and approving the protocol, the suitability of the investigators, facilities, methods and adequacy of information to be used for obtaining and documenting informed consent of the study subjects and adequacy of confidentiality safeguards.

4. IEC promotes fair ethical policies and procedures which will maximize the likelihood of achieving good and patient-oriented outcomes and enhances the ethical tenor between health care professionals and organizations conducting clinical trial or scientific research or MDS thesis or any other kind of study. **IEC should prevent unethical research.**

5. IEC overviews and monitors thoroughly, compliance of sites with Standard Operating Procedures (SOPs), regulations, guidelines and ETHICS. In the case of any serious adverse event occurring to the subjects involved in clinical trial or scientific research/study, the IEC shall analyze the data and record its findings for further action, if any.

Dr. Himanshu Aeran
Director Principal

For Information
Chairman
Executive Director
Director
Vice Principal

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

SEEMA DENTAL COLLEGE & HOSPITAL DIRECTOR PRINCIPAL

I. SHORT TITLE:

The following may be called as "Standard Operating Procedures for the Institutional Ethics Committee (EC SDCH) of Seema Dental College and Hospital, Rishikesh.

II. ADOPTION OF SOP:

Seema Dental College and Hospital, Rishikesh herein after referred "EC SDCH" has adopted this written Standard Operating Procedures (SOP) to ensure the protection of the rights and welfare of human participants in biomedical, experimental and behavioural research conducted at EC SDCH.

III. OBJECTIVE:

The objective of these Standard Operating Procedures of the Institutional ethical committee (EC SDCH) is to maintain effective functioning of the EC SDCH and to ensure quality and technical excellence and consistent ethical review of all the submitted health and biomedical research proposals and ongoing approved research studies involving human participants in accordance with the ICMR ethical guidelines for biomedical research on human subjects.

IV. AUTHORITY UNDER WHICH EC SDCH IS CONSTITUTED:

The Director Principal will appoint the Chairperson and all the committee members based on their competence, experience and integrity by sending an official request letter (Annexure 1A & 1B). Members will confirm their pal acceptance to the Director Principal by providing all the required information for membership (Annexure 2). The Chairperson will furnish any information or report to the Director Principal, SDCH when required.

V. ROLE AND RESPONSIBILITIES OF EC SDCH:

The EC SDCH will review all types of research proposals involving human participants with a view to safeguard the dignity, rights, safety and well being of all actual and potential research participants before approving the research proposals. The goals of research, however important, should never be permitted to override the health and well being of the research subjects.

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

The EC SDCH will ascertain whether all the cardinal principles of research ethics viz. Autonomy, Beneficence, Non maleficence, Respect for free and informed consent, respect for human dignity, respect for vulnerable persons, respect for privacy and confidentiality and justice are taken care of in planning, conducting and reporting of the proposed research. For this purpose, it will look into the aspects of protocol review , selection of participants, voluntary participation of potential participants, informed consent process, risk benefit ratio, distribution of burden and benefit, maintenance of privacy and confidentiality and provisions for appropriate compensations. It will review the proposals before the commencement of the study as well as review periodically until the completion of the study through appropriate well documented procedures. Such a review may be based on the periodic study progress reports furnished by the investigators and/or monitoring and internal audit reports furnished by the sponsor and/or by visiting the study sites.

The mandate of the EC SDCH shall be to review all research projects to be conducted at the institution involving human beings directly or indirectly , irrespective of the funding agency.

EC SDCH will provide advice to the researchers on all aspects of the welfare and safety of the research participants after ensuring the scientific soundness of the proposed research through appropriate Scientific Review Committee/Research Committee.

In case an ethics committee revokes its approval accorded to a trail protocol, it will record the reasons for doing so and at once communicate such a decision to the investigator as well as to the Licensing Authority.

VI. COMPOSITION OF EC SDCH:

EC SDCH will be a multidisciplinary and multisectorial body in composition and independent. The number of members of the Review Board may range from 7 to 15.

The Chairperson and member secretary will be from the institution of the EC SDCH. Other members will be a mix of medical/nonmedical, legal,

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

scientific and non-scientific persons and may also include members of public to reflect the differed points of view.

There will be representation of age and gender in the committee to safeguard the interest and welfare of all sections of the society. Members should be aware of local, social and cultural norms, as this are an important is an important social control mechanisms. EC SDCH may invite subject experts to take their views, whenever it is needed.

The EC SDCH will include:

1. Chairperson
2. One two persons from basic medical science area (one pharmacologist compulsorily, one female scientist compulsory)
3. One two clinicians from various institutes
4. One legal expert or retired judge
5. One social scientist / representative of non-governmental voluntary agency
6. One philosopher/ethicist/theologian
7. One lay person from the community
8. Member secretary

A sub-board of the main EC SDCH may review proposals submitted by undergraduate or post graduate students or if necessary, an EC SDCH may be separately constituted for the purpose, which will review proposals in the same manner as described above.

VII. MEMBERSHIP REQUIREMENTS:

1. All members will serve for a period of 1 year on renewable basis. New members will be included in the Ethical Committee Seema Dental College (EC SDCH) in such a way that there will be a mix of recently included members and members with some years of experience.

2. During the term, Director Principal in consultation with the Chairman can disqualify any member if, the contribution is not adequate and/or there is long period of member non availability.

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

3. A member can tender resignation of his office membership from the EC SDCH to the Director Principal through the Chairman after serving one month advance notice.

4. Director Principal can replace the member of EC SDCH as and when required.

5. Each member is required to sign the declaration and confidentiality agreement regarding EC SDCH activities.

6. Conflict of interest should be declared by members of the EC SDCH prior to review meeting.

VIII. QUORUM REQUIREMENTS

Minimum of 50% of committee strength + 1 member and not less than 5 members will be required to compose a quorum for the meeting of which at least one member will be from outside the institution, and one member will be a non-scientific member and one from opposite gender. All decisions will be taken in meetings and not by circulation of projects proposals. Quorum will have 5 members with following representations:

1. Basic medical scientists(preferably one pharmacologist)
2. Clinicians
3. Legal expert
4. Social scientist/representative of non-governmental voluntary agency/philosopher/ethicist/ theologian or a similar person
5. Lay person from the community

IX. CONDUCT OF EC SDCH MEETINGS

The Chairperson will conduct will conduct all meetings of the EC SDCH. In the absence of the chairperson an alternate chairperson an alternate chairperson will be elected from the members by the members present, who will conduct the meeting. The member secretary is responsible for organizing the meetings, maintaining the records and communicating with all concerned. He/ she will prepare the minutes of the meetings and get it approved by the chairperson and all the members.

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

X. INDEPENDENT CONSULTANTS

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

XI. APPLICATION PROCESS

1. All proposals should be submitted on any working day 2 weeks in advance of schedules meeting in the prescribed application form, the details of which are given.
2. All relevant documents should be enclosed with application form.
3. Required copies of the proposal along with the application and documents in prescribed format duly signed by the Principal investigator and the co investigators/ research scholars shall be guided to the Chairperson EC SDCH through member secretary. In his absence via any nominated by chairperson. Receipt of the application will be acknowledged by the EC SDCH.
4. Every application will be allotted an EC SDCH registration number to be used for all future correspondence and reference. The date of EC SDCH meetings will be intimated to the Principal investigator to attend the meeting and to make a brief presentation of the proposal and to clarify the points raised by the members.
5. The decision of the committee on the proposal will be communicated in writing. If revision is to be made, the revised document in required number of copies should be submitted within a stipulated period of time as specified in the communication or before the next meeting.
6. All research proposals/clinical trials funded/sponsored by Pharmaceutical companies, agencies, multinationals etc. will be charged on administrative fee/ processing fee as specified by the research secretariat/ECSDCH. Waiver of these fees is permissible for non-funded studies, departmental studies, and studies funded by organisations like

ICMR, UGC etc. in general, waiver of administrative fee is possible at the discretion of chairperson, EC SDCH.

XII. DOCUMENTATION

All research proposals shall be submitted along with the information and documents as specified

XIII. REVIEW PROCEDURE

1. The meeting of the EC SDCH will be held on periodic intervals every two months unless otherwise specified by the member secretary. Additional review meetings can also be held with short notice as and when required. Meetings will be planned in accordance with the need of the work load.
2. The proposals should be sent to the EC SDCH at least 2 weeks in advance of schedule meeting
3. The EC SDCH member secretary shall screen the proposals of their completeness and depending on the risk involved categorize them into three types namely exemption review expedited review and full review.
4. Decisions will be taken by consensus after discussion and whenever needed voting will be done. Decision of chairperson will be final.
5. Researchers will be invited to offer clarifications if needed. The principal investigator/ research scholar will then present the proposal in person in the meeting. When the principal investigator is not present due to unavoidable reasons the Co PI will present the proposal.
6. The decisions will be written as minutes of meeting and chairperson's approval shall be taken in writing.

1. EXEMPTION FROM REVIEW

Proposals which present less than minimal risk fall under this category as may be seen in following situations;

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

i) Research on educational practices such as instructional strategies or effectiveness of or the comparison among instructional techniques, curricula or classroom management methods.

EXCEPTIONS:

I) When research on use of educational tests, survey or interview procedures or observation of public behaviour can identify the human participant directly or through identifiers and the disclosure of information outside research could subject the participant to the risk of civil or criminal or financial liability or psychological harm.

II) When interviews involve direct approach or access to private papers.

EXPEDITED REVIEW

The proposals presenting no more than minimal risk to research participants may be subjected to expedited review. The member secretary of the EC SDCH and the chairperson of the EC SDCH or designated member of the committee of EC SDCH may do expedited review only if the protocols involve:

i) Minor deviations from originally approved research during the period of approval

ii) Revised proposals previously approved through full review by the SC SDCH or continuing review of approved proposals where there is no additional risk or activity is limited to data analysis.

iii) Research activities that involve only procedures listed in one or more of the following categories:

a) Clinical studies of drugs and medical devices only when-

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

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 nonresearch (clinical) purposes.

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

5. When in emergency situations like serious outbreaks or disasters a full review of the research is not possible, prior written permission of EC SDCH 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.

a) Research on interventions in emergency situation

When proven prophylactic, diagnostic and therapeutic methods do not exist of have been ineffective, physicians may be use new intervention as investigational drug (IND)/ devices/vaccine to provide emergency medical care to their patients in life threatening conditions. Research in such instance of medical care could be allowed in patients:

i) When consent of person/patient/responsible relative or custodian / team of designated doctors for such an event is not possible. However, information about the intervention should be given to the relative/legal guardian when available later

ii) When the intervention has undergone testing for safety prior to its use in emergency situations and sponsor has obtained prior approval

iii) Only if the local EC SDCH reviews the protocol since institutional responsibility is of paramount importance in such instances

B) Research on disaster management

A disaster is the sudden occurrence of the calamitous event at any time resulting in substantial material damage, affecting persons, community os states. It may be periodic, caused by both nature and humans and creates an imbalance between the capacity and resources of the society and the needs of the survivors or the people whose lives are threatened, over a given period of time. It may also be unethical sometimes not to do research in such circumstances. Disasters create vulnerable persons and groups in society, particularly so in disadvantages communities, and therefore, the following points need to be considered when reviewing such research:

SEEMA DENTAL COLLEGE & HOSPITAL
PRINCIPAL
RISHIKESH

i) Research planned to be conducted after a disaster should be essential culturally sensitive and specific in nature with possible application in future disaster situations

ii) Disaster affected community participation before and during the research is essential and its representative or advocate must be identified.

iii) Extra care must be taken to protect the privacy and confidentiality of participants and communities

iv) Protection must be ensures so that only minimal additional risk is imposed

v) The research undertaken should provide direct or indirect benefits to the participants the disaster affected community or future disaster affected population between the community and the researcher.

vi) All international collaborative research in the disaster affected area should be done with a local partner on equal partnership basis.

vii) Transfer of biological material if any should be as per government rules taking care of intellectual property rights issues.

Expedited review may also be taken up in cases of nationally relevant proposals requiring urgent review.

FULL REVIEW

All review presenting with more than minimal risk , proposals/protocols which do not qualify for exempted or expedited review and projects that involve vulnerable population and special groups shall be subjected to full review by all the members.

While reviewing the proposals, the following situations may be carefully assessed against the existing facilities at the research site for risk/benefit analysis.

SEEMA DENTAL COLLEGE & HOSPITAL
PRINCIPAL
RISHIKESH

XIV. Aspects considered during review of research proposals

1. Scientific design and conduct of the study
2. Approval by appropriate scientific review committee/ research committee
3. Examination of predictable risks/harms
4. Examination of potential benefits
5. Procedure for selection of subjects including inclusion/exclusion, withdrawal criteria.
6. Management of research related injuries, adverse effects
7. Compensation provisions
8. Justification for placebo in control arm if any
9. Availability of products, benefits to subjects after the study is completed if applicable
10. Patient information sheet , informed consent form in English and in local language
11. Protection of privacy and confidentiality
12. Involvement of the community wherever necessary
13. Plans for data analysis and reporting
14. Adherence to all regulatory requirements and applicable guidelines
15. Competence of investigators, research and supporting staff
16. Facilities and infrastructure of study sites
17. Criteria for withdrawal of patients, suspending or premature termination of the study in EC SDCH

XV. DECISION MAKING:

1. Members will discuss the various issues before arriving at a consensus decision. When consensus is not arrived at the decision will be made by voting procedure.
2. A member should withdraw from the meeting during the decision procedure concerning an application where a conflict of interest arises and this should be indicated to the chairperson prior to the review of the application and recorded in minutes.
3. Decision will be made only in meetings where quorum is complete
4. Only member can make the decision. The expert consultants will only offer their opinions.

SEEMA DENTAL COLLEGE & HOSPITAL * RISHIKESH * PRINCIPAL

5. Decision may be approve, reject or revise the proposals. Specific suggestions for modifications and reasons for modifications and reasons for rejection will be given.
6. In cases of conditional decisions, clear suggestions for revision and the procedure for having the application revised will be specified.
7. Modified proposals will be reviewed by an expedited review through identified members.
8. Procedures for appeal by the researchers will be clearly defined.

XVI. COMMUNICATING THE DECISION:

1. Decision of the meeting on the proposals will be communicated by the member secretary in writing to the PI/Research Scholar within 10 working days after the meeting at which the decision was taken in the specified format . A certificate of approval will be sent to the applicant within 2 weeks (Annexure 6). All the approvals will be valid for one year or for the duration of the project whichever is less. Investigator has to get his or her project re approved after one year if necessary.
2. The communication of the decision will include:
   a) Name and address of EC SDCH
   b) The date, place and time of decision
   c) The name and designation of the applicant
   d) Title of the research proposal reviewed
   e) The clear identification of protocol and version number , date
   f) Along with protocol, other documents reviewed- clear description of these documents along with version number and date
   g) List of EC members who attended the meeting – clear description of their role, affiliation and gender
   h) A clear statement of decision reached
   i) Any advice by the EC SDCH to the applicant including the schedule/plan of ongoing review by the EC SDCH

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

j) In case of conditional decision, any requirement by EC SDCH, including suggestions for revision and the procedure for having the application re reviewed

k) In case of rejection of the proposal, reasons for the rejection will be clearly stated

l) Signature of the member secretary with date

XVII. FOLLOWING UP PROCEDURES FOR APPROVED PROPOSALS BY PI/SPONSOR

1. EC SDCH will review the progress of all the studies for which a positive decision has been reached from the time of decision will the termination of the research
2. Progress of all the research proposals will be followed at a regular interval of at least once a year. But in special situations, EC SDCH will conduct the follow up review at shorter intervals basing on the need, nature and events of research project
3. Periodic status report of study should be submitted at prescribed intervals for review, along with information and documents as specified based on the safety concerns.
4. Final report should be submitted at the end of study.
5. Following instances and events will require the follow up review/renewed approval
   a) Any protocol amendment likely to affect rights, safety or well being of research subject of conduct of study
   b) Serious or unexpected ADR related to study or product, action taken by investigator, sponsor and regulatory authority
   c) Any event or information that may affect the benefit/risk ratio of the study
6. Protocol deviation, if any, should be informed with adequate justifications
7. Any new information related to the study should be communicated
8. Premature termination of study shall be notified with reasons along with summary of the data obtained so far

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

9. Change of investigator/ sites must be informed to the office of EC SDCH
10. Monitoring: oversight mechanism will be in place to monitor the approved studies. Actual site visits can be made especially in the event of reporting of adverse events or violations of human rights and appropriate action will be taken when required and communicated to the applicant including indicating modification / suspension/termination/continuation of the project. In case the EC SDCH desires so reports of monitoring done by the sponsor and the recommendations may also be sought.
11. Applicant must inform the time of completion of study and must send the result summary to ECSDCH. ECSDCH must receive a copy of final summary of study completed from the applicant.

XVIII. RECORD KEEPING:

1. All the documents and communications of EC SDCH will be dated, filed and archived in a secure place.
2. Only persons, who are authorized by the chairman of EC SDCH will have the access to the various documents.
3. All the documents related to research proposals will be archived for a minimum period of 3 years in the institute following the completion of the study.
4. No document will be retained by the EC SDCH member.
5. At the end of the meeting, every member must return the documents containing all the research proposals and documents to EC SDCH office staff.
6. Following documents will be filed and archived with proper label on the top of file for easy identification
   a) Constitution and composition of ECSDCH
   b) Curriculum vitae (CV) of all members of EC SDCH with records of training in Human ethics if any
   c) Standard operating procedures of ECSDCH
   d) Annual reports
   e) A record of all income and expenses of ECSDCH including allowances and reimbursements made to the EC Members

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

f) The published guidelines for submission established by the EC
g) Copy of all study protocols with enclosed documents. Progress reports and SAEs
h) Agendas and Minutes of all EC SDCH meetings duly signed by the Chairperson/member secretary.
i) Copy of all existing relevant national and international guidelines on ethics and laws along with amendments.
j) Copy of all correspondence with members, Principal Investigators and other regulatory bodies.
k) Record of all notification issued for premature termination of the study with a summary of the reasons
l) Final reports of the approved projects

XIX. UPDATING EC SDH MEMBERS:

1. All relevant new guidelines should be brought to the attention of the members.
2. The EC Members should be encouraged to keep abreast of all national and international developments in ethics through orientation courses on related topics bt its own members or regular training organised by constitutes authorities so that they become aware of their role and responsibilities. For drug trial review it is preferable to train the EC SDCH members in Good Clinical Practice. Any change in the regulatory requirements should be brought to their attention and they should be aware of local, social and cultural norms as this is the most important social control mechanism. This is needed for maintaining quality in ethical review.

XX. TERMS OF REFERENCE

Terms of reference will be maintained in the office if EC SDCH. This includes:

A) Membership requirements
B) Terms of appointment with reference to the duration of the term
C) The policy for removal, replacement , resignation procedure
D) Frequency of meetings

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

E) Payment of processing fee to the EC SDCH for review, honorarium consultancy to the members/ invited experts etc

The SOPs will be updated periodically based on the changing requirements. The term of appointment of members could be extended for another term and defined percentage of members could be changes on regular basis.EC SDCH would 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.

XXI. ADMINISTRATION AND MANAGEMENT

A full time secretariat and space for keeping records is required for a well-functioning EC SDCH. The members could be given a reasonable compensation for the time spared for reviewing the proposals. Reasonable fees can be changed to cover the expenses related to review and administrative processes for any third party (protocols submitted by researchers not employed by ECSDCH) submission as described. There should be provision for allocating reasonable amount of funds for smooth functioning of the EC SDCH

XXII. SPECIAL CONSIDERATIONS/PROTECTION OF VULNERABLE POPULATION

While all the above requirements are applicable to biomedical research as a whole irrespective of the specialty of research, there are certain specific concerns pertaining to specialised areas of research which require additional safe guards/ protection and specific considerations for the ECSDCH to take note of. Examples of such instances are research involving children, pregnant and lactating women, vulnerable participants and those with diminished autonomy besides issues pertaining to commercialization of research and international collaboration. The observation and suggestions of ECSDCH will be given in writing in unambiguous terms in such instances. ICMR guidelines as applicable will be followed for protection of vulnerable population.

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

Letter Ref No. Date:

From

Director Principal

Seema Dental College and Hospital

Rishikesh

To

_____

_____

Sub: Constitution of Institute Ethics Committee

Dear Sir

On behalf of Seema Dental College and Hospital, Rishikesh, I request your concurrence for possible appointment as a member of Institute Ethics Committee of SDCH. Kindly send your written acceptance in the enclosed format and provide short curriculum vitae along with the acceptance letter.

On receipt of your acceptance, I shall send you the formal appointment letter.

Yours sincerely

Signature:

Name:

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

APPOINTMENT ORDER

Dr/Mr/Mrs_____Date:_____

I am pleased to appoint you as_____of the Institutional Ethics Committee (EC SDCH) (Human Research) at Seema Dental College and Hospital Rishikesh w.e.f_____for a term of_____year/moths provided following conditions of appointment are met.

1. You should be willing to publicize your full name, profession and affiliation
2. You are willing to record all reimbursement for work and expenses, if any, within or related to an ECSDCH and make it available to the public upon request.
3. You consent to sign confidentiality agreement between you and ECSDCH regarding meeting deliberations, applications , information on research participants and related matters

The renewal of your appointment will be by consensus and 1 month notice on either side will be necessary prior to resignation/termination of appointment. Terms and conditions regarding the resignation procedure, disqualification procedures, replacement procedures etc may be found in the Standard Operating Procedures (SOPs) of EC SDCH.

We sincerely hope your association with EC SDCH will be fruitful to the institute and the community we serve.

Chairperson

(Name/Seal)

EC SDCH

Seema Dental College and Hospital

Rishikesh

Signature of Appointee

(Name & Date)

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

From

_____

_____

To

The Director Principal

Seema Dental College and Hospital

Rishikesh

Sub: Consent to be member of Institute Ethics Committee

Dear Sir

In response to your letter stated above, I give my consent to become a member of EC SDCH of Seema Dental College and Hospital, Rishikesh. I shall regularly participate in the EC SDCH meeting to review and give my unbiased opinion regarding the ethical issues

I shall be willing for my name, profession and affiliation to be published.

I shall not keep any literature or study related document with me after the discussion and final review.

I shall maintain all the research project information confidential and shall not reveal the same to anyone other than project related personal.

I herewith enclose my CV.

Thanking you

Yours sincerely

Signature

Name

Date:

SEEMA DENTAL COLLEGE & HOSPITAL
PRINCIPAL
RISHIKESH

SEEMA DENTAL COLLEGE AND HOSPITAL

INSTITUTE ETHICS COMMITTEE

INITIAL REVIEW SUBMISSION FORM FOR RESEARCH PROPOSAL

1. Title of the research proposal
2. Name of the Principal Investigator with qualification and designation
3. Name of the coinvestigator with qualifications and designation
4. Name of the Institute/Hospital/Field area where research will be conducted
5. Forwarding letter from the Head of the Department/Institute/ Guide
6. Protocol of the proposed research: clear research objectives, rationale for undertaking the investigations in human participants in the light of existing knowledge, inclusion and exclusion criteria for entry of participants. Precise description of methodology of the proposed research, including sample size, type of study design, intended intervention, dosages of drugs, route of administration, duration of treatment and details of invasive procedures if any. Plan to withdraw or withhold standard therapies in the course of research. Plan for statistical analysis of the study. Ethical issues in the study and plans to address these issues.
7. Proposal should be submitted with all relevant enclosures like proforma, case report forms, questionnaires, follow up cards, participant recruitment procedures and brochures if any, informed consent process, including patient information sheet and informed consent form in English and local languages. Investigators brochure for trail on drugs/devices/vaccines/herbal remedies and statement of relevant regulatory clearances. Source of funding and financial requirements for the project.
8. For any drug/device trail, all relevant preclinical animal data and clinical trial data from other centres within the country/other countries, if available
9. Usefulness of the project/trail

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

10. Expected benefits to volunteers /community. Benefits to other categories if any
11. Explain all anticipated risks (adverse events, injury, and discomfort) of the project. Efforts taken to minimise the risks. Proposed compensation and reimbursement id incidental expenses and management of research related and unrelated injury/illness during and after research period. Description of arrangements for indemnity, if applicable in study related injuries and description of the arrangements for insurance coverage for research participants, if applicable.
12. Agreement to report all serious adverse effects (SAE) to EC SDCH
13. Other financial issues including those related to insurance
14. An account of storage and maintenance of all data collected during the trail
15. Research proposals approval by scientific advisory committee
16. Statement of conflict of interest if any
17. Agreement to comply with the relevant national and applicable international guidelines, Good clinical practice (GCP) protocols for clinical trails
18. All significant previous decisions by other ECs or regulatory authorities for the proposed study and an indication of the modification to the protocol made on that account. The reasons for negative decisions should be provided
19. A statement on probable ethical issues and steps taken to tackle the same like justification for washout od standard drug or the use of placebo control
20. Curriculum vitae of all the investigators with relevant publications in last five years
21. Plans for publication of results/positive or negative/while maintaining the privacy and confidentiality of the study participants
22. Any other information relevant to the study
23. Signature of the Principal investigator with date

Note: the above information and enclosures should be furnished wherever necessary depending upon the nature of study proposal

SEEMA DENTAL COLLEGE & HOSPITAL
PRINCIPAL
RISHIKESH

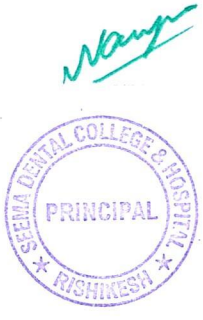
FORMAT FOR SUBMISSION OF PROJECTS INVOLVING RESEARCH IN HUMAN SUBJECTS FOR CLEARANCE BY ETHICS COMMITTEE OF SEEMA DENTAL COLLEGE AND HOSPITAL RISHIKESH

Submit the research project along with covering letter and sift copy with the following information to the member secretary, institution ethic committee. The principal investigator must submit protocol forwarded through the Head of the Department.

No research project shall be/can be started unless ethical clearance /approval are obtained. Please bear in mind that research projects which are earlier not submitted to the ethical committee

All submissions should be made in the prescribed Format of the Institution ethics committee with signatures of all the investigators. The submission must be accompanied with Participant Informed Consent Form and Participant Information Sheet, both in English and Hindi/Concerned local language, in a simple layman's language, in a narrative form, directed to participant, covering all the points. Also ensure all the pages are numbered.

Project submission time: submissions will be received on all working days.



FORM TO BE FILLED BY THE PRINCIPAL INVESIGATOR
FOR SUBMISSION TO EC SDCH
(for attachment to each copy of the proposal)

Proposed title:

	Name, Designation, Department and Qualifications	Address Email ID	No. of projects already with investigator	Signature
Principal investigator				
Co-PI 1.				
2				
3				
4				
5				
6				
Please attach detailed curriculum vitae of all investigators				

SEEMA DENTAL COLLEGE & HOSPITAL
PRINCIPAL
RISHIKESH

Tick appropriately

1. **Type of study:**

   - Cross Sectional ☐ - Clinical Trial ☐
   - Case control ☐ - Review ☐
   - Cohort ☐

   Participating centre:

   - Single center ☐
   - Multicentric ☐
   - Others(specify)

2. **Status of review**

   New ☐ Old ☐

3. **Clinical trials**

   Drug/vaccines/device/herbal remedies

   i. Does the study involve use of:
   ii. Is it approved and marketed
   iii. Does it involve a change in use, dosage, route of administration?
   iv. Is it investigational new drug?
   v. Investigators brochure submitted
   vi. In vitro studies data
   vii. Preclinical studies done
   viii. Clinical study is
   ix. Are you aware if this study is being done elsewhere?
   x. If yes, attach details

4. **Brief description of the proposal**—introduction, review of literature, aims and objectives, justification of the study, methodology describing the potential risks and benefits , outcome measures, statistical analysis and whether it is of national significance with rationale

5. **Subject selection:**

   i) Number of subjects:
   ii) Duration of study:
   iii) Will subjects from both sexes be recruited:
   iv) Inclusion /exclusion criteria given
   v) Vulnerable subjects

SEEMA DENTAL COLLEGE & HOSPITAL * PRINCIPAL * RISHIKESH

6. Privacy and confidentiality

Study involves: 1) Direct identifier ☐

2) Indirect identifiers ☐

7. Consent

Written ☐

Oral ☐

If consent not obtained, give reasons:

8. Risks & Benefits:

i) Is the risk reasonable compared to the anticipated benefits subjects/community/country?

ii) Is there physical/social/psychological risk/discomfort?

If yes, Minimal or no risk

More than minimal risk

High risk

iii) Is there a benefit to the subject?

Direct ☐

Indirect ☐

Benefit to the society ☐

9. Do you have any conflict of interest?

(financial/nonfinancial)

If yes, specify

Yes ☐

No ☐

10. Participant informed consent form

Attached English version ☐

Attached hindi version ☐

11. Whether any work on this project has started or not?

Yes

No

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

SEEMA DENTAL COLLEGE AND HOSPITAL RISHIKESH

INSTITUTIONAL ETHICS COMMITTEE

Ongoing approved research review submission form

1. Reference number
2. Month/year of approval
3. Number of ongoing review
4. Title of research proposal
5. Name of principal investigator with qualification and designation
6. Name of co investigators with qualification and designation
7. Duration of the project
8. Source of funding and financial allocation for the project/trial
9. Has subject recruitment begun?
10. If subject recruitment has not begin, give reasons
11. How many subjects have been screened?
12. How many subjects have been recruited?
13. How many more to be recruited
14. Is subject recruitment continuing?
15. Are there any drop outs?
16. Are subjects still receiving active intervention?
17. Have there been any adverse events? If yes, give details
18. Have there been any serious adverse effects?
19. Have there been any unanticipated study related problems?
20. Is there any new risk of benefit information? If yes, give details
21. Are there any interim changes to the protocol or consent form? If yes, give details
22. Does the scientific literature indicate changes in knowledge relevant to the conduct of the study?
23. list of attachments for review , if any
24. Remarks, if any
25. Signature of the principal investigator, with date

Note: The above information and enclosures should be furnished wherever necessary depending upon the nature of study proposal

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

SIX MONTHLY PROGRESS OF PROJECT

Institute Ethics Committee Reference No._____

Study title_____

_____

Name of Principal Investigator_____

Designation/department_____

Duration of the study_____

Date of starting of the study_____

Period of six monthly progress report : From_____to_____

Progress:

Side effects:

Amendments, if any:

Discontinuation reasons, if any:

Signature of Principal Investigator

Dated

COMMUNICATION OF DECISION OF THE INSTITUTIONAL ETHICS COMMITTEE (EC SDCH)

Protocol title:

Principal investigator:

Name and address of institution:

New review Revised review Expedited review

Date of review:

Date of previous review, if revised application:

Decision of EC SDCH

Recommended Recommended with suggestions
Revision Rejected

Suggestions/Reasons/Remarks:

Recommended for period of:

Please note:

- Inform ECSDCH immediately in case of any adverse events and serious adverse events
- Inform EC SDCH in case of any change of study procedure
- This permission is only for period mentioned above. Annual report to be submitted to EC SDCH
- Members of EC SDCH have right to monitor the trail with prior intimation

Signature of Member Secretary
EC SDCH

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

Data elements for reporting adverse effects occurring in a clinical trial

1. **Patient details:**
   Name
   Age
   Gender
   Weight
   Height

2. **Suspected drugs:**
   Generic name of the drug
   Dosage form
   Route of administration
   Starting date
   Duration of treatment

3. **Details of suspected adverse drug reactions**

4. **Details of the investigator**

   Name:
   Address:
   Date of reporting:

Signature of the Investigator

SEEMA DENTAL COLLEGE & HOSPITAL
PRINCIPAL
RISHIKESH

STANDARD OPERATING PROCEDURES FOR RESEARCH CELL
SEEMA DENTAL COLLEGE AND HOSPITAL
RISHIKESH, U.K

June 2022

Available at the institute website www.seemadentalcollege.org
SEEMA DENTAL COLLEGE & HOSPITAL
Veerbhadra Road, P.O. Pashulok, Rishikesh- 249203

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

The research cell of Seema Dental college and Hospital, Rishikesh (SDCH) has been constituted to review and approve all the clinical trials and research studies/ activities conducted by students and faculty of the institution
All the clinical studies and other types of clinical research undertaken in this institution are subjected to approval of regulatory authorities, approval of Institutional Ethics Committee (IEC) and compliance to competent authority guidelines on clinical research. The guidelines for clinical research include, Indian Council of Medical Research (ICMR), National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017, New Drugs and Clinical Trials Rules, 2019 and guidelines of Central Drugs Standard Control Organization (CDSCO), Guidelines for Good Clinical practice ICH E6(R2) etc.

SOPs of the research cell ensure that research is conducted in a manner that protects the rights and safety of study subjects and the integrity of the research data collected and essentially reflect "how" a procedure related to research is carried out in this institution.
SOPs will encompass all the departments in the institution to facilitate distribution, adoption and maintenance of one standard.

This standard operating procedure (SOP) describes the steps for fulfilling the regulatory, medical and ethical requirements for assessing the appropriateness and feasibility of implementing a conducting a research study protocol at SDCH.

Scope

This SOP applies to the activities involved in assessing protocol feasibility for all research studies conducted at SDCH, RISHIKESH involving human subjects.

SOPS need to ensure ongoing compliance by way of regular expert review.

1. Composition of the Research Cell: Dean/Principal/Head of Institution, Heads of all the departments of Seema Dental College and Hospital, Rishikesh Statisticians. Chairperson, Vice Chairperson, Secretary and Joint Secretary will be identified from among the members.

2. Appointments-The Research Cell members shall be appointed by the Director in consultation with the Heads of the various departments. The Chairperson, Vice Chairperson, Secretary and Joint Secretary shall be nominated by the Director.

3. The research cell will facilitate review and approval of Research Proposals

4. It shall review health research proposals submitted to it within a reasonable time and document its views in writing to the investigator(s).

The research cell shall provide independent, competent and scientific review of research proposals.

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

It may request the investigator(s) to explain any aspect of the study and shall make available acceptable standard format accepted by the committee for submissions of research proposals It shall obtain relevant documents which should include

• Summary of research proposal.
• Study proposal(s) and /or amendment(s)
• Written informed consent form(s) and questionnaire updates that the investigator proposes for use in the study.

The research cell shall consider the suitability of the investigator(s) for the proposed study with respect to relevant qualification, training and experience, as documented by current curriculum vitae.

PROCEDURE

Protocol Assessment

Every research proposal is assessed for feasibility of conductance with the existing staff and facilities.

Clinical/Scientific/Ethical Feasibility

- Clinical importance to patients/subjects.
- Scientific merit.
- Benefits and risks associated with the protocol.
- Consistency with the priorities of SDCH.

Operational Feasibility

- Availability of personnel and other resources required to conduct the study.
- Availability of patients meeting the inclusion / exclusion criteria of the study.
- The operational complexity of the protocol.
- Whether there are any conflicting studies in progress.

Regulatory Feasibility

- The Principal Investigator (PI) reviews the protocol to determine whether there is anything required that may be problematic when submitting the project to SDCH.

The PI must check the following points before submitting the protocol

- Research studies have the resources necessary to protect participants.
- Adequate time for the researchers to conduct and complete the research.
- Adequate number of qualified staff
- Adequate facilities
- Access to a population that will allow recruitment of the necessary number of participants.
- Availability of medical or psychosocial resources that participants might need as a consequence of the research.

Financial/ Legal Feasibility

- A detailed review of the costs, including time needed to complete protocol activities and patient care visits are determined by the PI.
- The PI must prepare the budget worksheet.
- The Legal expert will facilitate legal review of the contract.

Interaction with Institutional Ethics Committee:

Purpose

To describe the procedures related to communication with SDCH IEC (Institutional Ethics Committee) during the entire study duration right from study initiation to completion, and to describe what documents should be retained to reflect interaction with SDCH.

Scope

This SOP will apply to all studies being conducted at SDCH.

Procedure

Interactions with SDCH IEC continue throughout the duration of a research study to strengthen the team approach to the protection of participant safety in addition to enhancing compliance with applicable SOPs, guidelines and regulations governing research studies.

Initial Submission of project to SDCH IEC

1. Detailed description of project submission

- The PI/ Co-I should submit all study related documents to the SDCH IEC, no fewer than fourteen (14) days before the scheduled meeting.
- PI/Co-I must check the submissions and ensure that all mandatory forms and documents are enclosed. Comprising of :
    - Covering letter with brief description regarding the list of documents enclosed for IEC approval, including the no. of copies submitted, and date of all the documents.
    - Study protocol
    - Other related documents necessary for initial review as mentioned in the IEC
    - Curriculum Vitae and updated GCP certificate of the investigator and study team.

Note: One additional copy for PI Acknowledgement
The PI should keep a copy of the acknowledged (SDCH IEC stamp with sign and date) submission letter of the above mentioned documents

IEC Response

The PI should ensure that the letter of response from the SDCH IEC includes the following information:

- Clinical study identification, protocol number and title;
- Name and date of all documents reviewed by the SDCH IEC.
- Date of review by the SDCH IEC.
- Approval for the number of participants to be recruited in the study.

SHIVA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

- Decision/opinion/approval of the clinical study, including required modifications, if any; (Note: Reply to the SDCH IEC in case of any suggested modifications
- Signature of the SDCH IEC member secretary and date of the response.
- The PI should keep an original copy of the SDCH IECs approval letter.
- Immediately after receiving SDCH IEC approval, register the study on CTRI and if applicable on ClinicalTrials.gov.
- Notify SDCH IEC after receiving registration number.

Study Progress

PI can start project at SDCH after receiving approval letter from SDCH IEC and as study progress, PI must communicate with SDCH IEC for all required notification and reporting such as:

Protocol Amendments

a. Major Amendments

- Notify the SDCH IEC of any changes to the protocol and/or informed consent and/or of new information on the investigational product no fewer than fourteen (14) days before the next scheduled meeting.
- PI / guide must make sure that all changes or modifications in the amended version are underlined or highlighted along with detailed summary of changes.
- The number of copies of amendment /documents along with the covering letter should be submitted as per SDCH IEC requirements.
- Note: One additional copy for PI Acknowledgement
- The PI / CO-I / guide should obtain a copy of the acknowledged (SDCH IEC stamp with sign and date) amendment submission letter of the above mentioned documents, and file the same
- The amendments in the protocol and/or informed consent and of new information on the IP will be valid only after SVIEC approval, and should immediately implement the documents for the research after approval.

b. Minor amendments and notifications

Minor amendments are those that do not increase the risk or decrease the potential benefit to subjects and may be approved by the SDCH IEC.

Deviations/Violation and Waivers

- Submit protocol deviations/violations and waivers to the SDCH IEC for review and approval according to SDCH IEC and regulatory requirements.
- Deviation/ non-compliance/ violation /waiver happens when investigators fail to follow the procedures written in the approved protocol.
- Comply with national /international guidelines for the conduct of human research.
- Fail to respond to the SDCH IEC requests.
- PI/CO-I/ GUIDE must submit the deviations /violations/waiver reports.
- Protocol Waiver is analogous to a Protocol Deviation, except that prior SDCH IEC approval must be obtained before implementing the necessary departures from the protocol. Therefore, Protocol Waivers are anticipatory, while Protocol Deviations are not. E.g. Protocol Waiver means a prospective decision by an investigator to permit accrual of a subject who does not satisfy the approved inclusion /exclusion criteria for enrolment.

- SDCH IEC action could include one or more of the following:

- Inform the PI that SDCH IEC has noted the violation/ noncompliance /deviation and inform the PI to ensure that deviations /noncompliance /violations do not occur in future and follow SDCH IEC recommendations.
- SDCH IEC will enlist measures that the PI would undertake to ensure that deviations /noncompliance /violations do not occur in future.
- Call for additional information.
- Suspend the study till additional information is made available and is scrutinized.
- Suspend the study till recommendations made by the SDCH IEC are implemented by the PI and found to be satisfactory by the SDCH IEC.
- Suspend the study for a fixed duration of time.
- Inform the Director, principal /Head of institution, SDCH, Rishikesh.
- Revoke approval of the current study.
- Inform DCGI /Other relevant regulatory authorities.
- Keep other research proposals from the PI/ Co-PI under abeyance.
- Review and / or inspect other studies undertaken by PI/Co-PI.

Safety Information

- Safety information can be any information recently reported or obtained particularly regarding risks associated with the research.
- Safety information is categorized as Serious Adverse event (SAEs) and unexpected event reports of both onsite and offsite.
- The Principal Investigator must review safety information.
- It is recommended that the PI review of safety information must be documented.
- The Investigator must submit Serious Adverse Events (SAEs) and unexpected events reports, both onsite and offsite, including follow up reports for active study participants.
- Report all safety information to the SDCH IEC according to the regulatory requirements (eg. Investigational New Drug [IND] submissions, Council for International Organizations of Medical Sciences [CIOMS] reports, Suspected Unexpected Serious Adverse Reaction (SUSAR), Periodic Safety Update Report(PSUR), Data Safety Monitoring Board [DSMB] reports).
- File the safety reports and any associated correspondence.

Study Termination

a. Premature Termination / Suspension /Discontinuation of the study

- Research studies are usually terminated as per the recommendation of the SVDCH IEC, PI, or other authorized bodies wherein subject enrolment and subject follow-up are discontinued before the scheduled completion of the study.
- The SDCH IEC/PI other authorized bodies can prematurely terminate the study for the following reason but not limited to:
  - Protocol non-compliance/violation due to any reason.
  - Slow recruitment.
  - Frequency of SAEs occurring at trial site may require the study to be prematurely terminated for the safety of the patients.
  - Sponsor find treatment not effective.
  - Lack of funds, lack of adequate market potential, competing drugs have received marketing approval ahead of the test compound, etc.

- Based on the above mentioned reasons SDCH IEC secretary can send a notification letter for termination/suspension/discontinuation or query letter to request additional information to the PI.
- PI must reply immediately in case of any query generated or any further information requested from the SDCH IEC.

Managing Biological Samples:

Purpose

This SOP describes the procedures for collection, preparation, storage and shipment of biological sample.

Scope

This SOP will apply to all biological samples collected, processed, stored by PI.

Procedure

Collection of Samples

- After collecting the sample, the PI will record the details(the patient initials, patient ID and the date and time when the sample was obtained) of the biological sample collected.

Preparation and storage of Samples

- The sample either is stored as collected and/or processed as mentioned in the protocol or laboratory manual approved in the research proposal.

Managing Investigational Products (IPs):

Purpose

To describe the process and requirements for the receipt, storage, dispensing, and return or destruction of Investigational Product (IP) at SDCH/ research site.

Scope

This Standard Operating Procedure (SOP) will apply to all studies being conducted at SDCH/ research site.

Any new trial which is initiated during active period of the SOP will be covered under the SOPs, unless otherwise indicated. If necessary a study specific SOP may be prepared.

Procedure

Prior to receipt of Investigational Product (IP)/ Study Drug

- PI must identify an area with restricted access and appropriate temperature control for IP storage. This is area will be known as 'IP Storage Room'.
- Assign team members who would be responsible for IP receipt, storage, dispensing, accountability and recording the temperature for the storage area and returning or destruction of the IP/ study drug.
- The person must be identified on the study delegation log.

Receipt of Investigational Product (IP)/ Study Drug

- Upon receipt of the IP shipment at the SDCH/ research site, the PI/delegated member will unpack the IP box and check the IP inventory against the shipping form.
- Checking the inventory will include the following:

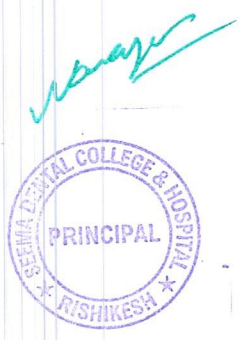
    - Checking the packaging numbers
    - Unique Kit numbers/IP number
    - Lot/batch numbers
    - Number of IPs in the container (s)
    - IP expiry date
- Any discrepancies (e.g. tampering/ breakage of the IP kit, mismatch in the number of kits, temperature excursions etc.) identified must be documented and informed to the sponsor/GUIDE/ point of contact immediately and seek advice for the next steps.
- Such IP must be stored separately and must be dispensed only after confirmation from the sponsor/Contract Research organization (CRO) /designee. This must be done by the person designated for IP accountability.
- If the inventory matches the drug received, the pharmacist/delegated person will sign and date (note: mention logger temperature present in the IP container on the receipt form) on the shipping receipt or Investigational Product Receipt Form, return a copy to the sponsor, and file the original .
- Shipment inventory must be done as per the study specific procedure
- The IP must be immediately transferred to the designated storage area at conditions as mentioned in the protocol.
- The temperature of the storage area must be recorded with a calibrated thermometer for the temperature range once daily or as mentioned in the protocol. It is strongly recommended that accurate temperature must be recorded.
- If available maintain the hard copy of auto generated temperature logger.

IP / Study Drug Storage

- Temperature of the IP storage area must be maintained on a 24-hour basis for recording temperature. The temperature will be recorded once daily or as mentioned in the protocol, except on holidays and Sundays. The capture of minimum and maximum values of temperature will be recorded if only specified by the sponsor/CRO.
- In case a temperature excursion is noted, the PI/ GUIDE/designated study team member must inform Investigator and the following telephonically followed by email at the earliest:
    - Inform the sponsor / CRO and document the same
    - Try to identify the cause of temperature excursion
- Take remedial actions in consultation with sponsor/CRO
- IP that has undergone a temperature excursion must be kept separately and must not be dispensed till a confirmation from sponsor/CRO is obtained i.e. the IP is "fit for use".

IP / Study Drug Dispensing

- IP must be dispensed by the PI/GUIDE/delegated member to subjects randomized on the study after fulfilling the eligibility criteria in accordance with the protocol.
- Upon dispensing the IP the PI/GUIDE/delegated member must note following in the source note and IP package:
    - Trial/Study ID number (both source notes and IP package)
    - Initial of the subject (both source notes and IP package)
    - Date of IP dispensing (both source notes and IP package)
    - Batch number and quantity of IP dispensed (in the source note)
    - Expiry date (in the source note)



- This information must be captured in Real time basis on the IP stickers available on IP containers, in the subject source notes as well as in the Drug Accountability Logs.

- The PI/GUIDE /delegated member will maintain a record of drug dispensed to and retrieved from each subject.
- The PI/GUIDE /delegated member will explain to each subject the drug accountability needs for the study (e.g., the need for the subject to return unused, partially used, and empty packages).
- Requests for IP resupply must be done as per the study specific procedures.

IP/ Study Drug Return

- The study subject will return all drug and study-related supplies to PI/GUIDE /delegated member on the specified visit mentioned in the protocol.
- The PI/GUIDE /delegated member will count the returned drug and compare this with the amount of drug expected to have been used since the previous study visit.
- PI/GUIDE /delegated member must document IP returned by the subject in the subject's source file as well as in the drug accountability logs as per the study requirement.
- In case of missing IP or extra IP, the PI/GUIDE /delegated member must obtain the information from the Subject and document the clarification provided in the source notes and drug dispensing log. This documentation should be done in real time basis
- The PI/GUIDE /delegated member will keep the Drug Dispensing Log and the drug accountability pages updated, regardless of when the monitor will perform final accountability.
- The PI/GUIDE /delegated member will store the returned drug separately in a secure area until it is verified by the Monitor.
- Whether the drug is to be returned to the sponsor or destroyed on-site will be determined by the instructions in the protocol.
- The documentation of the destruction/ return must be maintained.

Return of IP to Sponsor

- As specified in the protocol, the IP will be returned to the sponsor at intervals or at the end of the study. The PI/GUIDE /delegated member will follow the protocol or other instructions from the Sponsor or CRO to decide whether empty containers must be returned.
- The Monitor will perform the independent drug accountability review and will seal the drug that need to be shipped back to the Sponsor/CRO.
- The Monitor will arrange the preferred courier for the shipment of used and/or unused IP back to the sponsor/CRO.
- The PI/GUIDE will arrange for a gate pass for the shipment that needs to send back to sponsor/CRO.
- Unless instructed otherwise by the Monitor, the PI/GUIDE /delegated member will:
- Perform an inventory of the drug supplies.
- Compare inventory with the study medication records.
- Document discrepancies in the memo to file.
- Complete the Drug Return/Destruction Form (in presence of monitor) or similar form provided by the sponsor or CRO.
- Include a copy of the signed and completed Drug Return Form with the drug shipment and place the original in the study file.

IP Record Retention

At study completion, the PI/GUIDE will file all drug records with other regulatory documents in accordance with the record retention policy mentioned in the protocol

Site Initiation, Activation, Conduct and Closeout

Purpose
To describe the process, that ensures that the site is organized and prepared for the proper conduct of the research study at SDCH/research site. This standard operating procedure (SOP) also describes the processes to be followed at site initiation, activation, conduct and closeout of research study at SDCH.

Scope
This SOP will apply to all Pharma sponsored research study initiation, activation, conduct and close-out at SDCH.

Procedure
A research study should be initiated at a SDCH/research site only after investigator and Sponsor/CRO involved in the study is satisfied that essential documents, agreements and approvals are all in place. The site initiation process is designed to ensure that;

- SDCH/research site has all essential documents in place for the site to conduct the study in compliance with the approved protocol and applicable regulatory guidelines.
- SDCH/research site is aware of all the sponsor's procedures and SOPs for study conduct (such as safety recording and reporting, amendments, notification of any urgent safety measures/ violations or serious breaches) and has read and understood each.
- SDCH/research site is met with all the required regulatory and sponsor requirements.

Preparing site for SDCH/research site Initiation Visit

For preparing the SDCH/research site for initiation the investigator(s) or Clinical Trial Coordinator (CTC) should:

- Confirm the available date and time with the clinical research team that must attend the meeting and arrange the most suitable meeting date, time and place.
- Request an agenda for the visit from the sponsor; circulate the same to each team member.
- Confirm that investigator and team has reviewed the Protocol and Investigator's Brochure (IB) and any up-to-date information on investigational product (IP). The Investigator(s) must prepare a list of questions if any to be asked in the SIV.
- Ensure that the procedures stated in the study protocol are applicable at the site and fully understood.
- Confirm that all documents required by Institutional Ethics Committee (SVIEC) are available.
- Confirm that the clinical trial agreement (CTA), indemnification letter and budget are finalized and signed.
- Notify appropriate departments regarding the sponsor/CRO visit (e.g., Laboratories, pharmacy, CT scan, bone scan and x-ray, etc).

- File all essential documents in TMF (or sponsor-supplied Investigator Study File), and compile any outstanding documents to provide to the Clinical Research Associate (CRA) at the initiation meeting.

During the Site Initiation Visit

a. During the initiation visit the investigator(s) or Clinical Trial Coordinator (CTC) *should ensure that –*

- the Investigator's Trial Master File (TMF) contains the following mentioned applicable items and all the required regulatory documents:
  - Signed protocol and Investigator Statement
  - Signed and executed Investigator contract
  - CVs and licenses of key site study staff
  - Financial Disclosure forms
  - Investigator Undertaking (IU)
  - SDCH IEC approval letter for the protocol
  - SDCH IEC membership roster (updated)
  - SDCH IEC approved informed consent form
  - Institutional and/or other regulatory authority approvals
  - Valid clinical/other laboratory licensure
  - Laboratory normal value ranges
  - Notice that indicates the study has been submitted to the regulatory authorities (if applicable).
  - Investigator Brochure, if applicable.
  - Case Report Forms (CRF)
  - Investigational product inventory management forms
  - Any other essential documents.

- Provide the study members name involved in the study and their responsibilities in the duty delegation to the monitor/CRA.
- Provide original and updated curriculum vitae of all study personnel / Investigators involved, as per sponsor requirements (if not provided earlier).
- Ensure that the names and contact numbers of the relevant medical and study personnel of the sponsor are available and documented clearly.
- Ensure that all relevant study site personnel fill out the Site Personnel/Signature Log and Training Log.
- Check that the procedures and plans for storage, dispensing and return of IP have been agreed and finalized with the Sponsor and Pharmacist (if applicable).
- In case of paper CRF's: Check that the quantity of CRFs that have been requested or shipped to the study site are sufficient for the number of Participants/patients that are likely to be recruited into the study also allowing for the archiving of one set of intact, unused CRFs
- Check that other related supplies are available or are to be shipped to the study site at a later date, and that they are available in sufficient quantities.
- Check that laboratory facilities and arrangements for the dispatch of samples to the central laboratory are organized and that any specialized equipment that may be required will be available throughout the period of the trial, e.g. collection kits, centrifuge machine, freezer, etc.
- Ensure that monitor/CRA gives sufficient time to CTC for CRF completion training.

- Ensure and understand the requirements of the sponsors/CRO regarding source documents and raw data, which will be required during monitoring visits to enable the monitor/CRA to perform source data verification at each monitoring visit.
- Ensure that the procedures relating to the archiving of study records at the end of the study is agreeable to the sponsor.
- During the initiation visit the Investigator or delegate (for investigator initiated study)and monitor/CRA (for sponsor study) will provide a protocol-specific training session to all the members of the research team who will be involved in the research study.
- The investigator or monitor/CRA will ensure that the attendance sheets and other documentation are completed.

b. The protocol-specific training session will include, but is not limited to, the following:

- Aim and Objective of the protocol
- Time and events schedule for the protocol
- Subject recruitment
- Obtaining informed consent
- Procedure for dispensing the IP
- IP storage and records
- Protocol-specific forms and procedures
- Source documentation
- Adverse event reporting
- Additional information from the Investigator's Meeting (IM)
- Any other relevant information

c. The Investigator, monitor/CRA and CTC will:

- Develop a recruitment plan for subjects
- Identify a back-up to the primary CTC

Study Activation and Initiation Visit Follow-Up

a. In preparation for study activation

- Confirm that the sponsor sends a written summary of key discussions and agreements made during the SDCH/RESEARCH SITE initiation visit. Follow-up if necessary.
- Confirm readiness of the SDCH/RESEARCH SITE to start the study.
- Confirm the receipt of all study-related materials such as CRFs, laboratory supplies, investigational product(s).
- Distribute protocol summaries and worksheets, if not done previously (the sponsor may provide study-related worksheets, however the site can prepare one).
- Notify all appropriate departments that the study is ready to enroll participants.
- Initiate study recruitment strategies and begin enrolling study patients/participants.

Study conduct

a. Once the SDCH/RESEARCH SITE is activated and starts recruiting patients, the Investigator and CTC will ensure the following:

- All study activities are accomplished according to the protocol and applicable regulatory regulations.
- Subjects sign the correct version of the consent form before any study-related procedures are accomplished.

- Medical History along with physical examination and Vital signs will be captured by Principal Investigator and Sub investigator after voluntarily signing of ICF by patient
- Data collected in the Case Report Form (CRF) are supported by source documents.
- Protocol deviations/non-compliance/violations/waivers if any should be notified to the SDCH IEC and the same must be documented in the source documents and appropriate CRF.
- Adverse events are reflected in the source documents and captured in the CRF.
- Serious Adverse events (SAEs) are reported to the Sponsor/CRO within specified time frame.
- The IP is being dispensed correctly and IP accountability records are being maintained.

b. While the study is ongoing, the CTC will ensure the following:

- The Sponsor/CRO is informed of all significant study events and staff members are documenting critical interactions with the Sponsor/CRO.
- Biological samples are being obtained, handled, stored, and shipped appropriately.
- Study supplies remain adequate.
- Study records remain confidential.
- All equipment is calibrated regularly and maintenance records are being kept.

Premature Termination or Suspension of a Study

a. If the research study is prematurely terminated or suspended for any reason, the investigator/institution should:

- Immediately inform the SDCH IEC regarding the premature termination of the study in the format specified in the SDCH IEC SOP.
- Promptly inform the trial participants and include, where appropriate, the reason for suspension / early termination of the study.
- Assure appropriate therapy and follow-up for the participants, and, where required by the applicable regulatory requirement(s), should inform the regulatory authority (ies).
- The PI should maintain documents as specified in the TMF list and take measures to prevent accidental or premature destruction

In addition:

b. If the PI terminates or suspends a research study without prior agreement of the sponsor, the PI should:

- Promptly inform the sponsor and the SDCH IEC regarding the termination.
- Provide the sponsor and the SDCH IEC with a detailed written explanation of the termination or suspension.

c. If the sponsor terminates or suspends a research study, the PI should:

- In case the sponsor chooses to or is required to terminate prematurely or suspend the research study, then the sponsor should notify the investigator(s), institution(s), the ethics committee and the regulatory authorities accordingly. The notification should document the reason(s) for the termination or suspension by the sponsor or by the investigator / institution.

Site close-out

a. Preparing the site for study close-out visits

SEEMA DENTAL COLLEGE & HOSPITAL PRINCIPAL RISHIKESH

- After the last patient has completed all scheduled visits associated with the study, arrange a mutually convenient date and time with the monitor/CRA to conduct the study close-out visit.
- Request the monitor/CRA for the visit agenda so key research personnel such as PI, Co I, CTC, research nurse and other team members will be available, as appropriate.
- Ensure all regulatory documentation and case report forms (CRFs) not previously monitored are complete and available for review.
- Ensure all data queries received to date have been resolved.
- Inventory IPs supply and complete final accountability records. If previously instructed to return or destroy IP, assure all required documentation is filed in the appropriate TMF for monitor/CRA review.
- Arrange monitor/CRA meeting with the PI and/or Co I and CTC to discuss any outstanding issues.
- PI will ensure that all outstanding payments are cleared as per CTA.

b. Managing the study close-out visit

- Ensure all documentation (e.g., regulatory correspondence) is filed appropriately and ready for the monitor/CRA to review during the close-out visit.
- Discuss all open study-related issues and what steps will be taken to resolve them in order to satisfy the sponsor/CRO requirement(s).
- Review with the monitor/CRA the list of outstanding issues related to regulatory documents, source data verification, IP reconciliation, and any requirements for data retention and storage.
- Discuss any concerns regarding the possibility of a quality assurance audit and/or inspection by SDCH EC or external regulatory bodies. Include the CTC as appropriate.
- If the study involved electronic data capture, determine when hard copies/CD of all CRFs will be provided to TMC, if applicable.
- The PI is responsible for ensuring the appropriate follow-up, per the protocol, for any participant experiencing an ongoing unanticipated problem (e.g., serious adverse event) at study end and providing this information to the sponsor/CRO, assuring all requirements have been met.
- Arrange meeting of the PI and monitor/CRA to discuss any future considerations(e.g., publication of study data or future studies).

c. Follow-up after the study close-out visit

- For any remaining IP(s), ensure the item(s) is returned to the sponsor/CRO per their requirements.
- If the randomization code for any IP was broken for any reason, ensure complete documentation has been filed.
- Ensure return or destruction of all other study-related materials, such as unused lab kits and CRFs.
- Ensure any equipment on loan from the sponsor is returned or if mutually agreed by both the parties can be retained at the site.
- After all data queries have been resolved, check TMF, subject files and other study files for completeness.
- Arrange for transfer of study documents to secure storage.
- Submit the Final Closure Report to the SDCH IEC, for

Study Completion or Closure.

- Verify participant reimbursement or compensation if any have been distributed per the study budget, as outlined in the Informed Consent and CTA.
- If the informed consent and CTA, protocol or contract state subjects will be informed of their treatment arm, ascertain from the sponsor how and when this will be completed.

Applicable Staff

This SOP applies to all the personals of the clinical research team and others who may be responsible for site initiation, activation, conduct and close-out at TMC.

These include the following:

- Investigator/PI/GUIDE
- Research Team
- CTC
- Research Nurse
- Support staff

Study Team Training and Study Handover

Purpose

This SOP defines the procedure and recommendation of training of study team members and adequate handover to CTC/study team member, to ensure that the patient safety, protocol compliance, data integrity and overall quality assurance at the investigational site is protected and integrated as per the applicable regulations and guidelines.

Study team member must understand the responsibilities of the trials conducted at site and be appropriately qualified by education, training and/or experience to perform his or her research-related task(s). Some training may be obtained through internal hospital accepted training and certification program(s) or through external hospital accepted training and certification program(s).

The purpose of a handover is to ensure continuity of operations when the study team member, usually responsible, is not available due to temporary or permanent absence. A handover can be supported by a discussion to explain the status of the tasks, a summary of the work status in an email/ memorandum or, a more detailed file.

Scope

This SOP will apply to all study team members conducting studies in SDCH/research site

Procedure

Study Team Training

- On appointment, all study team members will be given an appropriate study depending on the job specification to possess the right experience and qualifications and further training may be provided to bring them up to the required level for specific tasks. Duty delegation /job responsibility document will be given to every Clinical Trial Coordinator (CTC)/ team member.
- The Investigators, CTC and other study team members must undergo training which will enable them to understand their responsibilities, applicable regulations, guidelines and research studies and training should be documented in the training log.
- Each Investigator, CTC and study team members will review and learn the site's SOPs. It is recommended that SOP training must be included in the orientation of new clinical

research personnel. All applicable clinical research personnel should be knowledgeable of new or revised SOPs.

- Good Clinical Practice (GCP) is a universal standard in clinical research that must be followed in every research protocol. GCP training and education are recommended for research team members, especially the Investigator and CTC. However, any member of the research team with a significant role in the conduct of a research study must be knowledgeable in GCP. All members of the clinical research team should GCP trained and certified.
- If scheduled, PI and CTC will attend the Investigator Meeting (organized by Sponsor) and complete all required training for a study. If PI is unable to attend the meeting, PI can recommend other study team member(s) to attend the IM. PI should be informed regarding the study contents discussed in IM.
- Before study initiation Sponsor/CRO will organize SIV meeting at site to train all study team members and all study team members should attend the meeting for thorough understanding of the study.
- PI and study team member(s) should be prepared to demonstrate all training received.
- CVs, GCP and other training certificates should be updated as required. It is recommended that an assessment of the employee's knowledge of the regulations and guidelines can be conducted upon recruiting and on a regular basis. It is recommended that an assessment of any additional protocol-specific skill requirements be conducted prior to activation of each new study.

Study Handover

If any study team member is planning for leave or to resign, he/she must ensure that the proper handover is given to concern person identified by the PI, the identified person should be briefed in time before the person goes on leave to allow for any follow up questions.

Prior to leaving the study, the existing study team member should complete the following:

- Training on protocol and procedures e.g. SOPs and explanation of relevant documents
- Information regarding study subjects, study documents and all study related activities
- Outstanding data entry and/or data queries
- Training to complete source documents
- Explanation on the objectives & priorities
- Notification to the sponsor of the study team changes
- Notification to the active subjects of the study team changes if the research team contact information will change for the subjects.
- Provide a list of study-specific contacts (e.g., sponsor, monitor, vendors involved etc.)
- Provide a list of outstanding issues
- The leaving person has to make sure that the documentations concerned for the tasks is up to date and easily available, and if needed, revise it when preparing the handover.

If there is a change in PI, the following documents need to be revised and completed;

- Inform Sponsor and IEC regarding the change in PI in the Study team.
- Consider revising the protocol and informed consent form, as appropriate. Also consider notifying current subjects; correspondence sent to all subjects must be approved by the IEC, if applicable.
- Update the Form FDA 1572 or the Investigator Agreements, Investigator Undertaking and other required forms
- Update the Duty Delegation log
- Ensure that the new PI has completed the SOP required training and study-specific training. Written hand over should be given in order to ensure the continuity of work.

The format can be a briefing note, a check list, or a schedule prepared to give all information.

When the study member returns from leave a hand over should be prepared to give updates on the status of the tasks.
The existing and new study team member should document the study handover in a note to file or other documentation in the TMF. The note should contain some of the items above and the date of the handover. The new study team member should obtain documented study-specific training and any required approvals prior to being added to the duty delegation log.

Applicable Staff
This SOP applies to all the existing personals of the clinical research team and any new member appointed who may be responsible for training and study handover as mentioned in this SOP(as per the delegation log).
These include the following:

- Investigator
- Research Team (listed in the delegation log)
- €TC

SEEMA DENTAL COLLEGE & HOSPITAL
PRINCIPAL
RISHIKESH