Standard Operating Procedure (SOP)

Faculty Responsibilities – M.Sc. Clinical Research Program & Ph.D. Clinical Research, Department of Clinical Research, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University (SRHU)

1. Purpose

To define the academic, research, mentoring, training, and industry engagement responsibilities of faculty members associated with the Clinical Research Programs, with an emphasis on structured learning, practical skills, and student development.

2. Scope

This SOP applies to all faculty involved in the academic and co-curricular delivery of the M.Sc. Clinical Research Program and Ph.D. Clinical Research

3. Responsibilities

S. No	Activity	Description
3.1	PG Teaching Sessions	Faculty must attend and contribute to daily PG classes (8:30 AM – 9:30 AM), promoting case-based and interactive learning. **Annexure 1. Timetable**
3.2	Curriculum Coverage	Deliver sessions as per university-approved syllabus. Ensure timely and relevant content delivery.
3.3	Teaching Methods	Use evidence-based strategies: PPTs, video lectures, case discussions, flipped classrooms, role-plays, group activities. **Annexure 2**
3.4	Assessment	Conduct daily and periodic assessments aligned with academic guidelines. Record and report outcomes. **Annexure 2**
3.5	Seminars/Journal Clubs	Conduct monthly academic events to enhance critical analysis and scientific communication.
3.6	Attendance	Faculty must sign attendance during class and remain present throughout the session unless pre-approved.

4. Research & Mentorship

S. No	Activity	Description
4.1	Research Participation	Faculty should be involved in at least one clinical research project (Intra-/Extramural).
4.2	Thesis Supervision	Every student must be guided by a faculty Supervisor (University) and co-supervisor (Industry). Regular thesis progress tracking and manuscript writing support are essential.
4.3	Mentor-Mentee Engagement	Provide one-on-one mentoring for assigned students and maintain mentoring documentation.

5. Capability & Skill Development

S. No	Activity	Description
5.1	Student Development Activities	Coordinate academic enhancement sessions like mock interviews, resume building, ethics debates, and soft skills training.
5.2	Capability Lectures	Deliver structured sessions on personality development, yoga & wellness, critical thinking, and research ethics.

6. Practical Exposure

S. No	Activity	Description
6.1	Clinical Trial Centre Visit & Study Start Ups SOPs	Guide student visits to SRHU's Clinical Trial Unit to understand operational workflows, documentation, and compliance. **Annexure 3**
6.2	Industry Visit	Organize at least one industrial visit per year to pharma/CRO units covering QA, PV, regulatory, and monitoring functions.
6.3	Hands-On Activity	Conduct practical modules as part of Curriculum.
6.4	Mini Projects	Supervise student mini projects on protocol writing, feasibility studies, case report documentation, mock pharmacovigilance analysis, etc.

7. Academic Events & External Engagement

S. No	Activity	Description
7.1	Trainings & Workshops	Organize and attend at least one faculty development programs or workshops annually in clinical research, ethics, or pedagogy.
7.2	Seminars/Symposia	Organize or participate in academic events; present papers/posters at conferences and moderate sessions.
7.3	Guest Lectures	Invite and coordinate expert sessions from industry, academia, or regulatory agencies.
7.4	Industry-Academia Collaboration	Promote partnerships with CROs, pharma companies, and health-tech sectors for internships, guest talks, and placements.

8. Special Academic Support Sessions

S. No	Activity	Description
8.1	Remedial Classes	Faculty must identify academically weak students through assessments and conduct **remedial classes** with focused revision, concept clarification, and interactive Q&A.
8.2	Peer-Assisted Learning (PAL)	Facilitate **peer-led sessions** where academically strong students' mentor and support their peers under faculty supervision. This promotes collaborative learning and confidence-building.
8.3	Breakthrough Sessions	Conduct **Breakthrough sessions**—open-ended academic support sessions that address student doubts, exam anxiety, or conceptual gaps in an informal setup.
8.4	Enrichment Tutorials	Faculty should also plan advanced tutorials for high-performing students to challenge and engage them further in research thinking, data analysis, or regulatory knowledge.
8.5	Documentation & Feedback	All special sessions must be recorded in a logbook or activity register, and student feedback must be collected to improve content and delivery.

9. Documentation & Review

All teaching, training, mentoring, and special session activities must be documented, reviewed annually, and aligned with the Clinical Research program's academic audit requirements.

Prepared By:

Name: _____

Designation: _____

Signature: _____

Date: _____

Reviewed By:

Name: _____

Designation: _____

Signature: _____

Date: _____

Annexure 1: Time Table

HIMALAYAN INSTITUTE OF MEDICAL SCIENCES
TIME TABLE – MSc Clinical Research
Semester-I (Aug 2024-Dec 2024)

Venue: Department of Clinical Research/ Department of Biochemistry/ HSST/ HSYS

HIMS/2024/ 169 –(2)

Date : 16th August 2024

Time	9:00-10:00	10:00-11:00	11:00-12:00	12:00-1:00	1:00-2.30	2.00-2.30	2.30-4.30 pm
Mon	CMCR506 General Epidemiology VV	CMCR504 Introduction to Clinical Research: NY	VAC: Elementary French: ACS			Sports	CMCR504 Introduction to Clinical Research: NY
Tue	CMCR506 General Epidemiology VV	CMCR504 Introduction to Clinical Research: NY	CMCR503: Genetics; Molecular Biology: NY	CMCR501 Biostatistics: AU		SDL	MOOC Course: NY
Wed	CMCR506 General Epidemiology :VV	CMCR501 Biostatistics: AU	CMCR502 General Biochemistry : MS	CMCR502 General Biochemistry: MS		Sports	Lab CMCR503: Genetics; Molecular Biology: NY
Thu	Lab CMCR506 General Epidemiology :VV		CMCR501 Biostatistics: AU	Tutorial for CMCR 501/502/503	LUNCH	SDL	PDP: AG/GS
Fri	Lab CMCR501 Biostatistics: AU		CMCR503: Genetics; Molecular Biology: NY	CMCR504 Introduction to Clinical Research: NY		Library	Lab CMCR502 General Biochemistry : Biochemistry Department
Sat	CDLa 101 Spoken English: SM	CDLa 101 Spoken English: SM	Special sessions/Capability Enhancement	Tutorial for CMCR 504/506		M3*/ Industry Interaction/ Alumni Sessions	YOGA

ACS: Dr Asha Chandola-Saklani, SM: Dr Suman Madhok, VV: Dr Vidisa Vallabh,MS: Dr Mayank Sharma, AU: Akanksha Uniyal, AG: Mr Ashish Gupta, GS: Ms Garima Sharma, NY: Dr Nikku Yadav
M3: Mentor-Mentee- Meeting: Ist Saturday

Vice Principal
Allied Health PG Programmes

Vice Principal
(Allied Health PG Programmes)
HIMS, SRHU
Jolly Grant, Dehradun-248011

Annexure 2:

Innovative Pedagogy:

The pedagogy employed is a dynamic blend of traditional and modern teaching methodologies designed to foster deep learning and active student engagement. It includes both didactic lectures to provide foundational knowledge and interactive lecture sessions that encourage student participation and dialogue. Brainstorming activities are integrated to stimulate creative thinking and collaborative problem-solving, while impromptu question-and-answer sessions are conducted to test comprehension and promote spontaneity in learning.

Students also participate in extempore seminars, which help develop their confidence, communication skills, and ability to think on their feet. The curriculum incorporates demonstrations (demos) for hands-on understanding of complex procedures and laboratory work, both in wet labs (for practical experiments involving biological or chemical substances) and dry labs (involving computational analysis or simulations). These are often supplemented by experiential fieldwork, which provides real-world exposure relevant to the subject matter.

Tutorials, group discussions, and student presentations form an integral part of the learning process, allowing for peer-to-peer learning and critical analysis of topics. Students engage in extensive reading and writing exercises to improve their academic literacy, and are introduced to early research orientation through exposure to scientific inquiry and project-based learning.

The curriculum is enriched with problem-solving assignments, live case studies, and a variety of field and computer-aided dry lab activities to build analytical and technical skills. Continuous assessment is carried out through a student participatory model, ensuring regular feedback and active involvement in their own learning progress.

Moreover, experiential learning is emphasized through community outreach projects, where students plan and execute field-based initiatives as part of their coursework. These assignments are thoughtfully aligned with the specific learning objectives and requirements of individual courses, making the learning process contextually relevant, socially responsive, and deeply immersive.

For assessing clinical competence **Miller's Pyramid** is used. It consists of four hierarchical levels:

- **Knows** – basic knowledge of facts and concepts.
- **Knows How** – ability to apply knowledge in context.
- **Shows How** – demonstration of skills in a simulated or controlled setting.
- **Does** – actual performance in real clinical practice.

Assessment

The assessment opportunities shall be broadly divided into:

- Formative assessment
- Summative assessment/ Term End Assessment

Assessment	**Type**	**Modes of Assessment**
Summative Assessment (100 Marks)	**End Term Semester Examination** **100 Marks**	• Structured question • PBQ • Short Answers Questions (SAQ) • Answer in brief • Give reasoning
Formative Assessment (100 Marks)	**Sessional I** **Sessional II**	25 25
	Day by Day Assessment (50)	
	Hands on activity **(30)**	• Student Knowledge & clarity of thought analytical ability • Hands-on skills • Effort (Data generation, Data generation, Data log, analysis,) • Compilation of work & submission (within time limit) • DOAP • Viva Voce • Record maintenance, attitudinal assessment, and timely submission
	Assignments **(5)**	• Student Knowledge & clarity of thought analytical ability, Originality • Regularity & Timely submission

		• Handling of QA
	Seminar **(10)**	• Content originality • Critical thought • Way of presentation/ body Language/ Presentation skills • Handling of QA/ Viva Voce
	Log-book (5)	• Day to day Assessment • Daily Skill Assessment

In brief: In accordance with UGC MERP guidelines Learning Assessment Components comprise a combination of Continuous assessment and End term examination. The weightage % distribution of marks generally follows 40:60 ratio (Formative (Continuous) Evaluation vs Cumulative).

The assignments will be assessed based on:

Learning assessment Component	Maximum Marks
Student Knowledge, Clarity of Thought, Analytical Ability, Originality	6
Regularity and Timely Submission	4
Total	10

Student seminars will be assessed based on:

Learning assessment Component	Maximum Marks
Content	2
Effort (Data Generation, Presentation/Pictorial/Graphical)	2
Presentation Skill and Body Language	2
Critical Thinking/Grasp	2
Viva (Handling of Questions)	2
Total	10

The Hands-on activities will be assessed based on:

Learning Assessment Component	Maximum Marks
Student Knowledge & clarity of thought analytical ability	2
Hands-on skills	2
Effort (Data generation, Data generation, Data log, analysis,)	2
Compilation of work & submission (within time limit)	2
Viva (Handling of questions)	2
Total	10

Annexure 3

Standard Operating Procedure for Clinical Trials

At

Clinical Trial Centre, Swami Rama Himalayan University

Swami Rama Nagar, Jolly Grant Dehradun-248140, Uttarakhand, India

Standard Operating Procedure for Clinical Trials at Site Himalayan Hospital Swami Rama Himalayan University

Context

1. Site Start up

1.1 Background

This SOP describes the start-up procedure for a clinical trial/research study at Swami Rama Himalayan University.

1.2 Purpose

To make sure the research site is able to conduct the proposed research plan effectively and completely as per the requirements of the protocol and with the available resources.

1.3 Scope

This SOP applies **to Responsible personnel**, **Investigator**, **Clinical Research Team** involved in the clinical trials conducted at Swami Rama Himalayan University.

1.4 Procedure

The responsibility to initiate the Clinical Trials/ Research studies in the institute is the prime responsibility of the Clinical Trial Centre – Swami Rama Himalayan University. Site Start up team in Clinical Trial Center (CTC) is responsible for following tasks:-

1.5 Confidentiality / Non Disclosure Agreement (CDA / NDA):-

i. To provide signed off CDA from the Principal Investigator to the Sponsor / CRO prior to any activity to conduct in Clinical Trial/ study.

ii. To keep a signed copy in Master file at site.

1.6 Feasibility:

i. Feasibility would be provided by the sponsor to the Principal Investigator/Site after the signingof CDA.

ii. Principal investigator/delegated study staff will fill the Feasibility Questionnaire within the timelines given by the sponsor / CRO / SMO.

iii. Filled Feasibility questionnaire would be provided by the site start up team within time frame to the Sponsor / CRO / SMO.

iv. All other documents required by Sponsor / CRO / SMO will be provided by the Site Start Upteam.

1.7 Pre-site Selection Visit:-

Pre-Site Selection Visit (PSSV) and Site Selection Visit (SSV) will be conducted at site after confirmation from Investigator.

1.8 Institutional Ethics Committee submission:-

Upon receipt of study related documents (refer to SOP of Institutional Ethics Committee), Site start up team will assist the Investigator to submit the same in Ethics Committee for EC review and approval.

1.9 IEC Approval:- Refer to IEC SOP

1.10 Clinical Research Coordinator will be assigned by the PI.

2. Clinical Trial Agreement

2.1 Background

All Sponsored research carried out at Swami Rama Himalayan University must have a fully executed "Tripartite or Quadripartite" contract known as a Clinical Trial Agreement (CTA)/ Clinical Study Agreement before the study starts. All parties (Sponsor/Contract Research Organization/ SMO, Institute and Investigator) must sign a written agreement that defines the scope of work and formalizes the understanding between the parties. This agreement must define the scope of work, establish acceptable payment arrangements, and address important issues such as the right to publish research results, protection of confidential information, conflict of interest and indemnification/insurance.

2.2 Purpose

All CTA / CSA received by the site must be checked and any alterations need to agree by all parties, before sent for signature on behalf of the Institute and Investigator. This SOPprovides a stepwise procedure where the Agreement is checked and validated on each contentpresent in the CTA.

2.3 Scope

A CTA is a legally binding contract, which evidences the agreement among parties and which defines each party's rights and obligations in relation to carrying out of research trial / study in the Institute.

2.4 Responsibility

- Investigator
- Legal Team
- SMO Team
- Clinical Trial Coordinator/ Member Secretary
- CTC Chairman

2.5 Procedure

Receiving the agreement:

Ideally the agreement should be received as early as possible for approval, to allow time for checking and for any changes to be made. The draft CTA along with proposed study budget will be received by the PI. The draft version of the CTA should be requested in electronic form preferably in word format, to simplify the process of making comments and changes. Any changes made to the electronic copy of the agreement should be tracked, so that the Sponsor/Contract Research Organization (CRO) can clearly see where changes have been made to be incorporated. For CTA make sure that the contents listed in Appendix 1 should be present in a CTA. If draft CTA received as a hard copy it should be stored in secure area with limited access.

2.6 Reviewing the agreement and study budget:

i. PI is responsible to prepare and compare the estimated expenses with proposedbudget, discuss with Site, negotiate on the same with Sponsor / CRO.
ii. The PI forwards the draft Agreement to Institute legal team for Legal review. The Legal team reviews the CTA and forward to PI with final comments.
iii. The PI forwards commented CTA to Sponsor / CRO.

2.7 Forwarding reviewed CTA to Sponsor/CRO/SMO:-

Any issues arising from the review should be addressed with the Sponsor/CRO. The PI forwards the commented CTA and Study Budget to the Sponsor/ CRO for their acceptability. In case, Sponsor/CRO has conflict between any clause(s), they revert back to the site with their comments and the CTA will again reviewed by legal of site to which the comment(s) pertains.

2.8 Signatures:-

Once the final version of the agreement (including all costing) has been agreed by all the parties, the Sponsor/CRO should be requested to send first clean electronic copy of CTA to review and approval then send printed copies (no. of copies must be same as no. of parties), with their signature(s), date. Institution authority will sign the only one page where the his/her name mentioned.

Once signatures are in place from all parties, one original copy of the agreement will be retained in the Investigator Site Master File, one original copy will be retained by the institute and the rest will sent to the Sponsor/CRO.

Note:- Institutional Overhead in Clinical Trials is 20% of total study budget

As per General Budget (Govt. of India) GST is applicable on clinical research

3. Principal Investigator (PI) Responsibilities:

3.1 Purpose

- To define Principal Investigator responsibilities and to provide guideline when performing clinical Research study (ies) under applicable regulatory requirements.
- Principal Investigator is responsible to oversee the conduct of the studies in the institute.
- Principal Investigator should ensure the right, safety and well being of human subjects.

3.2 Scope

Principal Investigator and other stake holder should be aware of responsibilities of PI in Clinical Research.

3.3 Applicability

It would applicable to all involved personnel of study protocol including Co/Sub- Investigator, research coordinators or other research staff of the clinical trial If the responsibilities have been delegated them by the PI.

3.4 Procedure

The Principal investigator:

i. Ensure that clinical studies are carried out according to (ICH-GCP) and local regulatory requirements.

ii. Should have an understanding that when a trial is sponsored by an agency/pharmaceutical company, they may be requested to follow their procedures in order to comply with company obligations. Agreement between all parties should be discussed and signed before initiating the trial.

iii. Ensure that they are appropriately qualified to conduct the trial.

iv. Should inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.

v. Should be able to demonstrate that adequate subject recruitment is likely to be possible, with necessary time available to conduct the study to GCP requirements, and with adequate facilities.

Note: Although a subject is not obliged to give his/her reason(s) for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the subject's rights.

i. Must declare any conflicts of interest, payments etc. from other parties.

ii. Must maintain a list of any delegated duties with respect to the trial, and the persons and qualifications of those persons to whom the duties are assigned.

iii. Must provide medical care to trial participants that are necessary as a result of any adverse events, serious adverse events, experienced during or following the trial that are related to the trial, and must be responsible for all trial-related medical decisions.

iv. Must possess, prior to trial commencement, a favorable Institutional Ethics Committee (EC) endorsement of trial protocol, patient information and consent documents, recruitment procedures, consent form updates and any other information given to subjects.

v. Must present all trial related documents to the IEC for review and approval including the Investigator's Brochure as well as updates.

vi. Must ensure that the trial is conducted according to the approved protocol.

vii. Must document any deviation and violation of the protocol for later review.

viii. Must ensure that no deviation from the protocol occurs without IEC endorsement, unless it is required to prevent imminent harm to subject.

ix. Must ensure accountability of the investigational product at the trial site(s).

x. Must ensure that subjects have made fully informed, written consent, with all trial procedures and risks adequately explained and that the principles and essential elements of Informed consent are up held and included in the information document.

xi. Should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.

xii. Should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions.

xiii. Should submit annual reports of the trial status to the IEC after 6 months or annually or after the completion of the trial as requested by the IEC.

xiv. Should provide written reports to the sponsor, the IEC and, where applicable, the institution promptly on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.

xv. Should comply with the applicable regulatory requirement(s) related to the reporting of all adverse / serious events to the regulatory authority (ies) and the IEC as per the time line.

xvi. Should promptly inform the trial subjects if the trial is prematurely terminated or suspended for any reason as well as the institution and should assure appropriate therapy and follow-up for the subjects, and where required by the applicable regulatory requirement(s), inform the regulatory authority (ies).

Note: If the investigator terminates or suspends a trial without prior agreement of the sponsor, they should inform the institution where applicable, and The Investigator/institution should promptly inform the sponsor and the IEC, and provide the sponsor and the IEC a detailed written explanation of the termination or suspension.

Should, upon completion of the trial, where applicable, inform the institution; the investigator should provide the IEC with a summary of the trial's outcome, and the regulatory authority (ies) with any reports required.

In case of Stem Cell Research the Principal Investigator should follow the guidelines set by ICMR/ NACSR, and refer to SOP for Stem Cell Research & Therapy.

3.5 In case PI leaves the Institution: (Before or after completion of the trial)

i. PI should inform prior to leaving the organization, in writing to IEC about the status of all his/her trials approved by IEC and submits a certified document stating that all trials have been conducted in compliance with applicable SOP.

ii. PI should submit all certified original copies of properly arranged trial documents.

iii. To the research team and a copy to IEC & Administration.

iv. PI cannot shift trial to another hospital without approval/ favorable opinion from the IEC.

4.0 Clinical Research Coordinators (CRC) Responsibilities

4.1 Purpose

To describe the operations and procedures for Clinical Research Coordinators and his/her responsibilities to achieve standards as per ICH E6, US FDA 21CFR, New CT rules 2019, India, ICMR and CDSCO-GCP guidelines as well as the relevant site SOPs.

4.2 Responsibilities:

i. The CRC assists the principal investigator (PI) and sub- investigators (Sub-I) with all the clinical study aspects and implementations. The CRC is responsible to coordinate all the clinical trial activities but can perform only those activities that are specified to him/her authorized by the PI in the delegation log. CRC Responsibilities include:

ii. Coordinate with study team members and Sponsor in the development and implementation of clinical trial at institute.

iii. To assist the Investigator / Co-Investigator in Screening, recruiting, and enrolling subjects into clinical trials and monitor their status as per protocol.

iv. Participation in Informed consent process (but no right to take consent on behalf of Investigator).

v. Perform Randomization process, if applicable
vi. Resolve Data base queries with help of Investigator.
vii. Plan/schedule subject's visits.
viii. Provide Diary Card to subject as per protocol.
ix. Arrange dispatch and shipment of samples, e.g. Blood, tissue samples, etc.
x. Complete subject's visits per protocol requirements.
xi. Proper maintain the Site Master File (SMF).
xii. Accounting for all test article and study drug supplies and inventories.
xiii. Investigational Product (IP) storage accountability.
xiv. IP dispensing and patient care in presence of Investigator / Co-Investigator.
xv. IP usage and reconciliation accountability
xvi. Acknowledge receipt of IP at the site.
xvii. Maintain Subjects Pre-screening/screening log, Temperature log and/or other applicable log
xviii. Prepare and maintain proper source notes.
xix. Data collection and entry in paper CRF or eCRF as per protocol.
xx. Adhere to study timelines.
xxi. Facilitate monitoring visit and inform to PI.
xxii. Prepare documents and make them available during monitoring visit.
xxiii. Facilitate SAE reporting according to study procedures.
xxiv. To assist Investigator to notify SAEs as per New CT rules 2019 to Institutional Ethics Committee (IEC)
xxv. Notify IEC of study related amendments.
xxvi. SAE Notification to the sponsor within 24 hours after receiving information of the event and within 7 working days to IEC.
xxvii. Adhere to rules and regulations and code of confidentiality throughout the study.
xxviii. Submit end of study report to IEC.
xxix. Attend study completion de-brief.

xxx. Storage of study documents should be confidential.

xxxi. Adhere to Hospital / Office of Research Policies.

xxxii. Gathering data, compiling information, and preparing reports.

xxxiii. Preparing and submitting trial specific information to the IEC and others, as assigned

xxxiv. Performing other duties as assigned

Incase if Clinical Research Coordinator leaves the Institution :(***Before the completion of the Trial*****)**

CRC should inform to the Investigator stating that he/she has completed all work assigned to him/her properly and information provided is true. Also ensure that he / she would be available for clarification as and when required pertaining to the trial.

5. 0 Informed Consent:

5.1 Purpose

To specify the procedure for obtaining voluntary consent by using the Inform Consent Document (ICD) [Inform Consent Form (ICF) + Patient Information Sheet (PIS)] fromsubjects who are eligible for participating in a clinical study as per the study protocol before start of any trial activity.

5.2 Scope

It is the responsibility of the investigator and/or delegated study staff to obtain written informed consent form, from eligible subject after being informed all aspect of trial and voluntary confirm subjects willingness to participate. This would minimize the possibility of coercion or undue influence.

5.3 Procedure

5.3.1 Informed Consent Document:

While seeking informed consent, the following information shall be provided to each subject. The Investigator is responsible for disclosing all these elements to the subject. Adequate information about the research is given in a simple and easily understandable unambiguous language in a document known as the ICF with PIS (approved by IEC). The latter should have following components as may be applicable:

i. Nature and purpose of study stating it as research.
ii. Duration of participation with number of subject.
iii. Procedures to be followed.
iv. Investigations, if any, to be performed.
v. Foreseeable risks and discomforts adequately described and whether project involves more than minimal risk.
vi. Benefits to participant, community or medical profession as may be applicable.
vii. Policy on compensation.
viii. Availability of medical treatment for such injuries or risk
ix. Benefit sharing in the event of commercialization.
x. Contact details of Investigator(s)/and Coordinator for asking more information on clinical trial.
xi. Information related to the research or in case of injury/death.
xii. Contact details of Chairman of the EC for appeal against violation of rights.
xiii. Voluntary participation.
xiv. No loss of benefits on withdrawal.
xv. Alternative treatments if available.
xvi. Steps taken for ensuring confidentiality
xvii. The subject must be explained about the possibility that the regulatory authorities,

IEC, and sponsor's monitors may inspect /audit their records.

Additional Elements of Informed Consent – When appropriate, one or more of the following elements of information shall also be provided to each subject:

A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently unforeseeable.

a. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
b. Any additional costs to the subject that may result from participation in the research.
c. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
d. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.
e. IEC will ensure that the information provided in the consent document is in a language understandable to the subject. IEC will ensure that technical and scientific terms are adequately explained using common or lay language. IEC would further ensure that the consent documents do not contain any exculpatory language through which the subject is made to waive or appear to waive legal rights or releases or appears to release the Investigator, the Sponsor, or the institution liable for negligence.

5.4 Responsibilities

5.4.1 Responsibilities of Investigator

i. Exclude the possibility of unjustified deception, undue influence and intimidation. Although deception is not permissible, if sometimes such information would jeopardize the validity of research it can be withheld till the completion of the project, for instance, study on abortion practices.

ii. Seek consent only after the prospective subject is adequately informed. The investigator should not give any unjustifiable assurances to prospective subject, which may influence the her/his decision to participate;

iii. If participant is ready to particiate in the study than take signed from the subject as an evidence of informed consent (written informed consent) if subject is illiterate, can not read and write in this case prefer a witnessed who is not belongs to the site , and in case the participant is not competent to do so, than legal guardian will signed the ICF.

iv. Renew or take fresh informed consent of each participant under circumstances described

v. The investigator must assure prospective subjects that their decision to participate or not will not affect the patient - clinician relationship or any other benefits to which they are entitled.

5.4.2 Responsibility of Institutional Ethics Committee [IEC]

Ensuring that all studies with human subjects are conducted as per the guidelines of the IEC as well as the regulatory agencies: ICMR, New CT rules 2019 and Indian GCP.

i. To protect the dignity, rights and well being of the potential research participants.

ii. To ensure that universal ethical values and international scientific standards are expressed in terms of local community values and customs.

iii. To assist in the development and the education of a research community responsive to local health care requirements.

5.5 Obtaining informed consent:

i. While obtaining the Informed Consent the Investigator must comply with the applicable regulatory requirements and ethical guidelines.

ii. The Investigator should provide "*ICD (ICF+PIS)"* provided by study sponsor of facts relevant to the study for consideration by the PI's site for obtaining informed consent from the study subjects.

iii. The latest IEC approved ICF must have date/version to ensure usage of the correct version.

iv. Consent process has to be done in a private environment in the presence of concerned persons only i.e. the Investigator/delegated staff, study coordinator, subject, LAR/Impartial Witness.

v. The trial subject enrolled in active study will not be taken up for case studies for academic or training programs.

5.6 Documentation of Informed Consent:

i. Investigator provides a copy of the latest ICF approved by Institutional Ethics Committee to the study subject for reading. ICF should be in the subject's vernacular language. Investigator reviews the ICF with study subject and addresses any questions within his/her scope of responsibility.

ii. The Investigator should ensure that the potential study subject has ample time to make a decision as to whether he / she want to be part of the trial or not.

iii. The Investigator discusses the elements of the ICF verbally and if required in a written format with the potential study subject and ensures that he / she understand the content and meaning of the ICF.

iv. The personnel responsible for taking the ICF should not unduly coerce or influence the potential study subject to participate in the trial.

v. Ensures that ICF is signed and dated prior to the study subject's participation in the study or prior to any testing to determine eligibility for participation in the study. Same notation along with time of signing ICF is made in the subject's research record.

vi. Ensures original signed ICF is entered into the patient's source document, that the study subject obtained another original / copy of fully executed signed and dated ICF by the investigator.

vii. If the ICF is amended during the course of the study, the Investigator ensures that all active study subjects (or the subject representative/Impartial Witness) sign an amended ICF (approved by IEC) as soon as possible. The communication of information provided to subject telephonically or on-site should be documented in the source documents.

viii. Signed original ICFs should be kept at Investigator's site master file and site personnel must keep record of subject's name and contact details (to take a copy of residence proof of subject is encouraged to prevent lost to follow up) for communication to subject.

5.6.1 If the subject is literate:

i. The subject must write his / her name, sign and date, the time of the signature in the signature sheet of the ICF as per requirement.

ii. Investigators should sign and date the form after the potential study subject has done the same.

5.6.2 If the Subject is Illiterate:

i. The subject is unable to read and write, then consent can be taken after ensuring its documentation by an impartial witness, if the volunteer can give only thumb impression then an impartial witness to the process should then sign. All the following must be ensured:

ii. The Investigator and impartial witness are present.

iii. A thumb impression of the patient is taken.

iv. The impartial witness signs and dates the ICF in the space provided.

v. 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.

5.6.3 Selection of Special Groups as Research Participants:

i. In economically backward

ii. Research on subjects undergoing psychiatric treatment

iii. Research Involving Pregnant Women or Foetuses

iv. Research involving neonates

v. Children

vi. Persons with Impaired Decision Making Capacity

vii. The subject is incompetent

viii. Patients with memory loss

ix. Geriatric subjects (Refer to "SOP on protection of vulnerable subject")

5.6.4 Confidentiality of Research Subject:

i. The investigator must safeguard the confidentiality of research data, which might lead to the identification of the individual subject. Data of individual participants can be disclosed under the following circumstances:

ii. Only in a court of law under the orders of the presiding judge or

iii. there is threat to a person's life or

iv. availability of new better treatment or in cases of severe adverse reaction may be required to communicate to drug registration authority or

v. If there is risk to public health it takes precedence over personal right to privacy and may have to be communicated to health authority.

vi. Therefore, the limitations in maintaining the confidentiality of data should be anticipated and accessed and communicated to appropriate authorities (IEC and/or

regulatory as the case may be.

5.6.5 Fresh Or Re-Consent Is Taken In Following Conditions:

i. Availability of new information which would necessitate change of Informed consent form.

ii. When a research subject regains consciousness from unconscious state or is mentally competent to understand the study. If such an event is expected then procedures to address it should be spelt out in the informed consent form.

iii. When long term follow-up or study extension is planned later.

iv. When there is change in treatment modality, procedures, site visits.

v. Before publication if there is possibility of disclosure of identity through data presentation or photographs (this should be camouflaged adequately).

vi. Identification of new "Reasonably foreseeable" risks or side effects judged to be "Definitely related" to the research.

vii. New information becomes available that may affect subjects' willingness to participate such as previously unknown risks or FDA market approval of a previously investigational agent used in the study.

viii. A change in PI contact and contact information of EC secretariat.

ix. If a subject wanted to enter again in the same study for which he withdraw consent. This would applicable as per protocol design.

5.6.6 Post Trial Access:

- Investigator along with the clinical research team should necessitate identifying post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care.

6.0 Subject Recruitment in Clinical Research

6.1 Purpose:

To document the policies and procedures for the recruitment of human subjects in clinical trial.

6.2 Responsibilities:

It is the PIs responsibility to ensure that eligible subjects meeting all the inclusion and exclusion criteria are enrolled in the study. The PI must ensure that informed consent is obtained voluntary after all information being provided him/her and has given opportunity to ask question with sufficient time to take decision to participate from all subjects prior to their participation.

6.3 Recruitment:

i. PI is responsible for recruitment of all trial subjects
ii. PI determines and identifies the set of potential candidates who meet the required inclusion and none of the exclusion criteria as per the protocol.
iii. After the EC approval has been obtained, the PI may calling up the potential candidates.

6.4 Delegation:

i. The PI delegates responsibilities to the clinical research coordinator and/or co investigator if required.
ii. A delegation log for the same has to be maintained with clear demarcation and delegation of responsibilities.

6.5 Enrollment:

i. When the PI finds a potential subject who met all the inclusion and none of the exclusion criteria, he /she are briefed about the study protocol.

ii. When the potential subject agrees to participate and signs the informed consent form, he/she is said to be enrolled in the study. (Refer to SOP on Informed Consent SOP)

iii. The subject details are entered in the subject identification log.

iv. Investigator may use referral sites to recruit patients, particularly in therapeutic areas in which appropriate study subjects may be difficult to find.

7.0 Investigational Product (IP) and/or Medical Device

7.1 Background:

No clinical trial for a new drug (refer to Indian Regulatory guidelines on New Drugs), whether for clinical investigation or any clinical experiment by the institution, shall be conducted except under, and in accordance with, the permission, in writing, of the LicensingAuthority.

7.2 Purpose

The SOP describes the handling and managing of all Investigational Product (IP), Medical Device which is used for the conduct of Clinical Trial.

7.3 Scope

The SOP applies to IP and Medical Device used for Investigator Clinical Trials under Investigator and or Pharmacy whichever applicable. All IP and Medical Device handling must be done and documented in accordance with the Sponsor's requirements. This SOP describes all handling processes from receipt of IP and Medical Device to return of IP and Medical Device to the supplier or destruction of IP and Medical Device

7.4 Guiding Principles

ICH-GCP requires that IP and Medical Devices should be manufactured, handled and stored in accordance with Good Manufacturing Practice (GMP). IP should be used in accordance with the approved Clinical Trial protocol.

The Investigator may delegate tasks as set out in this SOP, to the appropriate research staff member, however the Investigator retains ultimate responsibility for the conduct of the study, including adherence to the SOP.

The following documentations should be in place before IP and Medical Device is received at the clinical trial Site:

i. Ethics Committee approval letter
ii. Indemnity
iii. Insurance
iv. Regulatory Approval
v. Import license, if required
vi. Clinical Trial Agreement (CTA)

IP and Medical Device handling instructions should be known, including storage conditions. Adequate storage facilities specific to the IP and Medical Device should be available.

IP and Medical Device must be stored in a secure, limited access area.

Temperature logs for the IP and Medical Device storage should be maintained, if applicable.

An accurate inventory of the dispensing and return of the IP and Medical Device shall be recorded for each subject, using an IP and Medical Device accountability form.

All IP and Medical Device at the Research Site should be accounted for at any time point in a trial.

7.5 Procedures

7.5.1 Receipt and Inventory of Investigational Products, Medical Devices:

The investigator, the pharmacist or the person designated by the investigator should:

At the time of delivery of the investigational products, medical devices review the shipping instructions and ensure that they were followed. All documentation related to transportation and receipt of the investigational products, medical devices should be retained with the essential study documents.

Within a short time, make an inventory of products/devices received in order to ensure that the information on the shipment invoice corresponds to the products sent and received, including the quantity and lot number, if applicable. The result of the inventory should be documented and retained with the essential study documentation.

List any products/devices defects: packaging, labeling, quantity, etc. and follow-up with the sponsor or sponsor/investigator as soon as possible; report any inconsistency or divergence found during the inventory of investigational products, medical devices received. This inspection should be documented and retained with the essential study documentation.

7.5.2 Labeling and Coding of Investigational Products, Medical Devices:

The investigator shall ensure that the drug bears a label on which appears the following information both official languages:

i. A statement indicating that the drug is an investigational drug to be used only by a qualified investigator;
ii. Name, number or identifying mark of the drug;
iii. Expiration date of the drug;
iv. Recommended storage conditions for the drug;
v. Lot number of the drug;
vi. Name and address of the sponsor/sponsor-investigator;

vii. Code or protocol identification

viii. The Medical Device has a label that indicates:

ix. The name of the manufacturer;

x. The name of the instrument;

xi. The statements “Investigational Device".

xii. The statements “To be used by qualified investigators only”.

7.5.3 Storage of Investigational Products, Medical Devices:

i. The investigator, the pharmacist or the person designated by the investigator should:

ii. Establish and maintain controlled access for authorized personnel;

iii. Develop procedures to control physical access to the storage site;

iv. Store investigational products, medical devices in a lock.

v. Store investigational products (medical devices if applicable) in a location with appropriate and controlled temperature/humidity, as stated in the protocol and should record, if applicable, the temperature/humidity as indicated in the protocol or in another study document;

vi. The temperature/humidity should be recorded on all working days of the site.

vii. Store investigational products, medical devices as specified by the sponsor and in accordance with applicable regulatory requirements, ICH 4.6.1 and 4.6.4.

7.5.4 Distribution of Investigational Products:

i. The investigator, the pharmacist or the person designated by the investigator should:

ii. Inform each study subject about the correct use of the investigational product(s), medical devices and should check, at intervals appropriate for the study, that the instructions are being followed properly by all participants participating in the study.

iii. The investigator should ensure that investigational products, medical devices are used only in accordance with the approved protocol.

iv. Inform the subject of his responsibility to return all unused medication as well as all medication packaging (bottle, container, syringe, etc.) even if empty, as specified in the protocol.

v. Document any delegation of tasks, Documentation of delegation should be retained with the essential study documentation.

vi. Submit to the ethics committee all significant deviations from the drug dose / schedule that could have an impact on the health of the subject.

vii. The submitted documents should be kept with the documentation essential to the study.

7.5.5 Maintain IP and Medical Device Inventory:

i. IP and Medical Device dispensed to and returned from each subject to be documented on a trial specific Accountability Form. The following should be recorded:

ii. Subject Identifier

iii. IP Identifier

iv. Date of dispensed/returned

v. Quantity dispensed/returned

vi. Dated initials of person dispensing and collecting returned IP and Medical Device from the subject

vii. Record any inconsistencies.

7.5.6 Reconciliation of IP and Medical Device:

i. The complete IP and Medical Device accountability form must be signed and

ii. Dated by the investigator or authorized designee following reconciliation of IP and Medical Device.

iii. Ensure that the complete forms accounting for all IP and Medical Device are filed appropriately in the ISF.

iv. Document any inconsistencies

v. The supplier of the IP should confirm in writing if the IP is to be destroyed at the Research Site or returned to the supplier.

7.5.7 Return of IP and Medical Device to the supplier:

i. Following reconciliation of IP and Medical Device accountability, document the IP and Medical Device to be returned to the supplier on an IP and Medical Device Return Form.

ii. Pack all unused and/or returned IP and Medical Device in an appropriate shipping container(s), enclosed the signed IP and Medical Device Return Form and securely seal the container(s).

iii. Arrange for the IP and Medical Device supplies to be returned to the supplier by courier.

iv. Receipt of the returned IP and Medical Device should be acknowledged by the supplier, and documented accordingly.

v. Ensure that the returned original IP and Medical Device Return Form are filed appropriately in the ISF.

7.5.8 Destruction of the IP and Medical Device at the Hospital:

i. Follow Sponsor Instructions for The Destruction of IP and Medical Device, if available.

ii. Following reconciliation of the IP and Medical Device accountability, IP and Medical Device can be destroyed at site.

iii. If site was unable to destroy the IP, it can be done by the third party.

iv. Destruction must be documented, and all documents relating to destruction filed in the ISF.

8.0 Source Documents

8.1 Purpose

To provide guidance to research personnel when research records are establish during the clinical study. Documentation of source data is necessary for the reconstruction, evaluation, and validation of clinical findings, observations, and other activities during a clinical trial. Source documentation serves to substantiate the integrity of trial data, confirm observations that are recorded, and confirm the existence of subjects. This SOP also serves to ensure data quality by creating audit trails and enabling verification that data are present, complete, and accurate.

8.2 Scope

To describe the process of collection and storage of data and source documents and to ensure that management of the process complies with the principles of ICH-GCP. To achieve this goal and provide clean data to CRF/eCRF, the source documents represents the subject's data precisely and that the said data are complete, accurate, precise and up-to-date.

8.3 Site Responsibilities

The Investigator/researcher Ensures that, during the clinical study, the research team, which will be under his/her supervision, will comply with this SOP.

8.4 Procedures

8.4.1 Confidentiality and Direct Access to Data and Source Documents:

a. In the interest of accuracy of the source documents, which include pharmacy and laboratory documents, if applicable, the investigator should have a written subject document or computerized system for subject documentation which will make it possible to compare the source data/documents and the CRF.

b. Subjects authorize access to their data in the belief that all verified and collected information will be kept confidential by the sponsor, investigator, representatives authorized by sponsor and investigator, auditors and inspectors of the regulatory authorities.

c. Any person with direct access to the source data should respect the Declaration of Helsinki, GCP and applicable regulatory requirements for the maintenance of confidentiality of the identity of subjects and of the proprietary information of the investigator.

8.4.2 Delegation Log:

i. A delegation log identifying those who have access and those who can enter or correct source data should be kept in the Investigator Site File (ISF) or Site Master File (SMF) as an essential study document.

8.5 Definition of Source Documents:

Source documents can be defined in the protocol in order to allow their verification during the study. Moreover, the protocol should identify the parameters that should be entered directly into the CRF; in this case, these data will be considered as source data. The designation of source documents includes, but is not limited to:

Documentation of the process of obtaining informed consent (ICF);

The ICF signed and dated by the participating subject and the person who obtained the consent

The medical file including medical history, diagnoses and medical follow-up;

Any communication between the various parties, i.e. sponsor / investigator, investigator / subjects.

Examples of communication: email, telephone messages, etc. Demographic data: subject's initials, date of birth and gender;

Concomitant medications, current and previous, as the case may be, according to the protocol;

Inclusion or exclusion and randomization criteria;

Dates of study visits start and stop dates for medication, dates of laboratory tests and other diagnostic procedures;

Results of objective tests (X-rays, laboratory results, electrocardiograms, etc.) reviewed, signed and dated by the investigator or his authorized representative and interpretation of the result: "clinically relevant" or not;

Details of adverse events (AEs) or serious adverse events (SAEs), including beginning and end dates, etiology, relevant tests, treatment received and the consequences, as well as all available information on this topic in the source data;

Primary and secondary variables of effectiveness;

The subject number, the randomization number and the allotted CRF number, if relevant. Any document, in which clinical study data is recorded for the first time, is considered to be a source document (note, appointment book, subject's medical file, etc.). All these source documents should be handled and filed according to the applicable regulations.

8.6 Documentation of Source Data:

A. All source data collected should be kept in the subject's file or ISF from the time of collection or observation.

a. For documentation, the following standard practices should be observed:

b. Data should be entered in a sequential manner, without leaving any empty spaces;

c. Data should be dated and signed by the authorized person;

d. The date when the data were collected as well as the date of data entry, should appear for data obtained after a visit (late data);

e. If it is noted in the research record that data are missing and those data are then obtained/found at a later date, it cannot be inserted between existing lines or written in the margin, it should be inscribed following other entries with the notation of late entry; The notation must be signed/initialed and dated.

f. Data written by hand should be legible and written with permanent ink;

g. Data entered by several team members: each entry should be signed and dated by the authorized person who made the entry;

h. Work sheets or work forms provided by the sponsor to collect information necessaryto the protocol are an integral part of the source documents;

i. Missing elements (i.e. visit or tests not conducted) should be clearly reported in the source document;

j. Entries entered directly into the CRF are defined as source data. The data to be entered directly into the CRF should be mentioned in the protocol.

k. In the case of source data registered on thermal paper (i.e. electrocardiogram, respiratory function test, etc.), that a dated and signed photocopy of the original document has been made and is attached to the original document.

8.6.1 Correction in Source Data:

Corrections made to source data should follow the same procedure as corrections to CRFs: A single line through the data to be corrected (it should be possible to read the original data). The initials of the person who corrected the data and the date of correction Corrections should be made, preferably, by the person who made the entry or by others authorized to do so.

The use of liquid corrector or correcting material is prohibited.

8.6.2 Storage of Source Documents:

All the source documents generated during the clinical study (ies) must be kept under locked cupboards in a safe place with access only to authorized study personnel.

The source documents of each clinical study must be kept individual in a separate cupboard.

The master key of all the cupboards must be kept with PI.

9.0 Management of protocol deviations and violations

9.1 Purpose

To describe the policies and procedures about notification of modification, deviation or violations in approved research / study protocol

9.2 Scope

To emphasize Investigators responsibility to notify EC about modification, deviation or violations so these may not result in an increase in risk or a decrease in benefit to the human research participants.

9.3 Responsibility

Execution of SOP: Investigators, Delegated Study Personnel, Sponsor & Ethics Committee

9.4 Protocol Modifications

a. Investigators may not initiate any changes in research procedures or consent/assent form(s) without prior EC review and approval, except where necessary to eliminate apparent immediate hazards to the subject. Examples of modifications that require EC review include, but are not limited to, changes in:
    a. Study personnel
    b. Advertising materials (flyers, radio spots, etc.)
    c. Research procedures
    d. Subject populations (e.g., age range, no. of patients)
    e. Location where research will be conducted
    f. Consent/assent forms
    g. Recruitment procedures; or
    h. Date for completion of study.
    i. Subject information literatures and retention items.

b. If the investigator makes protocol changes to eliminate apparent hazards to the subject(s) without prior EC approval, the investigator must immediately report the changes to the EC for review and a determination as to whether the changes are consistent with the subject's continued welfare.

9.5 PROCEDURES

9.5.1Action for Investigator:

The Investigator is responsible for submitting a modification, deviation and violations in writing to the EC.

9.5.2 Action for Ethics Committee:

The EC's approval is sought prior to implementation of any change to the protocol. EC may audit any protocol reporting frequent deviations.

In case a protocol deviation takes place the Investigator documents the same; an explanation for the same is provided to the sponsor and a copy of the same is goes to the EC as well the research department.

Deviations undertaken to eliminate an immediate hazard would be considered an Unanticipated Problem and should be handled according to the specified SOP on unanticipated problems.

9.5.3 Reporting & Review

Deviation/Exception forms are to be completed for those events that qualify as a protocol deviation or exception are duly filled and reported to the EC. The EC member secretary will review the information, and either process for expedited review (where risk is not increased), chair review (where risk is increased but time considerations do not permit review at a meeting), or full committee review. Outcome of review will be informed to the investigator for review and action, if necessary.

9.6 Protocol Violation

If Protocol violation occurs on monitoring it should be brought to the notice of EC. An internal audit may be conducted by the institution or the EC as deemed necessary. The EC review the audit report and decide about the further course of action.

10.0 Patient Outreach Programme

10.1 Purpose

To describe the process of retaining study subject(s) on clinical trial complying with follow up visits and preventing subjects from becoming lost to follow up. To comply with the ethical principal of respect for persons participating in research and maximize their involvement in the research process, including proactive outreach activities for current, prospective, or past research subjects or their designated representatives.

10.2 Scope

This is applicable to subject(s) involved in clinical trials.

10.3 Responsibilities

Investigator

Delegated study staff.

10.3Procedures

10.3.1 Retention and Prevention of Lost to Follow Up:

Obtaining full and accurate information of subject(s) at the beginning of the study to avoid failure to locate subjects for future contacts.

Inform to the subject about their scheduled follow up visit prior to window period.

A subject follow-up schedule must be used to capture the scheduled and actual dates for all visits for all subjects, if provided.

Provide enrolled subjects with an EC approved subject Identification card/calendar or schedule of all their visits, if provided by the sponsor.

10.3.2 Locating subjects potentially lost to follow up in preferred order:

Investigator/delegated study staff/ Research Head will call telephone numbers for subjects, relatives and other contacts provided by the subject.

In case subject is not contacted through telephone, Investigator/delegated study staff/ Research Head send a certified letter or e-mail to the subject requesting to contact study personnel. In case subject is not contacted by above preferred methods, Investigator/delegated study staff/ Research Head will plan a personal visit to the address provided by subject. Assistance from the other services can be taken to locate the patient, if described in protocol.

11.0 Blood Sampling and Storage

11.1 Scope

The standard operation procedure of blood sampling and storage as requirement of protocol is to implement definitions, processes and standards as recommended by the ICH requirements for safety reporting. The purpose of this SOP is to provide the necessary definitions, policies, principles and guidance to personnel involved in sample collection and storage. It is applicable to all Investigators, study coordinators, Phlebotomists, Study nurses and all other personnel delegated in the delegation log of the concerned study.

11.2 Definitions

Blood Sampling Process:

i. Blood sampling for all trials will be conducted as follows.
ii. Subject will be taken to one of the Sample Collection rooms in the hospital
iii. All Vacuitainer and transfer tubes must be labeled with the subjects ID and visit ID.
iv. The delegated Phlebotomist on duty will perform blood sampling procedures as per the protocol.
v. If applicable, samples that need to be centrifuged can be done by the delegated site team as per the protocol, using centrifuge machines which are calibrated with the same being documented in the site master file.

11.3 Blood Sample Storage:

Blood samples will be stored in the following manner:-

i. Samples that need to be for one day or less till courier personnel arrive for shipment will be done as follows

ii. If sample is to be maintained at ambient temperature, it will be placed in a storage box or tube stand that maintains the tube in upright position. The box/stand will be placed in cool dry place at room temperature.

iii. If a frozen sample is to be sent, it must be stored in a labeled cryobox, in a Deep freezer at temperature defined by the protocol. The Deep freezer must be running continuous since 15 days prior to the visit concerned unless otherwise specified by the protocol.

iv. Blood sample must be retrieved at the time of shipping and packaged by the respective courier personnel. An invoice and declaration signed and stamped by the study staff, stating the value and purpose of the shipped samples and if it is hazardous, must be provided to the courier personnel.

v. Samples that need to be stored for duration longer than one day will be done as follows:

vi. Samples that need to be stored for duration longer than one day will be stored in a Deep Freezer as documented in the site master file at temperature conditions as defined by the trial protocol.

vii. The tubes, boxes, bags etc. used for storage of blood must be appropriately labelled using the method defined in the protocol and must be easily identifiable, distinguishable and retrievable.

viii The temperature must be maintained once in a week and the temperature must recorded on appropriate study temperature logs. If temperature records cannot be generated automatically from the freezer and need to be documented manually, they will be done once in every week at a fixed time, A list of site holidays will be provided to the sponsor (if applicable) on request prior to the start of the trial.

ix. If storage is not possible in the Research Department can be done in some other department in the hospital (such as Blood Bank, Pathology lab, Histopathology lab etc.) then the standard operating procedures for storage of samples of that department will supersede this SOP wherever a conflict arises.

12.0 Preparation for Monitoring Visit

12.1 Purpose

Monitoring of clinical trials is necessary to assure that the rights and safety of patients are protected and reported trial data is accurate, complete, and verifiable from source documents conduct of trial is in compliance with protocol, GCP and applicable regulatory requirements.

12.2 Scope

The scope of this operating procedure is to guide the research team in its preparation for an internal /external monitoring visit.

12.3 Responsible Personnel

I. Principal Investigator
II. Clinical Research Coordinator
III. Delegated Research Team

12.4 Procedures Information

The monitor must inform the site of an upcoming monitoring visit in advance along with the agenda for the visit. The investigator/delegated CRC must authorize monitoring and allow the monitors to carry out monitoring.

12.5 Scenario for a Monitoring:

A monitoring carried out by the Clinical Research Team Monitor(s) is done to ensure that the study complies with applicable standards and that data are accurate and of good quality. If carried out at the beginning of the study, a monitoring can serve to correct errors before the study is completed; however, it can be carried out at any time, in the course of the study or at the end. Investigator/Delegated Staff can be interviewed by the monitor on any findings.

A monitoring directed towards the investigator/CRC is carried out when there is reason to believe that there are problems with the site's data. Some of the problems can become apparent because of non-compliance of the site with the protocol, an overly low or high rate of adverse reaction or adverse events compared to other sites, a high rate of recruitment compared to other sites, etc. However, a monitoring can be done on a site for no particular reason.

12.6 Preparation for a Verification Monitoring:

i. The investigator/CRC should always be informed in advance in writing, of a planned visit for monitoring purposes, both parties (Site & Sponsor/CRO) will agree on a date that leaves a sufficient period for the Clinical research team to prepare for the visit.

ii. In order to prepare for a monitoring visit, the Investigator/CRC should verify that the original documents are available. The information contained in all the documents is complete, up-to- date and in consistent with the data or source documents.

iii. If there were retrospective entries or corrections, they should have been dated and signed by the person who made the entry or the correction.

iv. Procure original subject files (if required by monitor) from the Medical records Department (MRD)

12.7 Responsibility of Clinical Research Coordinator & Clinical Research Monitor in monitoring:

i. To inform all key & delegated personnel that the monitoring will take place, with the name of the monitor(s) and the scope of the monitoring and all dates agreed in advance in a timetable.

ii. Information should be provided by the monitor what documents (according to check list) should be made available during the monitoring and ensuring that this is available during the monitoring, including any documentation that has been archived.

iii. Prior to the monitoring, arrange appointments for the monitor with the Research Team (e.g. Principal Investigator and delegated person) and supporting departments (e.g. Pharmacy, Pathology, etc.) prefer time for monitoring is 10AM to 5 PM from Monday to Friday.

13.0 Management of unanticipated Risks and Problems

13.1 Purpose

Unanticipated Problems are any incident, experience or outcome that is unexpected, related or possibly related to participation in research and suggests a greater risk of harm to subjects or others. The purpose of this SOP is to enforce standards and procedures that ensure that all unanticipated problems are reported by investigators and reviewed by the Institutional Ethics Committee.

13.2 Responsibilities Investigator:

Identifies, documents, and reports unanticipated problems to the EC and the sponsor (if applicable). The regulatory team of the clinical research department assists the Investigator for the same.

13.3 Ethics Committee:

Is responsible for reviewing all unanticipated problems and assessing the risk and benefit faced by the human research participant or others, and suggesting further action where required.

13.4 Study Coordinator:

Assists investigator in documenting unanticipated problems and reporting to the EC

13.5 Criteria for identifying unanticipated problem:

Unanticipated Problems are any incident, experience or outcome that is unexpected, related or possibly related to participation in research and suggests a greater risk of harm to subjects or others.

It is important to remember that Unanticipated Problems must meet all three of the following criteria:

i. Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the EC-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied.

ii. Related or possibly related to participation in the research (possibly *related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).

iii. Suggests that the research places subjects or others at a greater risk of harm (physically, psychologically, economically, or socially) than was previously known or recognized

Adverse events focus on the harm; unanticipated problems focus on the "risk of harm".

iv. The vast majority of adverse events occurring in research with human subjects are not unanticipated problems. When conducting research with human subjects unanticipated problems occur that include other types of incidents, experiences, and outcomes that are not considered adverse events. These might include social or economic harm instead of the physical or psychological harm associated with adverse events. An example of social harm can include an incident where identifiable sensitive data was left unprotected and unauthorized individuals gained access to the information.

v. Unanticipated Problems also place subjects or others at *increased risk of harm*, but no harm may actually occur. The increased *risk* of harm is the key factor here. Subjects should always be informed of increased risk associated with the research and steps should be taken to eliminate or minimize the risk where possible.

13.6 Unanticipated Problems needed to be reported:

i. Breach of confidentiality (e.g., lost or stolen research data)

ii. Newly discovered information (e.g., from data analysis or publications) that indicates a greater risk to subjects than expected and that may affect adversely the safety of the subjects or the conduct of the clinical trial.

iii. Changes made to research without prior EC approval in order to eliminate apparent immediate harm.

iv. Incorrect dosing or labeling that adversely affects the safety of subjects

v. Risk to others (e.g., research staff, investigators) related to the research (e.g., physical harm)

vi. Adverse events which meet the definition of an untoward problem involving risks to subjects or others (unexpected, involve new or increased risk, and are related to the research)

vii. Unexpected serious adverse event

viii. Threats to subjects or others related to their participation in the research

ix. Changes in the research environment that increase the risk to subjects or others due to the research (e.g., political or social changes)

x. Higher occurrence of an adverse event or serious adverse event than expected

xi. Incarceration of subjects

xii. Any side effect adjudged to be related to participation in research that is not mentioned in the:

xiii. Protocol

xiv. Investigator Brochure

xv. Product labeling or package inserts

xvi. Informed consent document

xvii. Any medical condition or complaint that is adjudged to be related to participation in research and is not part of the subject's expected natural progression of an underlying disease, disorder or condition under study; or part of the subject's predisposing risk factor profile.

13.7 Procedure

13..7.1 Investigator Assessment:

The responsibility for identification, documentation and reporting of any unexpected problem lies with the Investigator. The Investigator should evaluate the event and assess whether it is an unanticipated problem based on Section 4 of this SOP. She/he must also evaluate causality and relatedness to participation in research.

13.7.2 Reporting:

Investigators must report the reportable events described above within regulatory timelines. In case the unexpected problem involves a medical procedure, drug or medical device, it must also be reported the sponsor and EC within timeline.

13.7.3 Ethics Committee:

i. Upon receipt of reports, EC Member Secretary, will review them and determine if the report meets the following criteria:

ii. Unexpected

iii. Related or possibly related to the research and

iv. Any indication that participants or others are at increased risk of harm.

v. If the report does NOT meet the criteria, the report is NOT an unanticipated problem involving risks to participants or others, and no further action is taken.

vi. If the report meets the criteria, the report is an unanticipated problem involving risks to participants or others and the EC will evaluate reports to determine if it involves more than minimal risk to subjects or others and determine the further course of action.

13.7.4 Actions by Ethics Committee

i. The EC member secretary and the members may make a decision for any of the following:

ii. Suspension of the research.

iii. Termination of the research.

iv. The PI has to submit a letter from the recruited subjects that they are willing to take part in the research upon knowledge of unanticipated problems.

v. Any other course of action deemed appropriate

vi. In case of non compliance to this the EC may take action as per the section 5.3.5.2 of SOP on Complaints and non compliance.

13.7.5 Research Department

i. Receipt of adverse events from sponsor:

ii. All safety reports (SUSAR LL and CIOMS Form) received from the sponsor will be notified to the ethics committee.

iii. The Investigator and/or Study Coordinator will file copies of these SAE and AE in the regulatory binder of the study

14.0 Archiving and Documentation

14.1 Definitions

Archiving in the context of clinical research relates to the collection for long term storage of essential documents that individually and collectively permit the evaluation of the conduct of a trial and the quality of the data produced.

14.1.2 Essential Documents are those documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced.

Trial Site- is the location(s) where trial related activities are conducted.

14.1.3 Investigator Site File (ISF) is the trial file held by the Investigator that holds all essential documentation, this file is set-up, maintained and located at the Investigator's site.

14.2 Purpose

This Standard Operating Procedure (SOP) describes the essential documents that are required in an investigator site file

14.3 Scope

This SOP refers to the essential documentation and the creation of the ISF for Clinical Trials

14.4 Responsible Personnel:

i. The investigator/CRC is responsible for set-up and maintenance of all essential documentation related to his/her trial, and is responsible for providing the Sponsor with any updated documents as requested throughout the trial until trial closure.

ii. This SOP must be read by all members of the team who are likely to file documents.

14.5 Procedures

14.5.1 Confidentiality:

Filing space should be available for the storage of investigator site files during the conduct of the clinical trial. Investigator site files will normally be stored in an investigator's office or local filing area.

14.5.2 Record Keeping:

Investigators must ensure that data are recorded and stored correctly and accurately. This not only includes data recorded on Case Report Forms but also all original source data (patient medical notes for example), laboratory test results, radiological images and pharmacy data (drug dispensing records and drug accountability records for example).

14.5.2 Period of Document Retention:

i. The investigator shall ensure that the documents contained, or which have been contained, in the Site master files are retained for at least 15 years after the conclusion of the trial / or specified in protocol.

ii. It is recommended that all records must be safely maintained by the IEC after the completion / termination of the study for at least a period of 5 years if it is not possible to maintain the same permanently.

14.5.3 Before the trial commences:

i. At the time of initiation, the trial site should have an ISF containing all essential documents which should provided by sponsor/CRO in case of clinical trials. Each file should be numbered consecutively, and be identified by trial title (short title), investigator name, site name and sponsor number.

ii. Each ISF will contain an index at the beginning of the file that indicates the sections where essential documents are filed.

iii. The Investigator should perform a review before the trial initiation visit (TIV) on site, once confirmation of all necessary approvals and other trial documentation are in place.

14.5.4 During conduct of the trial:

i. The Investigator must ensure that the ISF is maintained in an ongoing fashion and that all trial related patient logs (e.g. screening and enrolment) are maintained.

ii. Staff training must be documented and any new staff joining the team must be added to the delegation log and signed off by the Investigator before any trial related duties are performed (such as taking patient consent or reporting SAEs). Updates to the delegation log must be notified to the Sponsor so that they can centrally verify the correct delegation of roles (i.e. completion of an SAE form or assessing causality of an SAE).

iii. The following trial activities should be filed in the ISF as per protocol together with documented evidence of notification to the sponsor:

14.5.5 Deviation/violation forms:

i. SAE's/ADR's/ SUSAR's must be filed per patient/event

ii. Amendments

iii. Annual Safety Reports (ASRs)

iv. Annual Progress Reports (APRs).

v. It is important that site maintains amendment logs, indicating changes and dates of implementation. Old documents must be retained in the ISF but scored through by placing a line through any old documents no longer in use.

vi. All documents should be filed chronologically within each section to allow the most recent documents to be easily accessed.

vi. Investigator should ensure that the observations and findings are recorded correctly andcompletely in the CRFs and signed by the responsible person(s) designated, in the Protocol.

viii. Laboratory values with normal reference ranges should always be recorded on a CRF or enclosed with the CRF. Values outside the clinically accepted reference range or values that differ importantly from previous values must be evaluated and commented upon by the Investigator.

ix. It is important to ensure the ISF is kept up to date and all patients/staff logs are maintained accordingly. Any documents identified as missing must be obtained by the Investigator or the person to whom this task has been delegated.

x. Screening/enrolment logs should be filed in a separate section to the signed consent forms.

xi. The ISF must be retained within a secure place, with restricted access. Documents should be kept in a legible and well presented condition, it is necessary to retain a hardcopy of essential documents as there are currently no regulations regarding the electronic format of the ISF.

xii. It is a statutory requirement that the trial file be available at all times during the trial in the event of an audit/monitoring visit or Inspection.

xiii. If the interim storage of the investigator site file is found not to be in accordance with Regulations, the investigator will have to take action to ensure that the site file is stored appropriately

xiv. The study can be closed only when the Investigator (or the Monitor or CRO/sponsor if this responsibility has been delegated to them) has reviewed Investigator / Institution files and confirm that all necessary documents are in the appropriate files and can further be archived as per policy of the company.

14.5.6 After completion or termination of the trial (Archiving):

i. The Investigator shall notify the IEC of the declaration of trial end as defined in the protocol.

ii. Archiving of essential documents should occur after the trial has undergone the final close out visit for 15 years and the close out information has been issued by the Sponsor. The investigator will receive confirmation from the Sponsor that proposed off-site archiving arrangements are satisfactory.

iii. The Investigator must ensure that there will be sufficient funds available to cover the cost of archiving facility at the end of a trial. As such the cost of archiving trial documentation 50,000 + GST.

iv. The Investigator will inform the IEC and Sponsor of archiving of trial files. The archiving will be done by the PI.

15.0 SOP on Training Evaluation in Clinical Trials

15.1 Purpose

To specify the procedure for training provided to the Research team in terms of Site SOPs & Clinical trial protocol.

15.2 Scope

i. The scope of this operating procedure is to evaluate the research team on adherence to Site SOPs and clinical trial Protocol.

ii. To ensure planned and systematic actions are established to ensure Clinical trial is performed, data is generated, documented (recorded), and reported in compliance with SOPs and Clinical Trial Protocol.

15.3 Procedure

i. A member of the research team who involves in Clinical Research should follow the Site SOPs; planed systematic actions as required in clinical trial protocol.

ii. A member of the institutional personnel involved in clinical research trials is designated by the PI , Investigator to sign the study delegation log,

iii. He/she may participate in the SOP revision/ modifying process. They may also participate in the training of each standard operating procedures of Protocol & Site SOP.

iv. At the time of implementation of each SOP, need to ensure that clinical study personnel at the institution are trained in procedures and comply with this Site SOP.

v. Training on SOPS to research personal personnel involved in clinical trial will be provided by the person within the institution responsible for the site SOPs.

vi. This training should be documented by the individuals trained, signed and dated.

vii. PI will ensure that training of the study team in Site SOP and Protocol is documented. Training documentation should include the title of the training, participant name and training date, the person or organization that provided the training and a summary of the training. The training documentation can be filed individually for every participant or for the whole group.

15.5 Ensuring adherence to training:-

PI is responsible for ensuring that, during the Clinical Trial, the research team will comply with this site SOP and study protocol.

Operational techniques and activities undertaken within the quality assurance system of protocol to verify that the requirements for quality of the trial related activities have been fulfilled. The following documents will work as an external quality measurer to evaluate the training process: -

i. Documentations as per the clinical trial protocol.

ii. Monitoring follow up letters

iii. Audit report

iv. SAE and AE reporting with in time frame.

v. Customer feedback

vi. Protocol deviations& violations.

15.5.6 Responsibilities

i. Institute

ii. Investigator

iii. CRC

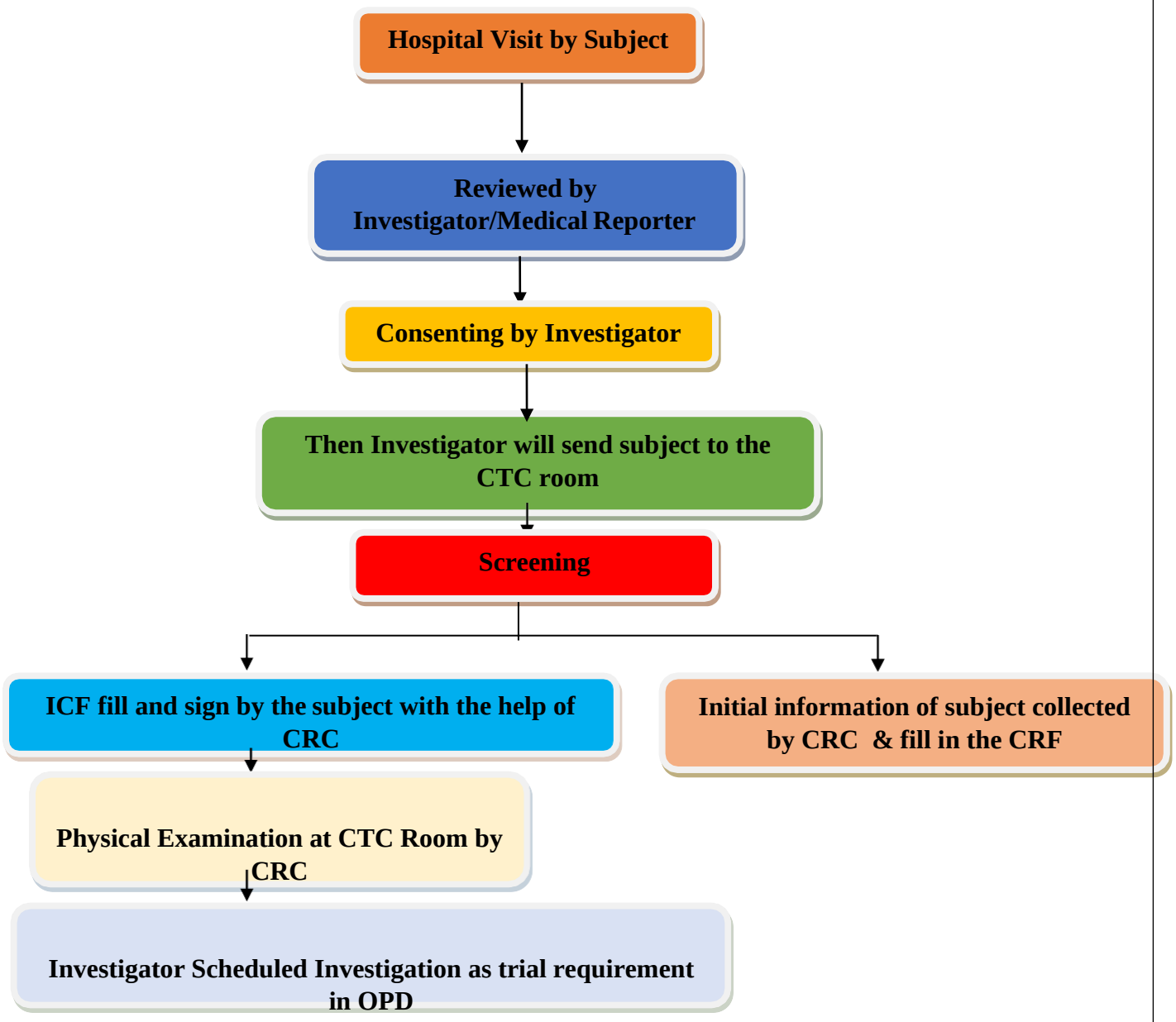
iv. SMO Team

Standard Operating Procedure for Clinical Trials at Site Himalayan Hospital Swami Rama Himalayan University

Check with Inclusion/ Exclusion criteria and Medical History by CRC & Investigator

If Subject agree to participate in the Study.

16.0 Objective: To lay out the procedure for the subject enrollment and visit



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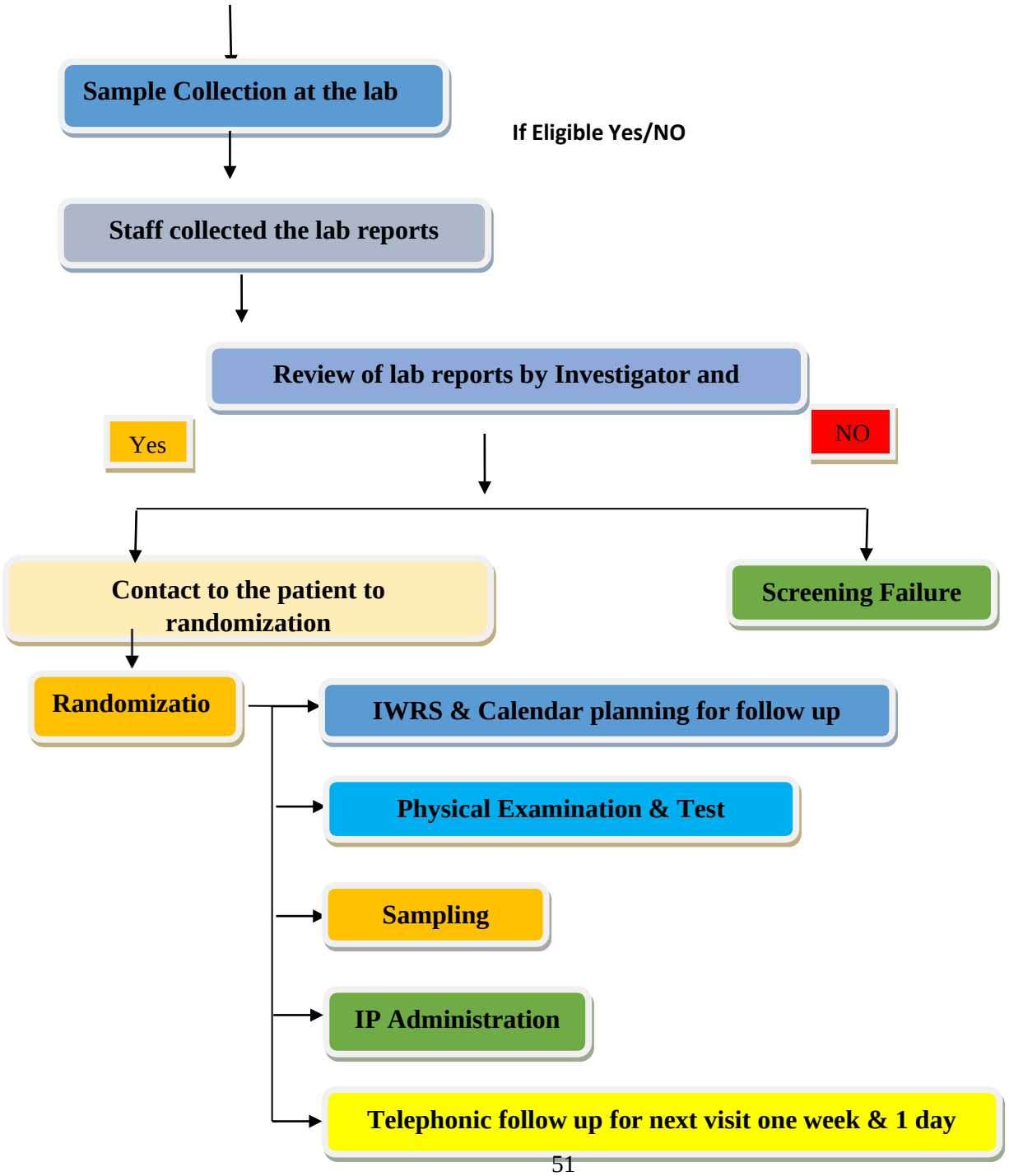

Duration of Validity: This SOP valid for 3 years

List of Abbreviations

ADR – Adverse Drug
Reaction AE – Adverse Event
CRC – Clinical Research Coordinator CRF – Case Report Form
CRO – Contract Research
Organization CTA – Clinical Trial
Agreement
DCGI – Drug Controller General of
India GCP Good Clinical Practice
GMP – Good Manufacturing
Practice IB – Investigators Brochure
ICF – Informed Consent Form
ICH – International Conference of
Harmonization ICMR – Indian Council of
Medical Research IDMC – Independent Data
Monitoring Committee INDA- Investigation
New Drug Application
IP – Investigational
Product ISF – Investigator
Site File
LAR – Legally Acceptable Representative
SRHU – Swami Rama Himalayan
University
IEC – Institutional Ethics Committee.

MOU – Memorandum of Understanding

MRD – Medical Record Department

NDA – Non Disclosure Agreement

PI – Principal

Investigator QA –

Quality Assurance QC –

Quality Control

SAE – Serious Adverse Event

SCRT – Stem Cell Research &

Therapy SOP – Standard Operating

Process

SUSAR – Suspected Unexpected Serious Adverse Reaction

References:

i. New Drug and Clinical Trials Rule 2019.
ii. Ethical guidelines for Biomedical Research on Human participants, ICMR
iii. Declaration of Helsinki.
iv. ICH-GCP Guidelines.
v. Indian – GCP

17.0 Objective: To lay down a procedure for finance, distribution of payments for hospital, Service charges and SMO.

17.1 Background

This SOP describes the payment pattern for a clinical trial/research study at Swami Rama Himalayan University.

17.2 Purpose

To make sure that the institute is able to pay effectively and completely as per the requirements of the study agreement.

17.3 Scope

This SOP applies to clinical trials conducted at Swami Rama Himalayan University.

- SRHU Clinical Research Team
- SRHU Finance Team
- SMO Team

17.4 Procedure

1. Firstly received Budget sheet from sponsor as part of Clinical Trial Agreement.

2. Will divide the whole budget in three parts viz, Hospital (without GST), Service (With GST) & Subject (without GST). Service includes PI fees, Sub Investigator Fee, CRC fees & Study start up amount.

3. Service part will further divided in two parties as per MOU. Viz., SMO & Institute MOU page no 5.

4. The payment to SMO will be done by Institute after receiving bills from SMO .

5. All invoices generated by Institute to sponsor.

6. The draft invoices for the services generated by SMO team in discussion with institute personnel and send to finance for final generation of e-Invoice.

7. The visit charges to the subject provided by institute after receiving the request from Clinical Trial Centre.

18 . To lay down a Performa for recording the vitals of enrolled participant

CLINICALTRIALCENTRE

Himalayan Hospital, Swami Rama Himalayan University Examination of Vital Signs

Study Site…….. Date&Time……..

Subject Initial…….. Subject Number:……..

Weight(kg):……. Height(cm):……

Blood Pressure(mmHg):…… Pulse rate (bpm):……

Temperature(^{0}F):…… Sp02(%)…….

Respiratory rate (min)……..

Signature of CRC:…… Signature of PI/COPI:…….

Normal Ranges:-

BloodPressure:130/90mmHg Pulse rate (bpm): 60-

120bpmTemperature(0F):100F Sp02(%):95-100%

Respiratory rate (min) 12-20 min

Standard Operating Procedure for Clinical Trials at Site Himalayan Hospital Swami Rama Himalayan University