PRAVARA INSTITUTE OF MEDICAL SCIENCES

(DEEMED UNIVERSITY)

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STANDARD OPERATING PROCEDURES

FOR CLINICAL INVESTIGATOR

DIRECTORATE OF RESEARCH
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OBJECTIVES

- To provide the investigator with general instruction to ensure that he / she understands and accepts the obligations incurred in undertaking the study
- To ensure that the study is planned, set up, conducted, documented and reported according to the protocol, related SOPs, ICH GCP and applicable regulatory requirements
- To ensure that the rights, safety, and welfare of study subjects are properly protected
- To ensure that data are generated, collected and documented with accuracy, consistency and integrity
- To ensure that the investigator is acquainted with the study procedures, verification procedures, audits and inspection procedures

GENERAL SOP

Clinical trials should be conducted in accordance with ICH – GCP, Schedule Y and the applicable regulatory requirement (S):

- Before a trial is initiated, foreseeable risk and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society
- A trial should be initiated and continued only if the anticipated benefits justify the risks
- The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society
- The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial
- Clinical trials should be scientifically sound, and described in a clear, detailed protocol
- A trial should be conducted in compliance with the protocol that has been received prior to the institutional ethics committee (IEC PIMS-DU) for approval or favorable opinion

- The medical care given to, and medical decisions made on behalf of subjects should always be the responsibility of a qualified physician or, when appropriate, of qualified dentist
- Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task (S)
- Freely given Audio visual informed consent should be obtained from every subject prior to clinical trial participation
- All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification
- The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(S)
- Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP) they should be used in a accordance with the approved protocol
- Systems with procedures that assure the quality of every aspect of the trial should be implemented

Patient protection-safety, well being, rights

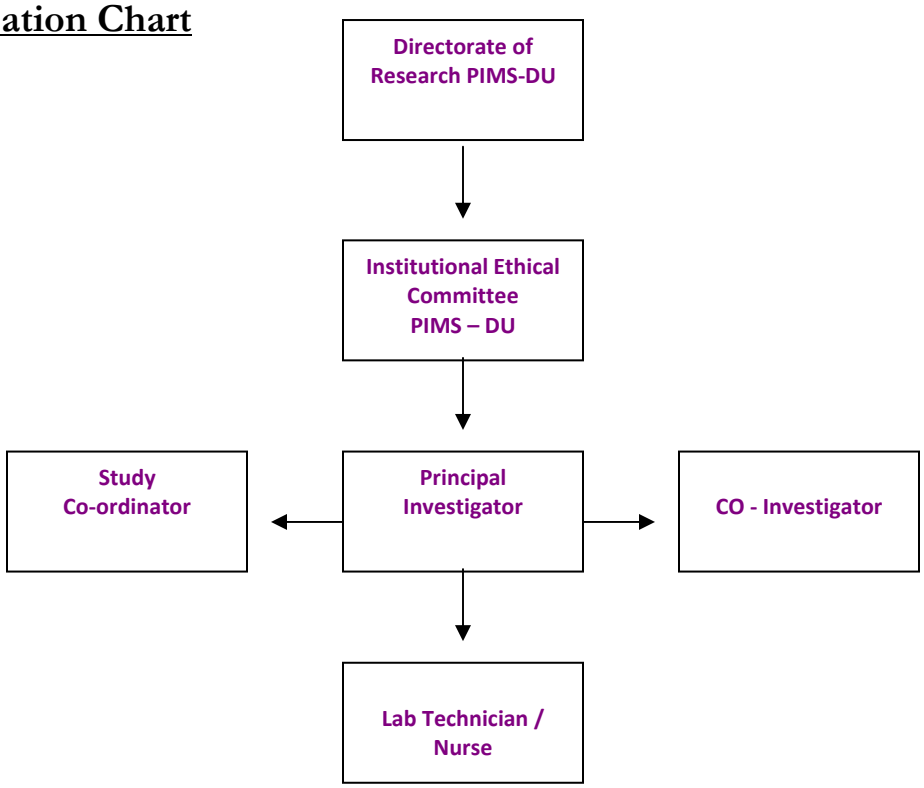
- The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society
- Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks
- Freely given Audio visual informed consent should be obtained from every subject prior to clinical trial participation
- The investigator should make a reasonable effort to ascertain the reason (S) for withdrawing prematurely from the trial, while fully respecting the subjects rights

Medical care of patient

- A qualified physician who is an investigator or sub-investigator must be responsible for all trial-related medical decisions

- The investigator should ensure that adequate medical care is provided to the trial subject for any adverse event, including clinically significant laboratory values related to the trial
- The investigator should inform the subjects primary physician about his / her participation in the trial if the subject has a primary physician and agrees that he / she be informed
- The investigator should make a reasonable effort to ascertain the reason (S) for withdrawing prematurely from the trial, while fully respecting the subjects rights

Organization Chart



Equipments, their calibration requirements:

- All the study related equipments are calibrated in a timely manner.
- Calibration certificates are kept in their respective files.
- In case of breakdown of study equipment, back up facilities for the same is present.

Hospital Registration:

- For all out-door patients, OPD registration is mandatory which can be done by patient or any of patient's relatives.

- For all In-door patients IPD registration is mandatory which can be done by patients or any of patient's relatives.

ICD PROCESS

- An informed consent is the process by which a study subject voluntarily conform his/her willingness to participate in trial.
- Before any subject enters a trial, and before study – related procedure begin, freely given Audio visual and written informed consent must be obtained from the subject.
- Only study subjects who have fully understood all aspect of their participation in the trial can make proper judgment and give their consent to participate in trial.
- Study subject found ineligible at screening (for medical reasons) should receive supportive counseling, any necessary and available treatment and referral for continued counseling.
- The Investigator can delegate the consent process to an appropriately qualified person; however, Investigator should see the subject afterward to ensure that the consent has been properly obtained. Verbal and written information given to the trial subject should be in simple terms and his/her first language. Medical terms should be avoided.
- Principal Investigator should ensure that sufficient time is given to the subject for informed consent process and resolve all quires raised by the patient till his satisfaction.
- The Investigator/designated persons should perform informed consent procedures fully with subject during recruitment.
- If subject is illiterate then written informed consent should be obtained from subject and his / her legally acceptable representative
- If the study subject and /or legally acceptable representative is (are) unable to read an impartial witness should be present during the entire informed consent discussion.
- After oral approval by the study subject and/or legally acceptable representative the witness must sign and personally date the informed consent form to attest that the information was accurately explained and apparently understood and that informed

consent was given freely by the subject and /or the study subject and /or legally acceptable representative be given a copy of the signed and dated informed consent form and any other written information.

- The original signed and dated informed consent form should be kept in the Investigator's file or respective subject's source file with study subject's data.
- Trial subject and /or legally acceptable representative should be kept informed throughout the trial of any new finding or information about the tested product which might be of consequence to their participation in the trial. They should receive updates of the signed and dated consent form as well as copies of any amendments to the written information.
- Updates of the original signed and dated consent form should be kept in the Investigator file or respective subject source file.

PATIENT SCREENING, ENROLIMENT AND FOLLOW-UP

- It is important that the Investigator resolves all questions from his/her staff concerning the interpretation of inclusion / exclusion criteria.
- The investigator should be able to delicate time to the recruitment of suitable trial subjects the consultation time for recruitment of each subject is likely to be longer than the time required for normal consultation.
- The Investigator must insure the unbiased selection of an adequate number of suitable study subjects as defined by the protocol.
- The investigator must allow study subject who meet the inclusion criteria the opportunity to decide for themselves whether or not be entered in to the study.
- In between study duration if the subject is admitted in the hospital then, on duty medical officer and nurses will take rounds and write their notes in the hospital file under supervision of Investigator as per hospital policy.

DOCUMENTION

JCH international guidelines for Good Clinical Practice and other applicable regulatory guidelines pertaining to clinical trial, require **direct access** to source data/document for trial, related monitoring, audits, IEC/IRB review, and regulatory inspection.

Source document are all original document, or certified copies containing data related to Clinical trial activities (source data), necessary for the reconstruction and evolution of the trial.

Source Document (non- exhaustive list)

- Informed consent.
- Subject medical file.
    - Medical and medication history
    - Serious adverse event
    - Instrument printouts
    - Traces and laboratory result scan and other report
    - Subjects visit dates.
- Subject identification list
- Clinical and office charts
- Product dispensing record, accountability
- Laboratory notes
- Trial agenda
- For IPD trial patient, original IPD file. Kept in medical record room of the institute and photocopies are kept in the source file of the trial subject.

LABS

- Site having separate department for laboratory, which is know as "Microbiology & Biochemistry Lab" which contains well equipped & well-furnished Biochemistry Lab. The site also can get lab Samples processed from external vendor as per requirement of the protocol.
- Lab technician draws blood & they process blood under supervision of study specific CRC. The CRC stores the sample at required temperature: packs it properly as per the protocol requirement and then dispatches the sample /samples to the central laboratory destination within time lines.
- Site is having good storage facility at -20°C & -40°C.
- Protocol specific & ICH- GCP training is provided to lab technician for better compliance.

- When report is received, it is checked by lab & validated by putting sign on it.
- These validated lab report are being reviewed by investigator or co-investigator, marking the comment whether these report are clinically significant or non significant. Also these are counter signed by the investigator co-investigator. Action is taken for clinically significant values as per requirement.
- The original lab reports are dispensed to the patient and photocopies are kept in the sources file of the trial subject.
- Expired central lab kits are destructed as per hospital destruction policy with prior permission of sponsor as per hospitals waste management policy.

LAB PROCEDURES

- Lab technician will perform the required procedures under supervision of study specific CRC.
- The original reports are dispensed to the patient and photocopies are kept in the source file of the trial subject.

EQUIPMENTS

- Principal Investigator should ensure that all the equipments used by study staff for study purpose are calibrated regularly.

STUDY DRUG

- The Investigator may assign an appropriate person (pharmacist/nurse/co-coordinator) to be responsible for investigational product storage and accountability at the site.
- The Investigator should ensure that the investigational product is properly received, stored and handled.
- The Investigator /designated person must:

  -Store the product in the condition that has been specified in writing and in accordance with the protocol and applicable regulatory requirement(s).

  -Record of temperature is maintained on a regular basis and sponsor is informed in case of any deviation.

  -Maintained records of the product's delivery, inventory and product return.

-Maintain up-to-date accountability on the trial 'Product Accountability log'.

-Ensure that the product is used only in accordance with the approved protocol.

- Document the use of the product by each subject, and if appropriate, check at regular intervals that each subject is following the instruction properly (compliance).
- Return any unused product to Sponsor at the end of the trial.
- Expired drug is returned or destructed as per hospital destruction policy with prior permission of sponsor as per hospital waste management policy.

IEC PIMS-DU

The meetings of IEC PIMS and functioning, quorum will be according to the SOPs of IEC PIMS-DU

ARCHIVAL

The Institute will retain all patient records for at least 15 years with the Institution in the Institution's Archival Department. After completion of the study, study related source documents/records should be kept in the archival room provided by Institution which is fire proof, water proof & rodent proof. The file should be properly labeled & packed.

The investigator should keep the file in a locked cabinet, in a secure area accessible only to the investigator and authorized study staff.

15 years after completion of the trial, written approval from sponsors must be obtained prior to destroying records.

Any changes in the address of the documents due to some shifting should be uniformed to the sponsor.

ADMINISTRATIVE /LOGISTIC

The study team assigned for the trial by the Directorate of Research directly receives all the trial related shipments/ couriers. All the shipments/ couriers are placed at appropriate places.

SERIOUS ADVERSE EVENT REPORTING

- The investigator & study staff is responsible for reporting the serious adverse event. The sponsor has to provide essential training for preparing initial & follow- up report of SAE before start of the study.

- Any Serious Adverse Event must be reported to sponsor, DCGI & Ethics Committee within 24 hours of knowledge of occurrence of Serious Adverse Event via Fax/e-mail. Notification to the EC should be accompanied with the serious adverse event report captured in the protocol specific SAE Form.
- Any relevant information concerning the SAE that becomes available after the SAE report from has been sent should be forwarded as soon as possible to sponsor, Ethics Committee & DCGI in follow up SAE.
- Any analysis report must be submitted to the Head of the Institute, Ethic committee and Expert committee formed by the Licensing Authority with copy to the Licensing Authority within 10 calendar incase of death of the trial subject & analysis report must be submitted to Head of the Institute, Ethics Committee and Licensing Authority within 10 calendar in case of SAEs other than death.
- In case of Hospitalization of the trial subject due to SAE, all the medical expenses incurred will be borne by the sponsor/ CRO of the study.
- The investigator must provide the best possible care available and follow the trial subject's SAE until complete resolution.
- SAE likely to be related to the investigational product and persisting at the end of the trial, or any SAE occurring after termination of the trial and likely to be related to the investigational product, should be followed up by the investigator until its complete resolution.

CRF

- Only authorized study personnel are allowed to enter data into the CRF and other required reports forms.
- The result of assessment should be first be entered into the subject file and then transcribed into the CRF. This will allow data to be verified during the process of source data verification.
- Data reported on the CRFs that are derived form source documents should be consist with the source documents or the discrepancies should be explained.
- The principal investigator or authorized person appointed by PI should review & sign the CRF appropriately.
- Study team should follow study specific guidelines for SAE/DCFs/CRF/IP etc.

CLOSE OUT

In a Close – Out visit, the Clinical Research Associate (CRA) visit the site to ensure the completeness of the investigator site field and all trial documents, including the regulatory documents.

It is responsibilities of the CRA to solve all edit queries and to ensure that all data are complete before the Close – Out visit is performed.

REVISION

The SOP would be revised every three years and the current SOP would be effective and in force till the new SOP is revised and in Place after review and approval.