



NATIONAL INSTITUTE OF AYURVEDA (Site SOP)

NATIONAL INSTITUTE OF AYURVEDA

Deemed To be University (De Novo)

Ministry of AYUSH, Govt. of India

Jaipur Rajasthan -302002

NIA SITE SOP . Version 1. Revision No. 0

Issue Date : 02-12-2020

Approved and Issued by : Prof. Sanjeev Sharma, Chairman of IRRB

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NIA : SITE SOP

Standard Operating Procedure (SOP) for Clinical Research at NIA;

Version 1. Revision 0

Prepared :Dr. Sumit Nathani, Member Secretary of IEC, NIA

Reviewed: Prof. Pawan Kumar Godatwar, Dean Research

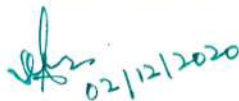
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Distribution List

Following are the Authorized Holders of Controlled Version No. 1 of NIA Site SOP for Clinical Research.

Copy No.	Name & Designation	Type of Copy
1	Prof. Sanjeev Sharma Chairman of IRRB	Printed
2	Prof. Pawan Kumar Godatwar, Dean Research	Printed
3	Dr. Bharthi Kumarmagalam, Member IRRB	Printed
4	Dr. Sumit Nathani Member Secretary, IEC	Printed
5	Office of Father Muller Research Centre	One printed + One word soft copy+ one PDF soft copy
6	Website of NIA	For reference of all investigators

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Amendment Record

Sl. No.	Date	Details of Amendment Done	Page No.	Reason for Amendment

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List of Abbreviations

AE	: Adverse Event
CDSCO	: Central Drugs Standard Control Organization
COI	: Conflict of Interest
CTRI	: Clinical Study Registry of India
CRO	Clinical Research Organization
DCGI	: Drug Controller General of India
DSMB	: Data and Safety Monitoring Board
NIA	: National Institute of Ayurveda
NIA Ethics Committee	: National Institute of Ayurveda Ethics Committee
NIA	: NIA College Hospital
NRC	: NIA Research Centre
GCP	: Good Clinical Practice
GLP	: Good Laboratory Practice
ICD	: Informed Consent Documents
ICMR	: Indian Council of Medical Research
IEC	: Institutional Ethics Committee
IP	: Investigational Product
LAR	: Legally Acceptable Representative
PI	: Principal Investigator
SAE	: Serious Adverse Event
SUSARS	: Serious Unexpected Serious Adverse Reactions
SOP	: Standard Operating Procedures
TOR	: Terms of Reference

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Introduction

National Institute of Ayurveda, Deemed To be University (De Novo) Ministry of AYUSH, Govt. of India undertakes clinical studies and other types of clinical research subjected to approval of regulatory authorities, approval of Institutional Ethics Committee (IEC), Institutional Research Review Board (IRRB) and compliance to competent authority guidelines on clinical research. The guidelines for clinical research include, Indian Council of Medical Research (ICMR), Good Clinical Practice Guidelines for Clinical Trials Ayurveda, Siddha and Unani medicine (GCP-ASU) etc..

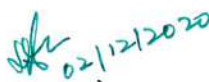
National Institute of Ayurveda will ascertain whether all cardinal principles of research ethics viz. autonomy, beneficence, non-maleficence and justice are taken care in the research involving human participants. The research center aims to protect the dignity, rights and wellbeing of the current and potential research participants; and to ensure that universal ethical values and international scientific standards are expressed in terms of local community values and customs. The site SOP of NIA ensures adherence to code of research ethics, uniformity in conducting the clinical research and compliance to all applicable guidelines on clinical research. All clinical studies should be reviewed and approved by the IEC & review by IRRB before initiation of the study, and it is mandatory to register regulatory clinical studies in the Clinical Studies Registry of India (<http://ctri.nic.in/>).

The investigator team should be trained in GCP/GL for ethics in clinical research the research team should refer to study specific SOPs for further details of carrying out the specific study protocol. The Institutional Ethics Committee of NIA, the NIA Ethics Committee reviews, approves and monitors the clinical research done at NIA. The researchers are instructed to refer the Policies and SOPs of NIA Ethics Committee for ethical guidelines on conduct of clinical research, and use the formats provided by NIA Ethics Committee for applying or submitting the reports to NIA Ethics Committee.

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1. SOP-1 : PREPARATION OF STANDARD OPERATING PROCEDURES OF

1.1.Purpose: To define the process for writing, reviewing, distributing and amending site SOPs of NIA. These SOPs ensure that the clinical research in NIA are conducted in accordance with relevant, National and International ethical guidelines. Uniformity of the processes of clinical research in NIA is ensured by SOPs.

1.2. Scope : Writing, verifying, reviewing, revising/amending and issuing the site SOPs of NIA

1.3. Responsibilities: The SOPs are reviewed and revised once a year. In the interregnum, amendments if required are done and notified. The Dean of Research, NIA appoints the teams for preparation/ revision of SOPs. The prepared SOPs are reviewed, approved and issued by Chief of Dean Research. The secretariat staff of National Institute of Ayurveda assist in clerical work and distribution

1.4. Procedure:

1.4.1. The author of this SOP shall take into account all the activities performed at NIA during the conduct of clinical research and prepare this SOP resulting in quality. The author(s) prepare a draft of SOP and distributes it to the persons who are authorized to review and approve for their review and approval. The review team may ask for any changes or corrections in the draft to the author(s). If there are any changes or corrections as required by the review team the author(s) makes the necessary corrections. After the corrections are made the final draft is sent to the review team again for final approval.

Once the approval is obtained by the author, he /she distribute the final documents for approval and signature. The final approved SOP is used and has to be followed by employees of NIA who have planned to conduct Clinical research in particular clinical studies and to train the study team members, according to their expertise. If the team feels the SOP has to be updated or revised, the same procedure has to be followed as done for preparation of SOP.

1.4.2. Each SOP will have following headings :

- 1) Purpose
- 2) Scope

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- 3) Responsibilities
- 4) Procedure in detail
- 5) Annexure (as applicable)

1.4.3. The header will have the title of the SOP document. The footer will have the version number, revision number, name and signature of reviewing, approving and issuing authority, date of revision and issue date.

1.4.4. Hard copies of the SOP are distributed to Chairman IRRB, Dean Research, Chairman Scientific committee and Member Secretary of NIA Ethics Committee Soft copy and one hard copy is available in the office of NIA. Soft copy in PDF will be issued to the PIs of the clinical research studies whenever they initiate a clinical research in NIA. Soft copy in PDF will be made available in the website of NIA for reference of all stakeholders.

1.4.5. The SOP will be reviewed once a year. The procedure for preparation will be followed for revision of SOP as well. When the revised SOP is made, it becomes the current version, and the previous version will be considered "obsolete". The Chief of Research will take back the "obsolete" version and then issue "current" version.

1.4.6. Secretariat will mark the "obsolete versions" and will keep only one copy of the "obsolete" version for reference. Other copies will be disposed off by shredding.

1.4.7. If any changes are required in the SOP in between (other than regular revision) due to any reasons, amendments will be made. The Chief of Research will assess the need for amendment and authorize the amendments and issue the soft copy in PDF within seven days of amendment approval.

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SOP-2 : Training of PI and Research Team

21. Purpose : To describe the process for initial training and thereafter continuous training and documenting the same, and to ensure all staff members involved in clinical research at NIA is properly trained according to ICH GCP, Indian GCP, ICMR and Schedule Y, NIA SOP and other applicable regulatory guidelines.

22. Scope: The training will include information the investigators and clinical research personnel need to properly conduct a clinical study, including SOPs.

23. Responsibility: The Chief of Research is responsible for monitoring training on guidelines and other applicable regulations on clinical research. The PI of the research team is responsible for ensuring training to all research team members. The NIA Ethics Committee member secretary ensures the training before IEC approval to the research protocol. The NIA Ethics Committee member secretary is responsible for updating the researchers on policies and SOPs of IEC, on annual basis.

24 Procedure:

2.4.1. The PI and the research team members should be trained on :

- 1) GCP
- 2) Guidelines from regulatory agencies
- 3) Site SOP
- 4) Study specific SOPs
- 5) Policies and SOP of NIA Ethics Committee

2.4.2. All new participating investigators and clinical research staff will be provided training to acquaint them with the principles of Good Clinical Practice and Good Laboratory practice

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2.4.3. The Principal Investigator is responsible for assuring that all research team members are trained appropriately in the site SOP and they have to be competent enough to conduct the study in accordance with all the regulatory guidelines.

2.4.4. Before conducting protocol activities, research staff shall receive protocol specific training provided by the Sponsor representative, monitor and/or the Principal Investigator. Study personnel will be trained on study specific SOPs prior to working on a clinical study.

2.4.5. Training methods may include, but are not limited to classroom, computer module or web- based.

2.4.6. Training records (copies) including certificates should be retained with study records for the duration of the study.

2.4.7. After a member is trained the trainer(s) who is qualified to provide with training will have to provide them with certificate duly signed by the trainer(s)

2.4.8. The training file should be updated following each training sessions attended. Training files are to be archived with the site upon termination of employment.

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SOP-3 : Communications to IEC

3.1. Purpose : To ensure that the PI obtains approval from IEC before initiating any research, and follows all the guidelines laid down by IEC for conduct of research

3.2. Scope : This SOP is applicable to all researchers who intend to carry out clinical research at NIA, and also to the sponsors and clinical research organizations

3.3. Responsibility : It is the responsibility of the PI to apply for review and approval of protocols by NIA Ethics Committee and to abide by all guidelines laid down by NIA Ethics Committee for conduct and reporting of clinical research at NIA.

3.4. Procedure :

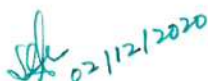
3.4.1. All the communications from PI should be addressed to Member Secretary, NIA Ethics Committee.

3.4.2. The Principal Investigator who intends to conduct a clinical research at NIA must submit a proposal and all essential documents to the IEC before the conduct of the study to obtain an approval from the IEC .

3.4.3. The PI should get updated with the policies and SOPs of NIA Ethics Committee, and apply to the IEC as per the instructions given in NIA Ethics Committee SOP. The documents mentioned by IEC should be submitted.

3.4.4. The detailed protocol (with version number and date), informed consent documents, proforma / case record forms, curriculum vitae of investigators, GCP/GLP training certificates, certificates of qualification, CTRI registration documents, IEC approval letter, are the minimum documents to be enclosed along with the application form.

3.4.5 . PI or the designated will coordinate with ethics committee for EC meeting date and accordingly PI or his/her designee is responsible for submitting all the documents to the IEC in a timely manner along with EC submission letter. The PI should present the research proposal in a meeting of NIA Ethics Committee as instructed by the IEC. He/should be give clarifications if any, and submit revisions as specified by the IEC.

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The PI should thoroughly go through the decision letter issued by IEC. The decisions of the IEC are issued in writing, and the research can't be initiated before getting the written approval from IEC.

3.4.6. The instructions and guidelines given by IEC for ethical conduct of research are mentioned in the decision letter as well as in the SOP of NIA Ethics Committee. It is the duty of PI and the research team to abide by the decision of NIA Ethics Committee.

3.4.7. While the PI may delegate responsibilities to specified study personnel for study preparation and management of communications with the IEC, the PI is the only person authorized to submit study documents to the IEC, including, a study application, renewal, amendment, adverse event report or termination/close-out. In unavoidable situations, the PI may delegate responsibility to another senior person who is part of the study. The PI is responsible for the content, accuracy and timeliness of submissions to the IEC.

3.4.8. The PI should check if the approval letter has the details of the members present and if the quorum has been met, it should also contain the date time and the venue of the meeting. The PI should also check if the approval letter has the name, version number and the language used in the documents approved is the same as submitted. If the PI finds any observation or error in IEC approval it should be communicated to the IEC and request for revised approval or clarification note.

3.4.9. Any protocol amendments, deviations/violations, adverse events, serious adverse events, progress reports, study closure reports (final reports) and other updates should be submitted to the IEC in a timely manner. Protocol amendments should be implemented only after the approval from IEC.


3.4.10. Whenever the IEC asks for submission of any study-related documents as a part of monitoring of research, it is the responsibility of the PI to submit such documents and clarifications in a timely manner. The PI should be present at the site during onsite monitoring of the study by the IEC.

3.4.11. The PI and his/her team should attend the trainings conducted by the IEC on clinical research guidelines, GCP, policies and SOPs of IEC.

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SOP-4 : Informed Consent Process

41. Purpose : The Informed consent documentation process is to be obtained from all the study participants before any study related procedure has been started. The purpose of this SOP is to ensure uniform implementation of informed consent process.

42. Scope : This procedure describes the methods and practice for the review, and documentation of the informed consent process for clinical research studies at NIA, to ensure that informed consent has been obtained and properly documented. If any Indoor Patients registered in Clinical Trial the informed consent (Annexure -1) should be part of Case Sheet.


43. Responsibility : The Principal Investigator or designated staff is responsible for the implementation of this SOP and ensuring that all staffs are appropriately educated. The PI is responsible for providing a complete and valid informed consent documents, and ensuring that it meets all state, institutional and regulatory requirements. The PI is responsible for ensuring approval of ICD by the IEC before it is used and to ensure that the approved version only, is being used; ensuring that potential study participants are informed properly and adequately regarding study procedures, Risk / Benefits, and other deemed necessary information detailed in the informed consent; to ensure that the Informed consent used is in the language the participant understands and is comfortable ; to ensure consent from legally acceptable representative if the potential participant is not comfortable and does not understand the vernacular language; to include an impartial witness as mandated by the guidelines; documenting that study procedures were discussed with the participant and that informed ; and questions the potential participant asked and the answers given should also be documented as informed consent process.

The PI or the authorized personnel is responsible for ensuring only the current valid consent form is used; to provide a copy of the signed and dated informed consent to the participant; filing a copy in the participant file; ensuring a copy of each version of the blank consent form is filed in the study regulatory binder.

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4.4 Procedure:

4.4.1. Prior to any study procedures, the Principal Investigator and authorized will review and discuss details of the research study using the consent form.

4.4.2. The potential participant will read and review the informed consent. He / She is given an opportunity to ask any questions regarding the study. He / She is given adequate time to decide on participation. He/ She will be given the freedom to decide on participating in the study.

4.4.3. The participant subjects should be informed the following

- (a) The type study and mode of interventions.
- (b) The purpose of the study and the participant's responsibilities.
- (c) The treatment(s) and the probability for random assignment to each treatment.
- (d) The procedures to be followed, including all invasive procedures.
- (e) The reasonably foreseeable risks or inconveniences to the participant and, when applicable, to an embryo, fetus, or nursing infant.
- (f) The reasonably expected benefits. When there is no intended clinical benefit to the participant, the participant should be made aware of this.
- (g) The alternative procedure(s) or course(s) of treatment that may be available to the participant, and their important potential benefits and risks.
- (h) The compensation and/or treatment available to the participant in the event of study-related injury.
- (i) Compensation for the anticipated expenses, if any, to the participant for participating in the study.
- (j) The approximate number of participants involved in the study .
- (k) That the participant's participation in the study is voluntary and that the participant may refuse to participate or withdraw from the study, at any time, without penalty or loss of benefits to which the participant is otherwise entitled.
- (l) That the monitor(s), the auditor(s), the IEC, and the regulatory authority(ies) will be granted direct access to the participant's original medical records for verification of clinical study procedures and/or data, without violating the confidentiality of the participant, to the extent NIA

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permitted by the applicable laws and regulations and that, by signing a written informed consent form, the participant or the subject's legally acceptable representative is authorizing such access.

(m) That records identifying the participant will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the study are published, the participant's identity will remain confidential.

(n) That the participant or the participant's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the participant's willingness to continue participation in the study.

(o) The person(s) to contact for further information regarding the study and the rights of study participants, and whom to contact in the event of study-related injury.

(p) The foreseeable circumstances and/or reasons under which the participant's participation in the study may be terminated.

(q) The expected duration of the participant's participation in the study.

4.4.4. If the participant agrees to participate, the participant will sign and date the consent form on the appropriate place.

4.4.5. In emergency situations, when prior consent of the participant is not possible, the consent of the participant's legally acceptable representative, if present, should be requested. When prior consent of the participant is not possible, and the participant's Legally Acceptable Representative (LAR) is not available, enrolment of the participant should require measures described in the protocol and/or elsewhere, with documented approval/ favorable opinion by the IEC, to protect the rights, safety and well-being of the participant and to ensure compliance with applicable regulatory requirements.

4.4.6. The participant or the participant's LAR should be informed about the study as soon as possible and consent to continue and other consent as appropriate should be requested.

Any queries regarding the study or related asked by the participant should be answered by the Principal Investigator or the designate to the complete satisfaction of the participant

4.4.7. If required a Legally Acceptable Representative (LAR) and an impartial witness should be present throughout the consenting process and sign and date at the appropriate place. The LAR

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is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to the participant's participation in the procedure(s) involved in the research. The impartial witness is a person, who is independent of the study, who cannot be unfairly influenced by people involved with the study, who attends the informed consent process if the participant or the participant's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the participant

4.4.8. The consenting person will sign and date the consent form on the appropriate place.

4.4.9. Before and after informed consent has been obtained, the coordinator will review the consent form document and ensure that the correct version of the Informed consent form was used; the participant and investigator have properly dated the consent form; all options and sections have been completed by the participant; initials or other participant identification is on each page of the consent form ; the delegated study team member files the original consent form in the participant file, provide a copy of the signed and dated consent form to the participant; and the entire consenting process has to be documented in the source as the informed consent process.

4.4.10. Audio Video recording of the entire consenting process has to be done provided the participant has accepted. Whenever there is any re consenting, audio video recording is mandatory.

4.4.11. Care should be taken to include all the concerned like the consenting doctor, participant, LAR, impartial witness, and others involved in consenting where ever applicable should be included in the frame of recording.

4.4.12. The recorded material should be kept confidential and can be accessed only by the authorized study team members.

4.4.13. If there are any changes in the national or international guidelines for Audio Video consenting, then they will be adhered to.

4.4.14. If there is any amended Informed consent form, the IEC approval is mandatory and without the approval the amended Informed consent form should not be used. While using the amended.

Informed consent all the procedures used while obtaining the initial approval and consenting procedure has to be followed.

4.4.15. The Principal Investigator or the authorized representative will document the Informed

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consent process using the signed and dated Consent form by the participant or his/her legally authorized representative, and if required an Impartial Witness and the investigator (or delegated staff) who obtained the participant's consent.

4.4.16. If a child in the age group of 7 years to 18 years should participate in a study an assent should be obtained along with a parental consent. For 7 to 12 years child, verbal assent is to be taken, and for above 12 years to 18 years age, written assent has to be taken.

4.4.17. The PI and the research team members should follow the guideline of NIA Ethics Committee, and refer to SOP of NIA Ethics Committee for the informed consent process.

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SOP-5 : Procedure for Screening and Enrollment of Research Participants

5.1. Purpose: The purpose of this Standard Operating Procedure (SOP) is to describe the procedures used by the Principal Investigator and his / her team to identify eligible subjects for a study.

5.2. Scope: All clinical research using human subjects conducted at NIA should maintain a subject screening and enrollment log and thus are responsible for screening and enrolling appropriate patients.

5.3. Responsibility: The Principal Investigator is the ultimate responsible person for identifying the eligible subject and enrolling them in the study. PI can even delegate the responsibility medical staff of the study team provides PI supervises.

5.4. Procedure:

541. The potential subjects for participation in the research will be based on the research protocol. The potential participants for the proposed research can be identified from patients coming to the hospital for treatment , patients list from the database, participants identified from the health camps organized and through advertisements

542. **Pre Screening :** Once intimation is received from the Sponsor / CRO about the selection of the site for a clinical study, the PI shall discuss the kind of patients required according to the study protocol with other sub investigators and other study team members, and identify the potential patients. An overview of the study could also be discussed with other doctors.

They can be identified either from the patients visiting the hospital / clinic for treatment or from the available medical records. If the Investigators do not have enough patients or do not have patients as per the protocol, then the Investigators shall write letters to their colleagues or other doctors, informing them the overview of the study and requesting them to send such patients to their hospital / clinic. This should be done only in the best interest of the patients. The overview of the study can also be discussed with doctors who are not part of the hospital. Doctors shall be requested to refer potential patients to the site if the patients show interest for participation in the study. If all this prescreening process is a part of the protocol, then all the prescreening procedures shall be done only after the protocol and all other documents have been approved by the IEC,

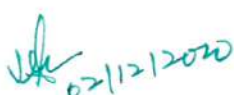
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other necessary approvals and only after the potential participant have given their voluntary consent.

All the details of such patients are maintained. As and when the study gets approved by all the required regulatory bodies are available with the Investigator, all study related procedure can be done only after a written signed dated informed consent obtained.

5.4.3 Screening :

- a) After obtaining all the approvals and once the site is initiated for the study, the pre- identified patients shall be contacted and requested to visit the site to discuss about the study. Other patients who may fit into the inclusion and exclusion criteria visiting the site can also be informed about the study.
- b) Before screening procedure is started all the medical records available with the patient should be collected and a detailed medical history taken. If from any of the inclusion and exclusion criteria the patient does not fit in the study then they need not be screened but if the Principal Investigator feels we can try with the screening process, then the patient can be screened according to the screening process after obtaining a voluntary informed consent, a photocopy of the same can be collected.
- c) All patients who voluntarily consent to participate should sign and date on consent form. A photocopy of the signed dated informed consent should be given to the subject. All study related procedures shall be performed only after the patient provides written informed consent.
- d) If the patients have not registered themselves in NIA hospital they have to be registered at hospital and it shall be ensured that all patients participating in a clinical study are registered.
- e) For studies that require history of the patient adequate steps have to be taken to collect the same from those patients to determine their eligibility. If such a patient is found eligible as per the inclusion and exclusion, then the patient can be randomized according to the protocol.
- f) The Principal Investigator should make sure that eligible patient is not participant of any other study or should not have been participant of a study if protocol necessitates.
- g) On randomization the Principal Investigator and the team should properly and clearly instruct the subject, the importance of drug compliance, the visit(s) and the investigation.
- h) If there are any specific instructions that has to be given to the subject, then all the instructions have to be provided to the subject.
- i) More than one contact details of the subject have to be obtained from the subject.

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j) If the protocol permits rescreening of the patient, it can be done according to the protocol.

544 Randomization:

a) Once the patient is found to be fit according to the inclusion and exclusion criteria, the subject can be randomized according to the protocol. The randomized subject will be provided with subject identification card.

b) It will be the responsibility of the Principal Investigator to fix an appointment and follow if the subject has to visit any other departments or hospitals for opinion or further management if required by the protocol.

c) The Principal Investigator decides on the next course of action if any Investigations show abnormal laboratory values. If a subject requires un-schedule visits then the study team should ensure the PI is present.

The Principal Investigator should inform the subject that in case he / she experience any untoward event (AE/SAE) he / she should contact the PI or the site team immediately.

d) If a subject wish to withdraw consent at any point of the study, the PI should make reasonable efforts to keep the patient informed the importance of continuing in the study but there should not be any coercion for the subject to continue in the study. If a subject withdraws from a study prematurely, it shall be ensured that all study specific procedures are performed as mentioned in the protocol. If there are any follow up visits as required by the protocol, the subjects should be informed and the dates are scheduled accordingly. The reasons for withdrawal of consent have to be obtained by the study team. e) However, the decision to participate or continue in the study shall solely lie with the subject.

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SOP-6 : Responsibilities of PI and the Research Team

6.1. Purpose : To delineate responsibilities required of qualified researchers in the role of Principal Investigator (PI) and Research team in clinical research so that the research is conducted in a ethical manner and as per all applicable guidelines.

6.2. Scope : This SOP applies to all the Investigators who are conducting clinical research at NIA

6.3. Responsibility : The Principal Investigator is the ultimate responsible person at the site for the studies that he/she is participating even though he/she has given some of the responsibilities to other members. But this doesn't mean that the assigned person is not responsible. They are responsible for the assigned job.

6.4. Procedure :

The PI and the research team should be well-versed with CGP / GLP and all applicable regulatory requirements.

6.4.1. Qualifications and Expertise of PI :

The PI must: Be qualified by education, training, and experience to assume responsibility for the proper conduct of the study. If the study involves the use of an investigational product, be thoroughly familiar with the appropriate use of that product as described in the study protocol. Be aware of and remain in compliance with GCP/GLP and applicable regulatory requirements. Maintain a list of qualified persons to whom he or she delegates significant study-related duties.

6.4.2. Responsibilities of PI : The PI retains ultimate oversight responsibility even when specific tasks are delegated to other site research staff.

PI responsibilities include:

- 1) Documenting the delegation of study responsibilities to qualified and adequately trained research staff.
- 2) Supervising study performance and overseeing the performance of study staff at the research sites.
- 3) Ensuring that: Participants' well-being and safety are protected.

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- 4) All study procedures are conducted at the research sites in accordance with the protocol and GCP.
- 5) Preparing a communication plan for all staff involved in the study.
- 6) Overseeing Investigational product accountability; If required it may be assigned to another study team member, but under supervision of the PI.
- 7) The PI should have sufficient time and be able to recruit the required number of suitable participants within the agreed period
- 8) The Investigator should be thoroughly familiar with the investigational product and its use and storage as mentioned in the protocol, Investigator's Brochure, product information and in other information sources provided by the sponsor.
- 9) The PI should be present and facilitate during the monitoring, auditing or inspection by the regulatory authorities, IEC, sponsors or monitors appointed by sponsors
- 10) He /She should have adequate number of qualified staff and adequate facilities and has to maintain a delegation log which should contain the names of persons, their roles and responsibilities in the study, and they should also be trained of their roles and responsibilities in the study by the PI.
- 11) Provision of adequate medical care in case of any adverse event to the participant is required during the study period.
- 12) The Principal Investigator or the designate is responsible for obtaining Informed Consent Form from a previously IEC approved version, according to the regulatory guidelines.

As and when there is a revision or update in the Informed Consent the Principal Investigator obtains an IEC approval and then has to use the same. The participant can refuse to continue in the study based on the revision of ICD. If the patient is not willing to participate in the study or if the study participant withdraws from the study, routine medical care should be provided. None of the study team including the PI should coerce or unduly influence the participant to continue or discontinue the study. None of the oral and written information concerning the study, should contain any language that causes the participant to waive or to appear to waive any legal rights, or that releases or appears to release the Investigator, the Institution, the Sponsor, or their agents from liability for negligence.

The Investigator, or a person designated by the Investigator, should fully inform the participant of

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all pertinent aspects of the study. Ample time has to be provided to the participant before he / she accepts to participate and all the questions asked by the participant should be answered to their complete satisfaction.

- 13) If a participant wishes to discontinue from the study pre maturely, the PI should make a reasonable effort to ascertain the reason(s), while fully respecting the participant's rights.
- 14) The PI should only follow the regulatory and IEC approved protocol, and if there are any amendments, the PI should obtain approvals and only after approvals should follow them.
- 15) All deviations and violations of the protocol are documented and the Investigator may implement a deviation from, or a change of, protocol to eliminate immediate hazard(s) to study participants without prior IEC approval/favorable opinion. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendment(s) should be submitted (a) to the IEC for review and approval/favorable opinion, (b) to the sponsor for agreement and, if required, and (c) to the regulatory authority(ies).
- 16) The Investigator should follow the study's randomization process, if any, and should ensure that the code is broken only in accordance with the protocol.
- 17) In a blinded study the PI should promptly document and explain why premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the Investigational Product(s).
- 18) PI should sign the clinical study agreement on behalf of the research team, along with the sponsor and head of the institution.
- 19) The PI and his/her team should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- 20) The Investigator/institution should maintain the study documents as specified in Essential Documents for the Conduct of a Clinical Study and as required by the applicable regulatory requirement(s).
- 21) The data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.
- 22) The financial aspects of the study should be documented in an agreement between the sponsor and the Investigator/institution.

Upon request of the monitor, auditor, IEC, or regulatory authority, the Investigator / institution should make available for direct access all requested study-related records.

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The PI should the study status to the IEC annually, or more frequently, if requested by the IEC.

23) All Serious Adverse Events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting.

24) For reported deaths, the Investigator should supply the sponsor and the IEC with any additional requested information (e.g., autopsy reports and terminal medical reports).

25) If the study is prematurely terminated or suspended for any reason, whether the Investigator or the sponsor terminates, all the study participants and the respective IEC should be informed and the reasons for early termination or suspension of the study should be clearly defined. In such situation all the regulatory guidelines should be maintained. Where ever required the regulatory authorities should be informed.

26) If the IEC terminates or suspends its approval/favorable opinion of a study, the Investigator should inform the Institution where applicable and the Investigator / institution should promptly notify the sponsor and provide a detailed written explanation.

27) The PI is responsible for all communications to IEC, regulatory authorities, head of the institution and the sponsors, on behalf of the entire research team.

6.4.3. Co Investigators: Are responsible for the medical care of the study participants, source documentation, informed consent process and other responsibilities as assigned by the PI

7.4.4. Responsibilities of the Research Site Staff :

Under the supervision of the PI at the site, examples of responsibilities for the Research Coordinator/Assistant may include: Ensuring that study data is accurately collected and reported. Reporting any study or participant problems. Maintaining regulatory files at the study site. Working with the Node Quality Assurance Monitor and data management staff to identify and resolve data and reporting issues. The Research Assistant's role frequently also includes interacting with study participants by performing assessments (e.g., the Addiction Severity Index) and protocol procedures. Nurses, pharmacists, and other staff are responsible for carrying out study procedures as described in the protocol (e.g., receiving and dispensing medications, conducting physical examinations, delivering behavioral interventions) and for assessing and reporting adverse events to appropriate staff.

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SOP-7 : Handling Investigational Product (IP)

7.1. Purpose : To describe requirements for control and record keeping of the inventory for Investigational Product.

7.2. Scope : SOP covers control and record keeping of all the IP obtained for use in human subjects' research. "Test article" includes the Investigational Product(s) which may be a drug or device, placebo(s) and/or comparator(s) used in the clinical study.

7.3. Responsibility:

This applies to the Principal Investigator and to delegated staff who is assigned for dispensing, control or inventory management of any IP.

7.4. Procedure :

7.4.1. An Investigator shall permit an IP to be administered or used only by subjects after obtaining consent for participation in the study and should be done only under the investigator's personal supervision. The PI may delegate Co investigator or a Sub- Investigator, who is responsible to the Investigator, to administer or dispense the test article. Though the designated person dispenses the IP, the accountability is with the PI

7.4.2. The received IP should be checked for any damage, quantity and maintenance of temperature. On receipt of the IP the concerned should be informed accordingly.

7.4.3. The Investigator or the designate should identify (if any codes) the IP and it should be given to the correct participant in the correct dosage as specified. The participant should be explained in detail the appropriate use of the IP.

7.4.4. If the participant develops any reaction, he/ she should be instructed to inform the PI or the authorized person immediately.

7.4.5. The IP should be stored in appropriate temperature, and should be recorded and documented. The IP storage area should be with limited access and should be recorded.

7.4.6. Accountability log should be maintained, the details should include the dates, batch number and if any code numbers, the total quantity received, quantity dispensed and returned by the participant and if there were any over dosage or any missed IP and the quantity returned to the

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sponsor or their representative or destroyed at the site

7.4.7. When the study is completed or discontinued the PI may return the remaining supply of IP to the sponsor or destroy the same as per regulations and with necessary precaution. This can be done only after the sponsor informs the PI. A destruction certificate will be provided by the PI to the Sponsor.

7.4.8. IP should not be used by the PI for any commercial use or in any other study.

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SOP-8 : Procedure for Source Documentation

81. Purpose : To describe the importance of source data and maintenance of Source documents during the conduct of a Clinical study

82. Scope: This SOP will cover all the documents which will form the Source Documents that will be used in clinical study and how the Principal Investigator and the team are responsible for maintaining the source documents.

83. Responsibility: The study team members like Principal Investigator, Co Investigator, Sub Investigator, Clinical Research Coordinator and other staff involved and who are authorized for accurate data collection, accurate reporting, interpretation and verification of the data collected and to maintain all the documents as specified in ICH GCP/GLP and other regulatory guidelines.

84 Procedure:

84.1. The Principal Investigator or the designee's responsibility is to take complete detail medical history (As required in the protocol) orally and by the reports that the patient has.


Thus collected data has to be entered in the hospital notes.

84.2. The original or the certified documents of the study participants pertaining to their illness, medical history or laboratory reports are considered as source document. On collecting the same they are photocopied and returned back to the participant and the date of collection are mentioned in the source. The photocopies (hiding the patient name) thus collected are verified with the original and certified by the Principal Investigator or the designate. Thus, collected documents are placed appropriately in the participants' file.

84.3. After the entries are made in the source documents if there are any corrections, appropriate corrective techniques have to be used. Original entry must be legible; the original entries should not be erased; whitener or any corrective fluids) should not be used; there should not be any overwriting

84.4. The corrections in the entries made should be: Only a line across the entries made and sign and date for the corrections made. If there are new entries to be made then the reasons for changes made have to be documented and initialed and date the corrections.

84.5. The laboratory reports have to be reviewed by the Principal Investigator and initialed and the date has to be entered. If there are any abnormality in the lab reports the Principal Investigator has to decide if they are clinically or not clinically significant and necessary medical action has to

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be taken.

8.4.6. The photocopies will include but not limited to old hospital / clinic reports (both OPD and in-patient hospitalization), ECG, X-ray and any other imaging report Lab reports, medical charts, old prescriptions, any other medical referrals and consultations.

8.4.7. All source documents have to be archived according to the sponsor or as per the regulatory guidelines.

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SOP-9 : Procedure for Reporting Adverse events (AE) and Serious Adverse Events (SAE)

9.1. Purpose : To define the way in which the safety reporting like Adverse Events and Serious Adverse Events are reported. The purpose of this Standard Operating Procedure (SOP) is to implement the definitions, reporting timelines, formats and standards as required by all required guidelines for reporting

9.2. Scope : For all the clinical research work done under NIA

9.3. Responsibility : Once the study is started and the participant has been enrolled into the study all the study team members including the Principal Investigator, Co – Investigator, Sub – Investigator, Clinical Research Coordinator and Research Nurse and other study related staffs are responsible for continued surveillance of AE, and SAE. In case if a situation arises the PI or the study team will report any such events promptly to the according to the prevailing guidelines.

9.4. Procedure:

9.4.1. Definitions:

- 1) **Adverse Event (AE):** An unexpected medical problem that happens during treatment with a drug or other therapy. **Adverse events** may be mild, moderate, or severe, and may be caused by something other than the drug or therapy being given.
- 2) **Adverse Drug Reaction (ADR):** An injury caused by taking medication, may occur following a single dose or prolonged administration of a drug or result from the combination of two or more drugs.
- 3) **Unexpected Adverse Drug Reaction:** An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g. Investigator's Brochure for an unapproved investigational medicinal product).
- 4) **Serious Adverse Event:** An adverse event is serious when the research outcome for the participant is death, life-threatening injury requiring hospitalization, prolongation of hospitalization, significant disability/incapacity, congenital anomaly, or requirement of intervention to prevent permanent impairment or damage.

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9.4.2. The Principal Investigator or the designee will instruct the participant to inform the site immediately if they are taking any tablets or meeting a doctor for any kind of illness. They would also be advised that they should have the prescription and laboratory reports (if any) to keep it safe and show to the study team member during their next visit to the site. The study team member photocopies the same. The study team member should follow with the participant until the resolution of the AE.

9.4.3. If the participant has not been to a doctor for consultation and taken the medicines from the pharmacy, the participant should be asked what all complaints they had and the drugs that they consumed. They should also be asked for the start and end of the AE as well as the medicines that they took for the AE. If they do not remember the exact dates then the closest possible dates can be obtained from the participant and be entered in the source.

9.4.4. It will be the responsibility of the Principal Investigator to provide with adequate medical facility for the participant. The medical care thus provided by the sponsor should be entered in the source.

9.4.5. If there are any abnormal lab values the PI should review whether they are clinically significant or very high or very low, enabling the participant to get admitted, then they are termed as SAE and the routine procedure is followed.

9.4.6. The AE should be assessed for causal relationship with the study medication and the seriousness of the AE should be assessed.

9.4.7. Serious Adverse Event Reporting: Any Serious Adverse Event (SAE) has to be reported according to the prevailing guidelines to the Sponsor, IEC and regulatory authorities.

Initial SAE report to be submitted by the Principal Investigator (PI) within 24 hours of occurrence. Due analysis should be submitted by the PI within 14 days from the occurrence of the SAE; Due analysis will also be submitted by the sponsor within 14 days.

9.4.8. Until the event is resolved the SAE should be followed up until resolution and the follow up report should be sent to the concerned.

9.4.9. All the information regarding the SAE should be documented in the source documents. The details in the SAE form should be captured only from the source. The fully completed SAE form should be signed and dated by the concerned as mentioned in the study specific site delegation log, and the SAE form should be shared with the person designate of the sponsor. All the source notes and the proof of the event should be filed in the source documents and wherever required

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photocopies of the same have to be taken and certified and filed in the source.

9.4.10. Review of Events: All AE, ADR, SAE will be reviewed by the Principal Investigator for the causality and further course of action, in accordance with the SOP and regulatory guidelines.

9.4.11. Safety reports: In multinational multi centric studies there will be various types of safety reports like (SUSAR, CIOMS Etc) that have to be reviewed by the PI and the appropriate site staff should also have an access to such reports and they have to be reported to the Institutional Ethics Committee. A copy of all the safety reports should be filed in the study specific site file

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SOP-10 : Procedure for Archival of Study Documents

10.1. Purpose : The purpose of this Standard Operating Procedure (SOP) is to describe the procedures used by the Principal Investigator and his / her team to archive the study documents at the end of the study.

10.2. Scope : Applicable and to be used by the PI and clinical research staff who are responsible for archiving the study documents.

10.3. Responsibility : The Principal Investigator shall arrange space and necessary material to archive the study documents.

10.4. Procedure:

10.4.1. On study completion it is the responsibility of the Principal Investigator to store all the study related data and documents in a safe and secured location according to all regulatory guidelines.

10.4.2. These shall be stored in a sealed cupboard or boxes, in a safe and secure location, with limited access. The documents should be archived in such a manner that they remain completely legible.

10.4.3. The area where these documents are stored should be pest controlled no water leakages with a fire extinguisher.

10.4.4 All the documents should be archived from the date of site closure as defined by the sponsor but not less than the regulatory requirement from time to time.

10.4.5. All the subject files shall be labeled with ----

1. DO NOT DESTROY
2. PRINCIPAL INVESTIGATOR CONTACT DETAILS
3. SPONSOR CONTACT DETAILS
4. PROTOCOL NUMBER
5. SUBJECT NUMBER / INITIALS
6. HOSPITAL REGISTRATION NUMBER

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- 10.4.6. The study documents should always be accessible for regulatory inspections and audits.
- 10.4.7. If a third-party vendor is assigned for storage of documents, then the location and the contact details of the vendor should be known to the Sponsor and the Principal Investigator.
- 10.4.8. The Principal Investigator should not destroy the documents without informing and obtaining approval from the Sponsor.
- 10.4.9. If the PI has to destroy the documents after the specified time period, he / she should make reasonable efforts to contact the sponsor before destroying the documents.
- 10.4.10. While destruction reasonable efforts must be taken to obtain the environmental clearance.
- 10.4.11. If the source documents are stored along with the hospital records in the MRD, the MRD in charge person should be kept informed about the importance of archiving and the safe and confidential keep of the subject file.
- 10.4.12. The PI informs the hospital authorities about the archival and it should be mentioned in the CTA.
- 10.4.13. If the documents are stored elsewhere or if the documents are archived with the help of a third party, the information about the vendor and location of the storage area shall be informed to the sponsors.
- 10.4.14. The fee for archival will be decided by the management at the appropriate time.
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3. NIA Ethics Committee Policies, 2019.
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