STANDARD OPERATING PROCEDURES (SOP)

Version : IECDYPMC:1.0

Date : 22.09.2016

INSTITUTIONAL ETHICS COMMITTEE

D. Y. PATIL EDUCATION SOCIETY

(Institution Deemed to be University) KOLHAPUR

(Deemed to be University Declared u/s 3 of the UGC Act 1956 vide Notification No. F.9-26/2004-U.3 dt. 01-09-2005 of the GOI)

Accredited by NAAC with 'A' Grade

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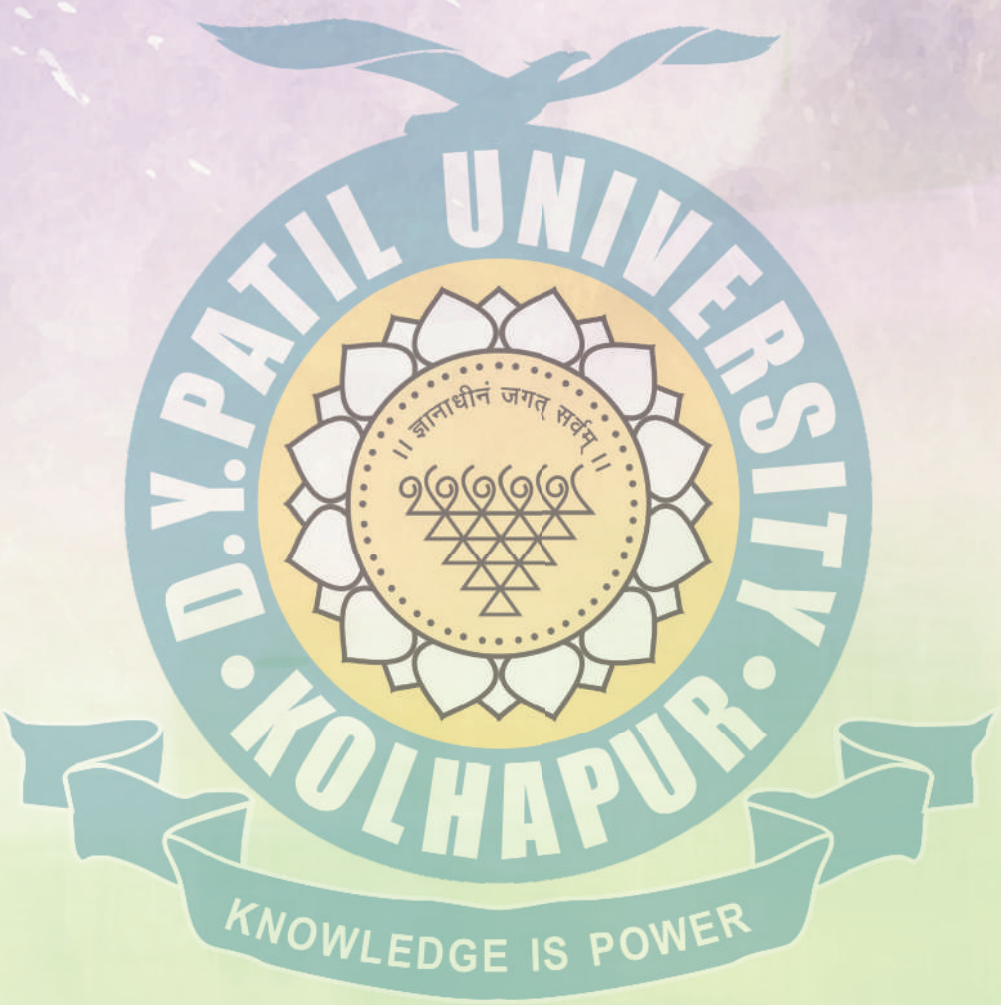
Institutional Ethics Committee


D.Y.PATIL UNIVERSITY
KOLHAPUR
॥ ज्ञानाधीनं जगत् सर्वम् ॥
KNOWLEDGE IS POWER

STANDARD OPERATING PROCEDURES

INSTITUTIONAL ETHICS COMMITTEE

For

D. Y. PATIL MEDICAL COLLEGE AND Dr. D. Y. PATIL HOSPITAL AND RESEARCH INSTITUTE

■ **Version**	:	IECDYPMC 1.0
■ **Date**	:	09-09-2016
■ **Authors**	:	Institutional Ethics Committee, D. Y. Patil Medical College, Kolhapur Member-Secretary : Dr. Shimpa Sharma
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■ **Confirmed by**	:	Academic Council, DYPU, Kolhapur
■ **Distribution**	:	Members of IEC (& Investigators of projects submitted to IEC)

CONTENTS

INTRODUCTION

The first International statement on the ethics of using human subjects in medical research, the Nuremberg Code, was formulated in 1947 and it laid emphasis on consent and voluntariness. In 1964, the eighteenth World Medical Assembly at Helsinki, Finland adopted a code of ethics for the guidance of doctors involved in clinical research. This is popularly known as the "Declaration of Helsinki".

Furthermore, in 1996, the International Conference on Harmonization (ICH) published a tripartite guideline for Good Clinical Practice (GCP) to harmonise technical requirements for registration of pharmaceutical products in three regions namely the United States, the European Union and Japan). Today, the ICH GCP guideline is followed globally for clinical research. This guideline elaborates the composition and functioning of an Institutional Ethics Committee to review clinical research proposals.

It is necessary to establish an Ethics Committee consistent with the ICH GCP Guideline and the Legislation applicable to all researchers so as to facilitate the ethical review of any human research project conducted within the Institution of origin and without.

The Ethics Committee ("EC") has been established to fulfil the following roles in the field of Medical Research.

Role of EC :

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

2. The EC will ensure that all the cardinal principles of research ethics viz. Autonomy, Beneficence, Non - Maleficence and Justice are respected in planning, conduct and reporting of the proposed research. For this purpose, it will look into the aspects of informed consent process, risk benefit ratio, distribution of burden and benefit and provisions for appropriate compensations wherever required.

3. It will review the proposals before start of the study as well as monitor the research throughout the study until and after completion of the study.

4. The committee will also examine compliance with all regulatory requirements, applicable guidelines and laws.

5. The mandate of the ECs will be to review all research projects involving human subjects to be conducted at the Institute, irrespective of the funding agency.

The Institutional Ethics Committee for D. Y. Patil Medical College and Dr. D. Y. Patil Hospital and Research Institute (henceforth called the "DYPMC & DDYPH") is guided by the ICH GCP guidelines for Good Clinical Practice and the ethical principles set forth in the Declaration of Helsinki.

STANDARD OPERATING PROCEDURES

1. Name

This committee will be known as the " INSTITUTIONAL ETHICS COMMITTEE, D. Y. PATIL MEDICAL COLLEGE, KOLHAPUR"

This name will remain unchanged until the members choose to change it by a vote of three-fourths of the current strength.

2. Purpose

The primary purpose of this committee will be:

1. To ensure the protection of the rights, safety and well-being of human subjects involved in a research project.
2. To provide public assurance of that protection.

3. Membership

The committee will consist of members who collectively have the experience and expertise to review and evaluate the scientific, medical and ethical aspects of a proposed research project. A list of committee members, their qualifications and their affiliations (hospitals, colleges etc.) described in §13 of this document will be maintained in the committee's records.

3.1 Composition of the Committee

a. The regular members of the committee will ideally include at least 7 and a maximum of 11 individuals including:

   i. Medical scientists and clinicians with expertise in diverse health care specialities.

   ii. A legal expert.

iii. A social worker/representative of a non-governmental organisation / theologian.

iv. A lay person from the community.

v. A Basic Scientist

vi. A person from the field of Media/Journalism

b. The committee will have representation from both men and women.

c. Members from other areas, such as a journalist or a member from a consumer protection activity, may be included in the committee.

3.2 Chairperson

a. The Chairperson will be selected and appointed by the Dean of the D. Y. Patil Medical College and the Padmashri Dr. D. Y. Patil Hospital & Research Institute (henceforth to be referred to in brief as DYPMC & DDYPH)

b. The appointed Chairperson will select and appoint members of the committee.

c. The Chairperson will be responsible for conducting all committee meetings, and will lead all discussions and deliberations pertinent to the review of research proposals.

d. The Chairperson will preside over all meetings and administrative matters pertinent to the committee's functions.

e. In case of anticipated absence, the Chairperson will nominate a committee member, as Acting Chairperson. The Acting Chairperson will have all the powers of the Chairperson for that meeting.

3.3 Members

a. The members will be selected and appointed by the chairperson, provided they are willing to work as an Ethics Committee member.

b. A member shall be willing to publicise his/her full name, profession and affiliation.

c. A member will sign a confidentiality agreement described in § 14.6 of this document

d. A member will have been trained in ethical issues or shall be willing to undergo training in ethical issues.

3.4 Member Secretary

a. The committee members will designate a Member Secretary from among themselves

b. In consultation with the Chairperson, the Member Secretary will be responsible for the following functions:

i. Receiving all research proposals.
ii. Numbering the proposals.
iii. Forwarding all proposals to committee members for review.
iv. Establishing time limits for receipt of reviewers' comments.
v. Preparation of agenda for all committee meetings.
vi. Inviting experts from relevant therapeutic areas to the scheduled meetings.
vii. Notification of review outcome to investigators of research proposals.
viii. Preparation and circulation of minutes (for approval of Chairperson within 7 days of the meeting and circulation to all members within 10 days of the meeting).
ix. Retention and safekeeping of all records and documentation.
x. Performance of other duties assigned by the Chairperson.

3.5 Tenure of Membership

a. A member will be a regular member for a period of up to 2 years.

b. Extension of membership will be determined by a vote of two-thirds of the members present in a quorum at a regular committee meeting.

c. There is no limit to the number of times that the membership can be extended.

d. New members will be appointed to replace members according to the process described in § 3.8 of this document.

3.6 Resignation of Members

Members may resign before completing their terms by writing their intention to the chairperson.

3.7 Termination of Membership

The membership will stand to be terminated under the following circumstances:

a. If a member resigns from the committee

b. If a member remains absent for 3 consecutive meetings without giving prior notice or giving a valid reason.

c. If a member is incapable of performing his/her duty as an ethics committee member

d. In case of demise of a member.

3.8 Appointment of New Members

a. New members will be selected and appointed under the following circumstances:

i. When a regular member completes his tenure and does not wish to continue his/her membership.

ii. If a regular member resigns.

iii. In case of the termination of membership of a regular member.

b. A new member will be preferably but not necessarily nominated from the same category as that of the member being replaced keeping in mind the necessity to include members from different backgrounds.

4. Responsibilities of the Committee

1. The committee's primary responsibility will be the protection of safety, rights, well-being and confidentiality of the research subjects.
2. The committee will review all research proposals submitted to it within specified time limits.
3. The committee will keep all information submitted to them confidential especially the proprietary information.
4. The committee will maintain concise but clear documentations of its views on the research proposal.
5. The committee will review the progress of each research project at appropriate and specified intervals.
6. The committee will review the qualifications of all investigators participating in the proposed research study.

5. Functions and Operations

5.1 Categories for submission of Research Proposal

a. Research Proposals submitted by Post Graduate students of the D. Y. Patil University, Kolhapur as part of their doctoral Dissertation or Thesis.

b. Research Proposals submitted by staff and students of the D. Y. Patil University which are non-sponsored research not involving use of unregistered drugs, investigational techniques as well as devices or any other surgical or non-surgical procedures.

c. Research Proposals submitted by staff and students of the D. Y. Patil University related to Health Sciences directly sponsored by Industry, Institutions and Funding agencies.

d. Proposals individually submitted by Medical Fraternity who are legally registered Medical practitioners but are not part of faculty of DYPMC & DDYPH.

5.2 Submission of the Research Proposal

a. **For research Proposals mentioned in section 5.1 a , 5.1 b. and 5.1 c** above, the procedure is as follows:

All prospective and retrospective studies involving human volunteers or patients to be conducted in DYPMC and DDYPH and/or directly or indirectly involving staff, students or facilities of DYPU, DYPMC and DDYPH shall have IEC permission before commencing such a study.

Each project along with a duly completed research protocol approved by the Institutional Research Committee (IRC) shall be submitted in soft copy to the Member Secretary of the IEC. The format approved by the IRC shall be used. It shall have the designation and signatures of Principal Investigator or Guide in case of Doctoral Dissertations. It must clearly mention any ethical concerns that may exist.

The project proposal shall be submitted in soft copy format and one hard copy. Each proposal shall contain the documents on A 4 size paper arranged in a file in the order mentioned below:

1) Summary of protocol (in not more than 500 words)

2) Protocol and any amendments to it with version and date (for review protocols)

3) The informed consent document (ICD), including any amendments / addenda and its translation(s) into regional language(s).

4) Case Record Form / Questionnaire.

5) Principal investigators current Curriculum vitae (for non-institutional researchers)

6) Subject recruitment procedures (e.g. advertisements/letters to doctors/posters)

b. For research ***Proposals mentioned in Section 5.1 (d) above,*** the submission process is as follows:

1) All prospective and retrospective studies (on drugs, investigational techniques as well as devices or any other procedure), involving human volunteers or patients to be conducted shall have IEC permission before commencing such a study.

Each project along with a duly completed research protocol approved by the Institutional Research Committee (IRC) shall be submitted in soft copy to the Member Secretary of the IEC. The format approved by the IRC shall be used. It shall have the designation and signatures of Principal Investigator or Guide in case of Doctoral Dissertations.

All details in the form such as type of patients, phase of drug trial, duration of study, sponsoring agency, budget of the trial, availability of permission and other relevant approvals of the Regulatory Bodies as relevant etc. shall be completed while submitting the proposal. It must clearly mention any ethical concerns that may exist.

2) Studies which plan to use a new drug shall submit along with the regulatory Body application form, a copy of the permission letter issued by the Regulatory authority to the pharmaceutical company/investigator. If the

regulatory authority approval is awaited, a letter of provisional approval from IEC will be issued and final IEC approval will be given after a copy of final permission is submitted to the EC. A study cannot begin until the final letter of permission is issued by the IEC.

3) In case a clinical study is planned on an "alternative system of medicine" a co-investigator from that system will be required on that study. For ayurvedic or herbal drugs, which are not marketed, a copy of the marketing/ manufacturing licence issued by Regulatory Body to the company shall be submitted.

4) A user fee will be charged for all sponsored projects, the exact amount of the fees pending final discussion to be undertaken at an appropriate time. The fees shall be collected at the time of submission of the project. The amount to be collected, as processing fee will be reviewed at the end of 1 year. The cheque must be drawn in favour of an Official account that will be opened in the name of the IEC, DYPMC in due course.

5) The project proposal shall be submitted in 5 copies. Each set shall contain the documents on A 4 size paper arranged in a file in the order mentioned below:

   i. Summary of protocol (in not more than 500 words)
   ii. Protocol and any amendments to it with version and date
   iii. The informed consent document (ICD), including any amendments / addenda and its translation(s) into regional language(s).
   iv. Case Record Form / Questionnaire.
   v. Principal investigators current Curriculum vitae.
   vi. Subject recruitment procedures (e.g. advertisements/letters to doctors/posters)

vii. Investigator Brochure This should give details of the study drug, toxicology studies, phase I, II, III data wherever available, safety information etc.

viii. Ethics Committee clearance of other centers (if multicentre study)

ix. Insurance policy

x. Clearance from the Regulatory Authorities as specified by Government of India

xi. Investigator's agreement with sponsor

xii. Investigator's undertaking to Institutional Ethics Committee

xiii. Regulatory Body marketing/manufacturing license for herbal drugs.

The guidelines for submission of a research proposal are as described in § 14.1 and the checklist for documents to be submitted is as described in § 14.3.

c) For Research protocols in Section 5.1 (d) above, the procedure will be as (a) or (b) above, depending on the nature and funding of the project as described in Section 5.1

5.3 Procedures

a. All communications with the committee shall be in writing.

b. The project proposals in the format mentioned in § 5.1. will be accepted in office address mentioned on cover (Office of Research Director, 1st Floor, D. Y. Patil Medical College, D. Y. Patil Vidyanagar, Kasaba Bavada, Kolhapur, India) on or before the 10th of every month.

c. The projects submitted by the 10th of a month will be circulated to all committee members and the proposal shall be reviewed for elements described in § 5.3.

d. A meeting, as described in § 5.4, will be held where each proposal will be discussed and decisions arrived at.

5.4 Elements of Review

The submitted proposal shall be reviewed for ethical principles as applicable to the standard of Care offered to the patient or participant and to scientific research.

The committee members shall review the proposal with reference to the following:

a. Scientific design in relation to ethical aspect
b. Justification / Rationale of the study
c. Selection criteria for subjects
d. Justification for use of placebo, if any
e. Potential benefits to the study subjects
f. Predictable risks to the study subjects
g. Criteria for discontinuation/withdrawal of subjects
h. Monitoring of serious adverse events
i. Compensation to subjects for participating in the study
j. Subject recruitment procedures
k. Patient retention activities.
l. Compensation for study related injury
m. Post trial benefits
n. Protection of privacy and confidentiality
o. Statistical analysis
p. Informed consent document in English and regional languages
q. Competence of investigators, supporting staff and infrastructure facility
r. Approval of regulatory authorities wherever applicable

5.5 Meetings

a. The committee will hold a regular meeting as per need for ethical review

b. When there are no research proposals to review, the meeting may be held less frequently, but not less than once every 6 months.

c. All members will receive notification of meeting schedules at least 2 weeks in advance.

d. The committee members will review all the proposals before the meeting.

e. The proposal may be sent to a subject expert for his/her assessment and opinion of the research proposal. The subject expert may be invited for the meeting.

f. The investigator and/ or co-investigator may be invited to the meeting to provide clarifications on the study protocol.

g. Quorum

Meetings will be held as scheduled provided there is a quorum. The quorum of the IEC will be at least five members (either primary or optional) with the following representations:

i. A basic medical scientist (preferably one pharmacologist),
ii. A clinician,
iii. A legal expert,
iv. A social scientist and
v. A lay person.

h. Hierarchy

i. There will be one Chairperson and one Member Secretary.

ii. The Chairman will be the head of the committee.

iii. The Member Secretary will be the guardian of all documents and funds in the committee's possession.

iv. All other members will be regular committee members with equal ranking.

v. A Treasurer will be appointed once sponsored projects are taken on by the IEC, DYPMC & DDYPH

i. Minutes

The Member Secretary will be responsible for coordination and recording of the proceedings of the meeting. The proceedings of the meetings shall be recorded in English and in the form of minutes. The minutes shall be approved by the chairperson. A copy of the approved minutes will be forwarded to the Office of the Dean, DYPMC, India.

j. Decision making

i. Decision for each proposal shall be by consensus. In the event of a consensus not being reached after discussion, decision will be taken by voting by all members.

ii. A majority vote for approval, disapproval, request for modifications, suspension or termination of a research proposal or an ongoing study is defined as one-half of the members who have reviewed the project.

iii. All members present at the IEC meeting will have the right to vote on the research proposals.

iv. Absent members will not have a vote.

v. Member(s) of the committee who is/are listed as investigator(s) on a research proposal will opt out from all deliberations on the proposal and will not vote on the proposal.

vi. An investigator or study team member invited for the meeting will

not vote or participate in the decision making procedures of the committee.

vii. Specific patient groups invited for the meeting will not vote or participate in the decision making procedures of the committee.

viii. In case the quorum is equally divided on a decision, the Chair Person will have a casting vote.

5.6 Review Outcome

The committee will document its view on the following:

a. Final Approval

b. Provisional approval subject to regulatory approval

c. Request for modification giving reasons

d. Request for additional information

e. Clear disapproval giving reasons.

f. Termination/suspension of an ongoing study giving reasons

5.7 Notification of Review Outcome

The outcome of committee's review shall be communicated to the investigator within 14 working days of the meeting. Thus, the decision will be communicated to the investigator within 30-45 days of submission of the proposal.

5.8 Approval

All sponsored projects will be given approval for the duration of the study from the date of the meeting on which the project was approved. The approval shall be in the format described in § 14.4. An annual progress report should be submitted to the committee.

All approval granted to dissertation projects of MD/MS students of DYPMC will remain valid till end of study except in the situation of non-adherence to protocol, serious adverse events and unexpected patient dropouts. The monitoring of the afore mentioned situations will be done on a 6-monthly basis as per the prescribed Progress Report proforma mentioned in the IEC Appendix 3

5.9 Review of the Modified Proposal

a. When modifications to the proposal, as recommended by the committee, are minor, the revised documents may not be re-circulated. The revised proposal shall be reviewed by either the Chairperson of the committee, the Member Secretary of the committee, or by one or more experienced reviewers designed by the chairperson from among the members of the committee. An approval may then be issued if the revised documents are satisfactory. The committee will keep all members of the committee informed of these approvals.

b. When modifications to the proposal, as recommended by the committee, are major, the revised proposal will be re-circulated and discussed again at next meeting.

5.10 Procedures for Appeal

For research proposals rejected/disapproved by the committee, the applicant may appeal for a repeat review within specified time of the receipt of the committee's decision. The Committee reserves the right to grant extension time of a variable duration on a case-to case basis for resubmission, depending on the required amendments. Failure to submit within this extension period, will lead to rejection of the proposal. The researcher may once again reapply by following the prescribed process. While doing so, the applicant shall give justification relevant to the issues/

objections raised by the committee.

5.11 Review of Amendments to the Approved Research Proposal

a. All amendments to the approved research proposal shall be submitted to the committee immediately for its review.

b. No changes in the protocol, case record form and /or ICD shall be initiated without prior written approval from the committee, except when necessary to eliminate immediate hazards to the subject, or when the change(s) involve only logistical or administrative aspects of the trial (e.g. change of monitor(s), telephone number(s).

c. The committee will be apprised of all changes made in any Approved Research Proposal which may have been reviewed by a single member or sub-committee of the IEC.

5.12 Expedited Review Procedures

a. The committee may use expedited review procedure in case of minor changes/ amendments in the previously approved research proposal that appear to involve no more than minimal risk to the study subjects.

b. Under an expedited review procedure, the review may be carried out by the Chairperson of the committee, or by one or more experienced reviewers designed by the chairperson from among the members of the committee The reviewers may exercise all of the authorities of the committee except that the reviewers may not disapprove the research.

c. An ongoing research activity may be disapproved only after review in accordance with non-expedited review procedure as mentioned in § 5.2

d. The committee will keep all members of the committee informed of these approvals under the expedited review procedure.

e. Only the Chairperson shall make the decision to allow an expedited review

5.13 Review of Subject Recruitment Procedures

All advertisements, letters to doctors, posters, notices to be used for recruitment of subjects shall be reviewed and approved by the committee prior to their implementation in the study.

5.14 Review of On-going Studies

a. The committee will conduct a continuing review of each on-going study by reviewing the reports described in § 6.

b. The committee may also ask for a status report from the investigator at earlier intervals as is felt appropriate to the degree or risk to the human subjects.

c. On the basis of the review, the committee shall recommend temporary suspension or termination of ongoing clinical trials for reasons such as patient safety.

6. Reports Required of Research Investigators

The research investigator shall submit the following reports to the committee:

a. Annual progress/status report: For studies whose duration is more than a year, the first report shall be submitted at least thirty (30) days before the completion of the year following the date of the first approval.

b. Subsequent reports shall be submitted at 6-monthly intervals following the first report.

c. In addition, the investigator shall also promptly report the following to the committee:

i. Deviations from/changes to protocol to eliminate immediate hazards to trial subjects.

ii. Changes that may increase the risk to subjects and /or affect the conduct of the trial.

iii. All adverse events that are both serious and unexpected within seven working days of the occurrence of the adverse event.

iv. New information that may affect adversely the safety of the subjects or the conduct of the trial.

d. Study completion report: A brief report of the study shall be submitted to the committee at the end of the study.

7. Withholding of Approval

For all sponsored projects, ethics approval may be withheld if unethical conduct is perceived and the same will be communicated to the funding agency.

Unethical conduct of research in non-sponsored projects will result in withdrawal of the ethics approval and negation of all data collected till that date.

8 On-going Training of Members

a. The Chairperson will identify the training requirements of the committee members.

b. The Chairperson and the Member Secretary will organize workshops or training programmes for the committee members.

c. The type of programmes, areas for training and mentors for these workshop or training programs will be decided by the committee members at a scheduled meeting.

d. Members shall also be deputed by the chairperson to attend workshops to train ethics committee members.

9 Records Retention

The committee will archive the following records for a period of at least five (5) years

a. Standard operating procedures (SOPs) of the committee
b. Guidelines for submission established by the committee.
c. Annual reports of the committee
d. Membership list
e. Curriculum Vitae of the members
f. Agenda of meetings
g. Minutes of meetings

The committee will also archive the following records for a period of at least five (5) years following the completion of a study :

a. One copy of all materials submitted by a research investigator
b. All correspondence by the committee with the research investigator regarding application, decision and follow –up
c. A copy of the decision and any advice or requirements sent to an applicant
d. All written documentation received during the study
e. The notification of the completion, premature suspension or premature termination of a study
f. A summary of the final report of the study

The records shall be made available to relevant statutory authorities upon request.

10 Reports to the Relevant Regulatory Authorities

The committee will make a yearly activity report for submission to the Appointing authority the Dean of DYPMC, Kolhapur, which will include the following elements:

a. A quantitative evaluation of the activities of the committee in a year
b. The list of the proposals reviewed in a year
c. Status of each study proposal

11 Location and Business Address:

The location and business address of the committee is as follows:

Member Secretary,
D. Y. Patil Medical College, D. Y. Patil University, Kasaba Bawada, Kolhapur
Tel. : 0231 2601235 / 36 Mobile: +91 9820017268
Fax : 0231 2601238 E-mail : iecdypIndia@gmail.com

12 Amendments to the Standard Operating Procedures

a. Amendments to the Standard Operating Procedures of the Independent Ethics Committee, D. Y. Patil Medical College shall be proposed in writing.

b. The proposal for amendment shall be submitted to the Member Secretary.

c. The proposal for amendment shall be presented to the regular members at a scheduled committee meeting.

d. Only regular members shall vote to accept or reject the proposed amendment.

e. A proposed amendment shall be approved by a vote of three-fourths of the members present in a quorum at a scheduled committee meeting, rounded to the next whole number.

f. If the changes on a final version are minor the version will be indicated as Version 1.1, version 1.2 etc. If there are major amendments, the version will be indicated as Version 2.

13 List of committee members with their affiliations and qualifications

The present composition of the Institutional Ethics Committee DYPMC, Kolhapur is listed in the table below:

No	Name	Designation	Qualification
1.	Dr. Mrs. S. S. Walawalkar	Chairperson	M.D. (Obst. & Gynac.)
2.	Dr. B. M. Tiwale	Scientific Member	M.Sc., (Med. Bio.) Ph.D. (Med. Bio.)
3.	Adv. Ravi Shiralkar	Legal Expert	B.S.L., LL.B.
4.	Dr. K. T. Jadhav	Lay Person	M.E., Ph.D. (Chemical Engg.)
5.	Dr. Abhay D. Chougale	Clinician	M.S. (Surg.)
6.	Dr. Archana G. Dhavalshankh	Basic Medical Scientist	M. D. (Pharmac)
7.	Dr. Sunita S. Patil	Basic Medical Scientist	M. D. (Pharmac)
8.	Dr. Vasanti Rasam	Social Scientist	M. A., Ph. D.
9.	Mr. Amit P. Mahadik	Lay Person	S.S.C.
10.	Dr. C. D. Lokhande	Scientific Member	M.Sc., Ph.D.
11.	Dr. Mrs. Shimpa Sharma	Clinician, Member Secretary	M.D. (Med.)

14 Appendices

14.1 Appendix 1 : Guidelines for Submission of a Sponsored Proposal to the Regulatory Bodies (to be prepared)

1. All prospective and retrospective studies involving human volunteers or patients, should have EC permission before commencement.

2. Each project along with a duly completed and approved research protocol should be submitted in soft copy as well as hard copy (4 copies). It should have the designation and signatures of Principal Investigator, all the co-investigators and the Heads of the concerned departments.

3. Studies which plan to use a new drug/s which have not been approved for use in India require permission from Regulatory Authorities of India as prescribed by the Government of India. For such studies, a copy of the permission letter issued by the relevant Regulatory authority or Body to the pharmaceutical company/ investigator also needs to be submitted to the IEC. If the relevant permission is awaited, a letter of provisional approval will be issued by the IEC and the final IEC approval will be given after a copy of permission from the relevant Regulatory Body is submitted to the IEC. No study should be initiated until the final letter of permission is issued by the IEC.

4. A clinical study planned on an "alternative system of medicine" shall require a co-investigator from that system. For ayurvedic or herbal drugs, a copy of the marketing/ manufacturing license issued by the relevant Regulatory bodies to the company should be submitted.

5. For all projects sponsored by pharmaceuticals, a user fee in INR will be charged. Government sponsored projects will also be charged a user fee in INR and projects outside the DYPMC & DDYPH which are not sponsored, will be charged a nominal fee. The fees shall be collected at the time of submission of the project. The exact fee to be charged will be decided at a later date.

6. Two sets of the project proposal need to be submitted. Each set shall contain the documents mentioned below on A 4 size paper arranged in a plastic file in the order mentioned below:

i. EC application form duly filled.

ii. Summary of protocol (in not more than 500 words)

iii. Protocol and any amendments to it with version and date

iv. The informed consent document (ICD), including any amendments / addenda and its translation(s) into regional language(s). A format of the ICD is available in the office of the EC. The ICD should be customised for the study using this format.

v. Case Record Form / Questionnaire.

vi. Principal Investigator's current curriculum vitae for non-doctoral research

vii. Subject recruitment procedures (e.g. advertisements/letters to doctors/ posters)

viii. Investigator Brochure (for sponsored projects). This should give details of the study drug, toxicology studies, phase I, II, III data if available, safety information etc.

ix. Ethics Committee clearance of other centers (if multicentre study).

x. Insurance policy / Statement regarding compensation of study related injury by sponsor

xi. Regulatory Authority clearance [for Phase I, II, III studies]

xii. Investigator's agreement with sponsor

xiii. Investigator's undertaking to Regulatory Authority [for Phase I, II, III studies]

xiv. All other clearances wherever applicable from relevant Regulatory authorities

xv. Regulatory authority marketing/manufacturing license for herbal drugs.

7. After initiation of the study, the EC requires submission of the following:

All adverse events occurring in the study, deviations from, or changes in the protocol to eliminate immediate hazards to the trial subjects, new information that may adversely affect the safety of the subjects or conduct of the trial.

8. The EC expects to be informed annually about the status of the study.

(a) For studies which are completed within the EC approval period, a study completion report should be submitted to the EC, by the principal investigator. If a study was not initiated, or was withdrawn or terminated, the same should be informed to the EC giving reasons.

(b) For studies which will continue for more than a year, annual progress report must be submitted. The request for extension of approval (beyond duration of study on submission) should be accompanied with a project report mentioning the following: no. of screened patients, randomised patients, active patients, no. of patients who have completed the study, no of patients who have dropped out/ withdrawn, no. of patients who had an SAE, report of an interim analysis if available. The approval will be extended after the EC reviews the annual project reports and the request for extension. A user fee in INR will be charged for extension of approval of projects sponsored by pharmaceuticals the exact amount to be determined at a later appropriate date.

9. The Standard Operating procedures of the IEC, DYPMC and DDYPH, V 1.0, dated 09.09.2016 should be available with the Member Secretary of the IEC.

14.2 Appendix 2 : Regulatory Body Application Form

Title of the project _____

_____

	Name	Designation	Dept. & Institute
Principal Investigator			
Co-Investigator 1			
Co-Investigator 2			

Non-sponsored study ☐ Sponsored study ☐

If non-Sponsored Study:

Thesis/dissertation ☐ Other Academic ☐

(Please mention approx. date of submission of thesis/ dissertation: _____)

If Sponsored study

1. Indian ☐ a) Government ☐ b) Industry ☐ c) Institutional ☐

2. International ☐ a) Government ☐ b) Private ☐ c) UN agencies ☐

3. Industry ☐

Address of Sponsor:	Research Fund will be deposited in:
Total Budget: INR _____	(Please give details of allocation of budget in attachment.)

1. Type of Study : Prospective ☐ Retrospective ☐

Single center ☐ Multicentric ☐ If multicentric, how many centres _____

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2. Does the study involve use of: Drug / Vaccine ☐ Device ☐ Alternative Medicine ☐

Any other ☐ Not Applicable ☐ If other, please specify _____

i) Is the test drug / device marketed in India Yes ☐ No ☐

Is it marketed in other countries: Yes ☐ No ☐ Specify _____

If marketed in India, please attach package insert

If not marketed in India, please attach regulatory Authority permission.

ii) Is the test drug an Investigational New Drug (IND)? Yes ☐ No ☐

If yes, please submit Investigator's Brochure which contains data of pre-clinical studies.

If IND, please also attach Regulatory Authority permission

iii) Does the test drug involve a change in use, dosage, route of administration?

Yes ☐ No ☐

If yes, please attach copy of relevant permission.

If other, please specify_____

3. Clinical Study is : Phase I ☐ Phase II ☐ Phase III ☐ Phase IV ☐

4. Subject selection:

i) Number of subjects at this centre If multicentric, total number of subjects

ii) Vulnerable subjects Yes ☐ No ☐ (If yes, tick the appropriate boxes)

pregnant women ☐ children ☐ elderly ☐ fetus ☐ illiterate ☐ handicapped ☐

seriously/terminally ill ☐ mentally challenged ☐ economically/socially backward ☐

any other ? If other, please specify_____

Iii) Special group subjects Yes ☐ No ☐ (If yes, tick the appropriate boxes)

employees ☐ students ☐ nurses/dependent staff ☐ any other ☐

If other, please specify _____

5. Does the study involve use of

i) Fetal tissue or abortus Yes ☐ No ☐

ii) Organs or body fluids Yes ☐ No ☐

iii) Fecombinant/gene therapy Yes ☐ No ☐

If yes, please submit a copy of permission from relevant Authority

iv) Ionising radiation/radioisotopes Yes ☐ No ☐

If yes, please submit a copy of relevant Authority permission.

v) Infectious / biohazardous specimens Yes ☐ No ☐

vi) Will pre-existing/stored/left over samples be used? Yes ☐ No ☐

vii) Will samples be collected for banking/future research Yes ☐ No ☐

viii) Will any sample collected from patient be sent abroad? Yes ☐ No ☐

If yes, please submit a copy of relevant Authority permission.

ix) Is there any collaboration with any foreign lab., clinic or hospital Yes ☐ No ☐

If yes, please submit a copy of relevant Authority permission

6. Will any advertising be done for recruitment of Subjects? Yes ☐ No ☐

(Posters, flyers, brochures, etc.) If yes, kindly attach a copy

7. Data Monitoring

i) Is there a Data & Safety Monitoring Board/Committee (DSMB)? Yes ☐ No ☐

ii) Is there a plan for interim analysis of data? Yes ☐ No ☐

iii) For how long will the trial data be stored? _____ years

8. Is there compensation for participation? Yes ☐ No ☐

If Yes, Monetary ☐ In kind ☐ Specify amount / type: _____

9. Are there any arrangements for compensation of trial related injury? Yes ☐ No ☐

Please submit a copy of the insurance policy if it is available.

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We hereby declare the information given above is true and that we do not have any financial or non - financial conflict of interest.

Signature of Principal Investigator : _____

Signatures of Co- investigators:

1. _____
2. _____
3. _____

Forwarded by Heads of Department(s)

_____ _____

Stamp/Seal of the Department(s)

14.3 Appendix 3 : Check List of Documents

No	Document	Attached Yes/No	Comment
1	EC/Regulatory body application form		
2	Summary of protocol		
3	Protocol		
4	Amendments to protocol		
5	Informed consent document in English		
6	Informed consent documents in Regional languages (Total)		
7	Back translations of Informed consent documents		
8	Amendments to the informed consent document		
9	Case Record Form / Questionnaire		
10	Principal investigators Current Curriculum Vitae		
11	Subject recruitment procedures: advertisement, letters to doctors, notices		
12	Investigator Brochure		
13	Ethics Committee clearance of other centers (Total No.)		
14	Insurance policy		
15	Clearance from Regulatory Authority for Drugs		
16	Investigator's agreement with sponsor		
17	Investigator's undertaking to Governmental Authority		
18	Governmental Authority approval		
19	Regulatory Authority marketing/ manufacturing license for herbal drugs.		
20	Other Documents as relevant		
21	Progress report Form for PG Dissertation		

14.4 Appendix 4 : Format of Consent Document

I, Mr/Mrs/Ms ..... Gender ..... Age: .....

Residing at .....

do hereby confirm that:

(i) I have been asked by the student/researcher of D Y Patil Medical College ("the Medical College") whether I wish to participate in a study under the aegis of the Medical College;

(ii) The nature of the study being undertaken by the student/ researcher, as well as the extent of my participation in it, have been duly explained to me in a language that I understand;

(iii) The potential risks and consequences associated with this study have also been duly explained to me in a language that I understand;

(iv) I also understand that my participation in this study is only for the benefit of advancement in the field of medical research and that at no point in time is my participation being solicited for any pecuniary gain by the researcher or the Medical College;

(v) I have also been explained that I am in no way obliged to participate in the study and that, once I have agreed to participate in the study, I am still free to withdraw from participation in the study at any point in time upon notifying the Medical College in writing in the prescribed form without assigning any reason;

(vi) There will be no financial transaction between myself, the researcher and/or the Dr. D. Y. Patil Medical College for my participation in that study;

(vii) I have been explained that any data collected out of my participation in the study will only be used for academic purposes and/or for further medical research;

(viii) I have also been reassured that any publication of the data collected during the course of the study or any publication of its conclusions, shall be done on a 'no

names' basis and shall under no circumstances reveal my personal identity. Any personal details likely to reveal my personal identity shall at all times remain confidential;

(ix) I understand that if any accident or undesirable medical complication arises out of a procedure or treatment done solely for the purpose of research, I will be offered treatment, free of cost, by the Dr. D. Y. Patil Hospital & Research Institute, Kolhapur. Any additional compensation considered necessary by the Institutional Ethics Committee may also be given to me.

(x) The contents and effect of this consent form have also been duly explained to me in a language that I understand;

By affixing my signature/thumb print hereto, I am therefore freely and voluntarily signifying my consent, intent and willingness to participate in the study of the student researcher for the purposes of the postgraduate dissertation under the egis of the Medical College. I also certify that my right to privacy has not been infringed in any manner.

[SIGNATURE/THUMB PRINT OF PARTICIPANT]

DATE :

WITNESSED BY :

(1) NAME :

TITLE/CAPACITY :

SIGNATURE :

(2) NAME :

TITLE/CAPACITY :

SIGNATURE :

14.5 Format of Assent Form

I, Mr/Mrs/Ms ..... Gender ..... Age: .....

Residing at .....

do hereby confirm that I am the legal guardian/parent of the child named .....
....., age ..... studying in .....

(i) I have been asked by the student/researcher of D .Y. Patil Medical College ("the Medical College") whether I wish to allow my ward to participate in a study under the aegis of the Medical College;

(ii) The nature of the study being undertaken by the student/ researcher, as well as the extent of my participation in it, have been duly explained to me in a language that I understand;

(iii) The potential risks and consequences associated with this study have also been duly explained to me in a language that I understand;

(iv) I also understand that my ward's participation in this study is only for the benefit of advancement in the field of medical research and that at no point in time is his/her participation being solicited for any pecuniary gain by the researcher or the Medical College;

(v) I have also been explained that he/she is in no way obliged to participate in the study and that, once I have agreed to allow him/her to participate in the study, he/she is still free to withdraw from participation in the study at any point in time upon notifying the Medical College in writing in the prescribed form without assigning any reason;

(vi) There will be no financial transaction between myself, the researcher and/or the D. Y. Patil Medical College for the participation in that study;

(vii) I have been explained that any data collected out of this participation in the study will only be used for academic purposes and/or for further medical research;

(viii) I have also been reassured that any publication of the data collected during the course of the study or any publication of its conclusions, shall be done on a 'no names' basis and shall under no circumstances reveal the personal identity of my ward. Any personal details likely to reveal his/her personal identity shall at all times remain confidential;

(ix) I understand that if any accident or undesirable medical complication arises out of a procedure or treatment done solely for the purpose of research, my ward will be offered treatment, free of cost, by the Dr. D. Y. Patil Hospital & Research Institute, Kolhapur. Any additional compensation considered necessary by the Institutional Ethics Committee may also be given to me on his/her behalf.

(x) The contents and effect of this consent form have also been duly explained to me in a language that I understand;

By affixing my signature/thumb print hereto, I am therefore freely and voluntarily signifying my consent, intent and willingness for my ward to participate in the study of the student /researcher under the egis of the Medical College. I also certify that my right to privacy has not been infringed in any manner.

[SIGNATURE/THUMB PRINT OF PARENT/GUARDIAN]

DATE :

WITNESSED BY :

(1) NAME :

TITLE/CAPACITY :

SIGNATURE :

(2) NAME :

TITLE/CAPACITY :

SIGNATURE :

14.6 Appendix 6: Confidentiality Agreement

(To be printed on the letterhead of the Ethics Committee)

CONFIDENTIALITY AGREEMENT

The undersigned accept that the confidential information contained in the proposals submitted to the Ethics Committee for review in the EC meeting dated_____ shall be maintained in confidence with the same degree of care, the EC holds its own confidential information and shall not be disclosed to any third party. However, we understand that EC records may be subjected to review by the relevant regulatory authorities.

Name	Signature	Date
Dr. Mrs. S. S. Walawalkar		
Dr. B. M. Tiwale		
Adv. Ravi Shiralkar		
Dr. K. T. Jadhav		
Dr. Abhay D. Chougale		
Dr. Archana G. Dhavalshankh		
Dr. Sunita S. Patil		
Dr. Vasanti Rasam		
Mr. Amit P. Mahadik		
Dr. C. D. Lokhande		
Dr. Mrs. Shimpa Sharma		

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The Standard Operating Procedures of the Ethics Committee, DYPMC, Version 1.0, dated are verified and confirmed by the following EC members

No	Name	Signature	Date
1.	Dr. Mrs. S. S. Walawalkar		
2.	Dr. B. M. Tiwale		
3.	Adv. Ravi Shiralkar		
4.	Dr. K. T. Jadhav		
5.	Dr. Abhay D. Chougale		
6.	Dr. Archana G. Dhavalshankh		
7.	Dr. Sunita S Patil		
8.	Dr. VasantiRasam		
9.	Mr. Amit P. Mahadik		
10.	Dr. C. D. Lokhande		
11.	Dr. Mrs. Shimpa Sharma		

D. Y. PATIL MEDICAL COLLEGE, KOLHAPUR
Institutional Ethics Committee

Addendum to SOPs for Institutional Ethics Committee

The Standard Operating Procedures (SOPs) for Clinical Trial Investigations is hereby reviewed and resolved to attach with SOPs for Institutional Ethics Committee as addendum.

Sr. No.	Name of Members	Position	Sign.
1	Dr. J.L. Nagaonkar	Chair Person	
2	Dr. Mrs. Vasanti Rasam	Social Scientist	
3	Dr. Sushma Jotkar	Clinician	
4	Advt. Ravi Shiralkar	Legal Expert	
5	Dr. K. T. Jadhav	Social Scientist	
6	Dr.Jarinabanu. C Tahashildar	Medical Scientist	
7	Dr. C. D. Lokhande	Scientific Member	
8	Dr. Mrs. Shimpa Sharma	Member Secretary	
9	Mr. Amit P.Mahadik	Lay Person	

Date:

Place: Kolhapur

Dr.D.Y.Patil Medical College, Hospital and Research Institute, Kolhapur

Clinical Trial site SOP- Version-1.0-2022

SOP-I. SOP- **Clinical trial Investigators**

Effective date: 01-Apr-2022 to 31-Mar-2025

Prepared By:

Dr.Rajesh Jagannath Khalyalappa Department of Medicine, Dr.D.Y.Patil Medical College, Kolhapur	Signature with date

Reviewed By:

Dr.Shimpa Sharma Member-secretary	Signature with date

Approved By:

Dr.Rakesh Kumar Sharma Dean, Dr.D.Y.Patil Medical College, Kolhapur	Signature with date

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Note: When a trial is sponsored by another agency/pharmaceutical company, the Investigator may also be requested to follow their procedures in order to comply with company obligations. Agreement between all parties will be discussed before initiating the trial.

Aims: To define Investigators' responsibilities and to provide instruction, when performing clinical study (ies) facilitated by Dr. D Y Patil Medical College- Kolhapur

I. Objectives:

i. To provide the Investigator with general instruction to ensure that he/she understands and accepts the obligations incurred in undertaking the study.
ii. To ensure that the study is planned, set up, conducted, documented, and reported according to the protocol, related site SOPs, Recent IEC SOPs, ICMR Guidelines, ICH GCP and applicable local regulatory requirements.
iii. To ensure that the rights, safety, and wellbeing of study subjects/Participants are properly protected.
iv. To ensure that data are generated, collected, and documented with accuracy, consistency, and integrity.
v. To ensure that the Investigator is acquainted with the study procedures, verification procedures, audits, and inspection procedures.
vi. To be responsible for the third- party staff (Site management organization employees), whoever working in the respective clinical trials.

Co-investigators:

Co- investigators are authorized healthcare professionals who work alongside the PI at a trial site, e.g. other Consultants in the department, Post Graduate Medical students). The co- investigator may conduct all or part of the PI's duties, and must be available to act up

as PI if the PI is unavailable for any length of time (e.g. annual leave) or in an emergency situation that could affect the safe conduct or oversight of the trial.

Note: PI/Co-I is not affiliated with the Dr. D Y Patil Medical College, Kadamwadi-Kolhapur, those cannot be delegated to the clinical trial team.

II. Prior to initiation of the study:

The Investigator should:

i. Be interested in the scientific aspects of the study and ensure that the study is responsive to the needs of public health within the country of the population in which it will be conducted.

ii. Ensure the confidentiality of the product, the protocol and trial procedures by giving a confidentiality agreement in writing to CRO/sponsoring agencies.

iii. Have sufficient time free from other obligations to prepare and conduct the trial.

iv. Clinical trials are time-consuming and the Investigator should ensure that sufficient time can be dedicated to the study, including for informing and supervising study staff.

v. Review Investigator's Brochure and any up-to-date information on the investigational product.

vi. The Investigator must be familiar with the product, including pre-clinical toxicology, pharmacology, pharmacokinetics and up-to-date clinical data.

vii. Review and discuss investigators' SOPs and protocol with the Clinical Monitor

viii. The Investigator should clearly define: Factors that may alter the feasibility and acceptability of the trial. An adequate recruitment rate for the trial by providing retrospective data on numbers of patients who would have satisfied the proposed entrance criteria during proceeding time periods.

ix. Make sure that the procedures stated in the study protocol are applicable in his/her center and fully understood. The Investigator should ask the Clinical Monitor to clarify any points of possible misunderstanding.

x. Make sure that there are sufficient medical, paramedical and clerical staffs to support the study and deal with foreseeable emergencies.

III. Make sure that the facilities are sufficient to allow the study to be undertaken efficiently.

Ensure:

- Confidentiality and safety conditions for trial subjects.
- Adequate equipment/facilities for subject follow-up, examination and care.
- Adequate facilities for Investigational Medicinal Products storage
- Adequate facilities for laboratory assay of the Subject's blood parameters investigations.
- Adequate facilities for retention of trial documents, ensuring the confidentiality of all information about trial subjects and information supplied by Dr. D Y Patil Medical College, Kadamwadi-Kolhapur /sponsoring agencies.
- Make sure that the IPD trial subject should be in the house in the Private Wards

IV. Arrange an archive of trial documents according to GCP and regulatory requirements. It is important to check.

- The duration of retention of patient records with the Institution's archive. In case the Institution's archive does not ensure the retention of documents for the period of time requested by the sponsor.
- The Investigator must arrange for the retention of the subjects' source documents/records for the period requested by the sponsor and regulatory requirements.

V. If the IEC and others approve the trial, sign the final copy of the protocol and confirm in writing that he/she has read and understood, and will adhere to, the protocol, study procedures and ICH Good Clinical Practice, will collaborate with the monitor, and accords with Sponsoring agencies on publications policy.

Submit requested documents to the Dr. D Y Patil Medical College, Kadamwadi- Kolhapur, including:

- Signed agreement to comply with this SOP
- Approved protocol, signed and dated.
- Approved informed consent form and other subject information, advertisement (local language and English translation).
- Investigator's and co- investigator's curriculum vitae (CVs).
- Recent ICH- GCP training certificate
- Authorized Staff Form
- Product exportation/importation authorization.
- Laboratory certification/recent list of normal laboratory ranges, dated and signed by lab head/Investigator.
- Lab Accreditation certificate
- Final Clinical trial agreement
- Signed agreement that the product will not be used before the Site Initiation Visit has been made and authorization obtained from the SMO Clinical Research Coordinator (if applicable).
- Ethics Committee accreditations
- Visit archival facilities at Dr. D Y Patil Medical College, Kadamwadi- Kolhapur

VI. During the Study:

The trial can be initiated (begin screening and/or enrolment of trial subjects) only after the Clinical Monitor has satisfactorily conducted a Trial Initiation Monitoring Visit and the SMO Clinical Coordinator has given written authorization.

i. Delegation of duties: PI can delegate the CRC/Sub- I/Phlebotomist when the study is ongoing at site. PI should provide a comprehensive list of study staff members and the duties that have been delegated to them by the PI. It is applicable for both observational

and interventional clinical trial studies at Dr. D Y Patil Medical College, Kadamwadi-Kolhapur

ii. Completion of the delegation log:

The Clinical trial delegation log provides documented evidence of the appropriate delegation of the PI's responsibilities. The delegation log must state clearly the name of the person, their role and the activities they are delegated by the PI as well as being signed and dated by the PI prior to the activity being undertaken by the individual. All key personnel must be on the delegation log. The PI may delegate activities to a named person in a large department such as pharmacy, and the relevant trials pharmacist would then take responsibility for the conduct of that activity by the department. The dates of entries must be in chronological order and the PI must NOT pre-sign logs (for members of the research team to add names and tasks at a later date).

iii. Investigator's File, Including Storage and Retention:

On initiation of the study, the Investigator must prepare a file containing all the documents related to the trial. During the study, the Investigator is responsible for updating the File and regularly adding trial-related documents.

The Investigator should keep the File in a locked cabinet, in a secure area accessible only to the Investigator and authorized study staff. The Investigator File and associated source documents should be retained for the time agreed with /sponsors. Patient identification codes should be kept for at least 15 years after completion of the trial.

iv. Written approval from sponsors and site administrations, PI must be obtained prior to destroying records.

- Lab kits
- IPs
- Study Documents (after completion of 15 years)

★Lab kits and IPs as per sponsor requirements, during the study

v. The Investigator's File contains:

Administrative and Regulatory Documents

- Composition of Ethics Committee
- IEC Accreditation details
- Lab head CV and MRC
- Local regulatory requirements.
- IEC and other authorities' written approval for all documents (protocol, informed consent(s) and any written information including advertisements for recruitment of study subjects).
- Protocol initial submission letter and initial Local EC Decision letter.
- Correspondence with the Ethics Committee and the Authorities, including Protocol submission. Amendment submission, if any.
- SAE Initial, Follow Up and Final reports and SAE review report by Ethics Committee.
- Protocol modification notification, if any.
- Interim report/written summaries of the trial, if applicable.
- Final Report/written summaries of the trial, if applicable.
- Product importation authorization.
- Correspondence about product importation.
- For studies under IND, a copy of the completed and signed Form FDA 1572 and FDA 3455
- Investigator's and Co/Sub-investigators' C.V.s.
- New Investigator and Sub-investigators' C.V.s along with recent ICH-GCP certificate.
- Authorized Staff Form (ASF).

vi. Investigators/sub-Investigators qualifications and agreements

- The investigator(s) should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirement(s), and should provide evidence of such qualifications through up-to-date curriculum vitae and/or

other relevant documentation requested by the sponsor, the IEC, and/or the regulatory authority (ies).

- The investigator 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.
- The investigator should be aware of, and should comply with, GCP and New Drugs and Clinical Trial Rules, 2019
- The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authority (ies).
- The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.
- PI should Signed a confidentiality agreement
- PI should Signed an agreement stating that products will not be used before the Trial Initiation.
- Monitoring Visit has been made and approval from the SMO Clinical Coordinator obtained.
- Sub investigator should be affiliated with Dr. D Y Patil Medical College, Kolhapur.

vii. Correspondence and Monitoring

- Correspondence with sponsoring agencies (including the telephone call, E-mail etc). Notes of meetings with sponsoring agencies.
- Summary list of site visits (copy).
- Site Initiation visit Report (copy).
- Notification by Investigator to/Sponsor of serious adverse event and related reports.
- Documentation of serious adverse event reporting by/Sponsor to other investigators.
- Investigator interim report/summaries of the trial for /sponsoring agencies, if applicable.

- Investigator final report/summary of the trial for/sponsoring agencies, if applicable.
- Sponsoring agencies should inform through Mail/Telephonically Prior to Visit for site monitoring.
- Copies of the Investigator's interim report/written summaries of the trial to the Local EC and authorities.
- Monitoring visit of IEC members at the site: PI/CRC should arrange/ready for all study-related documents for Monitoring. IEC secretariat will inform via mail/letter about the IEC monitoring visit. IEC members will select randomly which have approved and ongoing studies at the site.
- To ensure to submit the SIV and SMV report to Ethics Committee

viii. Compliance with the study protocol

- The investigator/institution should conduct the trial in compliance with the protocol agreed by the sponsor and, if required, by the regulatory authority (ies) and which were given approval/favorable opinion by the Local EC. The investigator and the sponsor should sign the protocol, or an alternative contract, to confirm the agreement.

- The investigator should not implement any deviation from, or changes in the protocol without agreement by the sponsor and prior review and documented approval/favorable opinion from the Local EC of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change in monitor(s), change of telephone number(s)).

- The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.

- The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard(s) to trial subjects without prior Local EC 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,
  c) To the regulatory authority (ies)

xi. Adequate sources:

- The investigator should be able to demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
- The investigator should have sufficient time to conduct and complete the trial within the agreed trial period.
- The investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely manner.

VII. After Completion of the study:

- The CRA has to confirm the closeout visit in writing to the Investigator/study site. The letter will detail all persons expected to attend, and all administrative documents, IMP, and regulatory documents required for review at this visit. The CRA will confirm recruitment status at the end or premature end of the trial. If the site is closed prior to the end of the trial, a reason for early closure should be clearly documented.

- The CRA will ensure that all Serious Adverse Events (SAE's) have been reported by the Investigator to the Sponsor and that the investigator is aware of any future reporting requirements and follow up on any ongoing SAEs. If applicable, a line listing of all SAEs/SUSARs that have occurred at the site should be filed in the TMF. If closing the lead site in a multi-center trial, a line listing for all the SAEs/SUSARs at each site should be filed in the TMF.
- The CRA will ensure that all outstanding data queries are resolved at the time of the close out visit.
- All outstanding issues from previous monitoring visits will be resolved or appropriately documented.
- The CRA will verify that final drug accountability is complete
- If applicable, the CRA will ensure that Sponsor authorization for IMP destruction has been obtained and that the destruction or return of unused or partially used IMP is appropriately commented and documented in the Pharmacy file.
- PI along with the study CRA review the all-study related documents in study close out visit. After completion of the study, all the study documents should be archived

SOP-II. SOP- **Obtaining Informed Consent Form**

Effective date: 01-Apr-2022 to 31-Mar-2025

Prepared By:

Dr.Rajesh Jagannath Khalyalappa Department of Medicine, Dr.D.Y.Patil Medical College, Kolhapur	Signature with date

Reviewed By:

Dr.Shimpa Sharma Member-secretary	Signature with date

Approved By:

Dr.Rakesh Kumar Sharma Dean, Dr.D.Y.Patil Medical College, Kolhapur	Signature with date

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SOP-II- Obtaining of Informed Consent forms

I. Policy:

The ethical conduct of clinical investigations is based on the voluntary consent of the subject, who has been appropriately informed about a study's risks and benefits and is designed to protect the rights, safety, and wellbeing of human subjects. It is the responsibility of the investigator to ensure compliance with all ethical standards, guidelines and federal and state regulations have been met through the language of the informed consent document, and that informed consent itself has been properly obtained from the subject or the subject's legal representative.

II. Objective:

This SOP gives the procedure for obtaining informed consent from all trial subjects.

III. Scope:

Applicable for all Clinical trials at the site

IV. Definition-

Informed Consent: A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the study that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.

V. PROCEDURE:

1) All the clinical trial-related ICFs should be obtained in the respective Principal investigator OPD.
2) Procedure for Obtaining Informed Consent from Volunteers for participation in the study

3) The Subject Information sheet and the Informed Consent form will be given to the subject on the day of Screening.
4) The Study Coordinator/designated person will issue a copy of the Institutional Ethics Committee approved 'Subject Information Sheet and Informed Consent Form' (SIS/ICF) to the subject in the language best understood by him/her.
5) Investigator/designated person will give study-related information from the Institutional Ethics Committee of approved 'Subject Information Sheet and Informed Consent Form' to the volunteer.
6) Investigator/designated person will inform and explain the subject about the purpose of the study, the study procedure, the risk and discomforts associated with the study procedure and restrictions, the adverse effects of study drug, housing period, total blood loss, duration of the study, the remuneration, number of volunteers to be included in study, voluntary participation, withdrawal from the study, identity confidentiality etc, from the IEC/ approved 'SIS/ICF'. The name of the subject to whom the SIS/ICF is issued and sign and date of the person counseling the subject will be documented in the source document.
7) Investigator/ designated person will take the Informed Consent in one-to-one manner, the Investigator/ designated person will answer to all personal queries of the subject or their Legal Acceptable Representative (LAR) or Guardian during this session.
8) Investigator/designated person will inform that the eligible and interested subject or the volunteer's Legally Acceptable Representative (LAR) will have to sign the SIS/ICF and if the subject is unable to read and if the Legally Acceptable Representative (LAR) is unable to read then an impartial witness who is independent of the study will be present during the entire informed consent discussion and will explain the contents of the SIS/ICF to the subject or the volunteer's legally acceptable representative in the best language understood to the volunteer.

9) Each subject will be given sufficient time and opportunity to enquire about the study drug or the study procedure or consult his/her family physician to decide for his/her participation in the study.

10) The Investigator(s), Sponsor or the staff will not coerce or unduly influence the potential volunteer/subject to participate or to continue to participate in the study.

11) Investigator/Physician/ designated person will ensure that the subject as understood all the aspects of the study including the purpose of the study, the study procedure, the risk and discomforts associated with the study procedure and restrictions, the adverse effects of study drug, housing period, total blood loss, duration of the study, the remuneration, number of volunteers to be included in study, voluntary participation, withdrawal from the study, identity confidentiality etc, from the Human Ethics Committee approved 'SIS/ICF' and is participating in the study willingly.

12) Investigator/designated person will document the name of the subject to whom the SIS/ICF is issued and the name of Investigator/designated person counseling the volunteer, in the source document.

13) The volunteer/volunteer's legally acceptable representative (LAR) will write all the details like his/her name, address, date of birth, qualification, occupation, annual income of the volunteer, name of nominee(s), a relation of the nominee with the subject, address of the nominee, and sign the ICF (declaration) with a date.

14) In case of the volunteer/legally acceptable representative is unable to read/write then the subject will give the left thumb impression at the appropriate place and the impartial witness will write the volunteer's name and date below the thumb impression and all the respective details as mentioned above in the ICF, with the consent of the volunteer. The impartial witness will write his/her name, address and contact details, sign and date the declaration for witnessing the entire process of obtaining the informed consent of the volunteer.

15) The impartial witness by signing the consent form attest that the information in the consent form and any other written information is accurately explained and is apparently understood by the subject of the volunteer's legal representative or the guardian and that the informed consent was freely given by the subject or the volunteer's legal representative.

16) The Investigator/Co- Investigator will sign and date and will put his/her name in the ICF.

17) Site coordinator will give a photocopy of signed consent to the Subject/Legally Acceptable Representative.

18) The researcher has an obligation to convey details of how confidentiality will be maintained to the participant.

19) After the completion of the consent process the study designee record all protocol-related information in source documents.

20) If the patient is literate and unable to write in ICF then LAR can write the details on behalf of the patient and no LAR signature is required to authenticate the same. But reflection of the movement should be recorded in the ICF process.

VI. Applicable rules and regulations:

- FDA 21 CFR 50.20—General Requirements for Informed Consents
- National Ethical Guidelines for Biomedical and Health Research Involving Human Participants- 2017
- HHS 45 CFR 46.116—General Requirements for Informed Consent
- New Drugs and Clinical Trial Rules, 2019

SOP-III. SOP- **Roles and Responsibilities of Study CRCs**

Effective date: 01-Apr-2022 to 31-Mar-2025

Prepared By:

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SOP-III- Roles and Responsibilities of Study Coordinators

1. Purpose

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

Study team members must understand the responsibilities of the trials conducted at the site and be appropriately qualified by education, training, and/or experience to perform or their research-related task(s).

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

2. Scope:

This SOP will apply to all study research coordinators at the site management office in Dr.D Y Patil Medical College, Kolhapur.

3. Responsibilities:

i. Study start-up activities like Feasibility/Synopsis and Clinical disclosure agreements.
ii. Reviews and develops a familiarity with the study protocol (e.g. study procedures and timelines, inclusion/exclusion criteria, confidentiality).
iii. Document date of training and signatures of study personnel trained on the study-specific training log.
iv. Collect documents needed to initiate the study and submit them to the sponsor (e.g. forms 1572, CVs, etc.)

v. Conduct or participates in the informed consent process, including interactions with the IEC and discussions with research participates, including answering any questions related to the study.

vi. Obtain appropriate signatures and dates on forms inappropriate places. Assures that amended consent forms are appropriately implemented and signed/Dated.

vii. Screen subjects for eligibility using protocol-specific inclusion and exclusion criteria, documenting each potential subject's eligibility or exclusion. Creates and utilizes Eligibility Checklist to inclusion/exclusion criteria.

viii. Coordinate participant tests and procedures, including scheduling and registration of subjects with hospital Outpatient/in-patient departments at the site (e.g. radiology for CT scan).

ix. Collect data as required by the protocol. Assure timely completion of Case Report Forms

x. Maintain study timelines per the event schedule (e.g. subject visits, procedures and data entry are completed within the allotted time window per study protocol).

xi. Maintains adequate inventory of study supplies. If handling investigational drugs/devices, follows the sponsor protocol and/or UCSF Policy on Investigational Drug/Device Accountability.

xii. Complete study documentation and maintains study files in accordance with sponsor requirements and Medical College policies and procedures including, but not limited to, consent forms, source documentation, narrative notes if applicable, case report forms, and investigational material accountability forms.

xiii. Maintain effective communication with sponsor, research participants, IEC and PI during the course of the study.

xiv. Work with the PI to manage the day-to-day activities of the study including problem solving, communication and protocol management.

xv. Report all findings and correspondence from external or internal study monitoring and audits to the research manager and department Chair in a timely manner.

xvi. Assist the PI in reporting of research-related incidents, including protocol deviations or potential violations, as well as findings and correspondence from external or internal study monitoring and audits to the Ethics Committee in a timely manner.

xvii. Assist the Principal Investigator in the submission of accurate and timely closeout documents to applicable Federal agencies, Medical College entities, and the sponsoring agency in accordance with Federal regulations and Hospital/Medical College policies and procedures.

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

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

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

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

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

When the study member returns from leaving a handover should be prepared to give updates on the status of the tasks.

The existing and new study team members should document the study handover in a note to file or other documentation in the TMF. The note should contain some of the items above and the date of the handover. The new study team member should obtain documented study-specific training and any required approvals prior to being added to the duty delegation log.

4. Procedure:

Appointment Procedure:

The site clinical research coordinators have been appointed through respective site management organizations. Before assigning the CRC to Dr.D Y Patil Medical College, the Organization has to intimate the site personnel via mail or letter for communication with a proper appointment letter and period of agreement (If applicable).

Study Team Training:

1. On appointment, all study team members will be given an appropriate study depending on the job specification to possess the right experience and qualifications and further training may be provided to bring them up to the required level for specific tasks. Duty delegation/job responsibility document will be given to every Clinical research Coordinator/team member.

2. The Medical Director and department of clinical research recommend that all Investigators, CRC, and other study team members must undergo training that will enable them to understand their responsibilities, applicable regulations, guidelines, and research studies and training should be documented in the training log.

3. Each Investigator, CRC, and a study team member will review and learn the site's SOPs. It is recommended that SOP training must be included in the orientation of new clinical research personnel. All applicable clinical research personnel should be knowledgeable of new or revised SOPs.

4. Good Clinical Practice (GCP) is a universal standard in clinical research that must be followed in every research protocol. GCP training and education are recommended for research team members, especially the Investigator and CRC. However, any member of the research team with a significant role in the conduct of a research study must be knowledgeable in GCP. All members of the clinical research team should GCP trained and certified.

5. If scheduled, the PI and CRC will attend the Investigator Meeting (organized by Sponsor) and complete all required training for a study. If PI is unable to attend the meeting, PI can

recommend other study team members (s) to attend the IM. PI should be informed regarding the study contents discussed in IM.

6. Before study initiation the Sponsor/CRO will organize an SIV meeting at the site to train all study team members and all study team members should attend the meeting for a thorough understanding of the study.

7. In the study start-up activities like feasibility/study synopsis CRC should be intimate to the site personnel.

8. The PI and study team member(s) should be prepared to demonstrate all training received. CVs, GCP, and other training certificates should be updated as required. It is recommended that an assessment of the employee's knowledge of the regulations and guidelines can be conducted upon recruiting and on a regular basis. It is recommended that an assessment of any additional protocol-specific skill requirements be conducted prior to activation of each new study

9. Study team members should attend the course to acquire training or to update themselves.

10. PI can also train the study team and should maintain the training record.

11. It is recommended that the PI and study team must maintain the Site SOP training Record.

12. Entry into a Study drug store at site: The access will be given only to blinded/unblinded pharmacist who is delegated (Delegation log) in a clinical study for the IP management. The entry access will be restricted.

5. Applicable Staff:

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

These include the following:

- Investigator
- Research Team (listed in the delegation log)
- Clinical Research Coordinator

Staff responsible for Implementation:

- The department and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

- The department and PI will ensure that at the time of implementation of the SOP, the research team at the clinical research unit in Dr. D Y Patil Medical College, Kolhapur, are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

- It is the responsibility of each individual who are about to go on short / long term absences or leave their current position / the Agency/third party employees to prepare a hand over file.

SOP-IV. SOP -**Reporting of SAEs/ AEs**

Effective date: 01-Apr-2022 to 31-Mar-2025

Prepared By:

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I. OBJECTIVE:

This SOP gives the procedure for handling and reporting the Adverse Events and Serious Adverse Events encountered during the clinical studies at Dr.D.Y.Patil Medical College, Kolhapur

II. SCOPE:

Applicable to all Clinical studies.

III. PRECAUTION: Nil

IV. DEFINITION:

a. Definitions:

Serious Adverse Event: Any untoward medical occurrence that at any dose results in death, is life- threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

Serious Adverse Event or Serious Adverse Drug Reaction: An AE or ADR that is associated with death, inpatient hospitalization (in case the study was being conducted on out-patients), prolongation of hospitalization (in case the study was being conducted on in-patients), persistent or significant disability or incapacity, a congenital anomaly or birth defect, or is otherwise life threatening.

- Adverse Event: An AE is any untoward medical occurrence in a patient or clinical investigation of subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

- Unexpected Adverse Event: Any adverse event occurring in one or more subjects such that, the nature, severity or frequency of which is not consistent with either:

a) The known or foreseeable risk of adverse event associated with the procedures involved in the clinical study that are described in (a) the protocol- related documents, such as the IEC- approved Study protocol, any applicable investigator brochure, and the current IEC- approved informed consent document and (b) other relevant sources of information, such as product labeling and package inserts; or

b) The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event (if applicable).

1) Relatedness/ Causality assessment of Adverse Event to an Investigational Drug:

Relatedness/ Causality assessment of Adverse Events will be as per the WHO- UMC causality assessment system as mentioned.

WHO- UMC Causality Categories

Causality term	Assessment criteria*
Certain	• Event or laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or

Probable/ Likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible)
Conditional/ Unclassified	• Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Un assessable/ Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient or contradictory • Data cannot be supplemented or verified

*All points should be reasonably complied with

2) Severity: The degree of an adverse event is divided into mild, moderate, or severe.

- Mild: Minimal interference in day-to-day activities, Special treatment may not be required to treat adverse event, Symptoms are transient.

- Moderate: Discomforting events, interference in day-to-day activities, therapeutic measures are required to treat adverse event.
- Severe: (As mentioned in the 'Definitions' section above) Severe discomfort, Day-to day activities are impossible, major therapeutic intervention is required to treat adverse event.

V) PROCEDURE:

1.0 Handling of Adverse Event

a. The Clinical Investigator/Medical Officer will explain the expected adverse events identified in the Study Protocol/product literature or package insert in the study meeting held prior to the conduction of the Clinical study.
b. The designated person will monitor the subject(s) for any untoward or unfavorable and unintended sign (including abnormal Clinical laboratory finding), symptom during the Visits and study housing. The designated person will also consider any Adverse Event occurring after discharge of the subject from the clinical facility (during washout period, during the anticipated duration of action of the drug(s) or also thereafter at the discretion of the Clinical Investigator).
c. On occurrence of an Adverse Event the designated person will examine the subject and will give assurance or provide appropriate medical care to ensure well being of the subject in accordance with currently acceptable clinical standards and guidelines.
d. The designated person will further ask the subject about the adverse event in detail to ascertain the severity and/or circumstances contiguous to the adverse event, including any medication taken (if any) after discharge from the study center, so that the event can be judged clinically.
e. Whenever required, the designated person will also inquire about the progress of the adverse events to the subject telephonically. The subject is also requested to report the Adverse Event at any time to the designated person.

f. The designated person will review the post study clinical laboratory report (pathological report) for any out of range values, these values will be compared with the baseline reports values to determine its significance for evaluation of any Adverse event. If any clinically significant observation(s) are found in the Clinical laboratory reports then it will recorded in the Adverse Event Form of the CRF, attached as Annexure- 01, and the designated person will inform the subject about the evaluation and will request him/her to report to the Study center for follow up.

g. The designated person will record the follow ups in the 'Telephonic Communication and Subject Follow- up Form' of the CRF, attached as Annexure- 02

h. The decision for any further diagnostic test(s) or specialist consultation is required for the management of the adverse event, will be done on the discretion of the Clinical Investigator/Co- Investigator.

i. The designated person will monitor the subject or follow up with the subject till the resolution of the Adverse Event.

j. designated person will record the Adverse Event, time of occurrence, time/date of resolution, the assessment of causality, severity, expectedness/unexpectedness and course of treatment or action (if appropriate), in the 'Adverse Event Form' of the CRF of the respective subject.

k. If in the judgment of the Clinical Investigator/Co- Investigator the continuation of the subject proves harmful to him/her, then will take the decision to terminate the subject from the study. The termination details will be recorded in the 'Subject Drop- Out/Withdrawal/Termination Form' of the CRF of the respective subject. Handling of Serious Adverse Event (SAE).

l. In case of occurrence of any Serious Adverse Event, Clinical Investigator/Co- Investigator/Medical Officer will give preliminary treatment (if required) to the subject in the Emergency Care Unit (ECU) of Hospital. As per the 'Standard Operating

Procedure for ECU maintenance and handling Emergency Situation' and then will shift the subject to the emergency facility (if required).

m. The subject will be monitored till the resolution of the Serious Adverse Event or on the discretion of the Clinical Investigator/Co-Investigator.

n. The Medical Officer will record the Serious Adverse Event, time of occurrence, time/date of resolution, the assessment of causality, severity, expectedness/unexpectedness and course of treatment or action (if appropriate), in the 'Serious Adverse Event Form' of the CRF of the respective subject, The Medical Officer will keep all the relevant medical record including the hospital record along with the CRF of the respective subject.

o. The Medical Officer will also record details in the 'Logbook for Serious Adverse Event details.

p. Clinical Investigator/Co-Investigator will review the details recorded in the respective subject's CRF and in the 'Logbook for Serious Adverse Event Details'.

q. The termination of the subject from the study due to a Serious Adverse Event will be documented in the 'Subject Drop-Out/Withdrawal/Termination Form' of the CRF of the respective subject.

2.0 Reporting of Adverse event:

Reporting of the adverse event by the Investigator:

- Unanticipated problems involving risks to subjects should be reported promptly.
- Summary of the adverse events and any unanticipated problems involving risks to the subjects should be reported at continuing review.
- Any information about risks associated with the clinical study, should be reported at continuing review.
- A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure (e.g agranulocytosis, hepatic injury)

- A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with drug exposure, but uncommon in the study population.
- Multiple occurrence of an AE that, based on an aggregate analysis, is determined to be an unanticipated problem. There should be a determination that series of AEs represents a signal that the AEs were not just isolated occurrence and involve risk to human subjects. A summary and analyses supporting the determination should accompany the report.
- An AE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations.
- A Serious Adverse Event that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence.
- Any other AE or safety finding that would cause the sponsor to modify the investigator's brochure, study protocol, or informed consent documents or would prompt other action by the IEC to ensure protection of human subjects.
- An AE observed during the conduct of a study should be considered an unanticipated problem involving risk to human subjects, and reported to the IEC, only if it were unexpected, serious, and would have implication for the conduct of the study (e.g. requiring a significant, and usually safety-related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent, or Investigator's brochure). An individual AE occurrence ordinarily does not meet these criteria because, as an isolated event, its implications for the study cannot be understood. Many types of AEs generally require an evaluation of their relevance and significance to the study, including an aggregate analysis of other

occurrence of the same (or similar) events, before they can be determined to be an unanticipated problem involving risk to human subjects.

2.1 Reporting of the adverse event by the Investigator to Sponsor:

There is no severity or expectation threshold to trigger the investigator's responsibility to report to the sponsor adverse events related to the drug. The sponsor however is required to report only serious, unexpected and related adverse event experiences to the Regulatory.

- Adverse events that could be reasonably regarded as caused by or probably caused by the drug, to be reported promptly unless the event is alarming, in which case, to be reported immediately;
- Serious adverse events, to be reported immediately unless the protocol or other document indicates otherwise. It is essential to specify clearly in the protocol and the adverse event reporting section of the protocol, what is and is not expected as well as what is and is not regarded as serious.
- The time lines for notifying of SAE both death and other than death events by the Investigator to Sponsor as per 122 DAC of New Drugs and Clinical Trial Rules.2019 is within 24 hours of identifying the event

2.2. Reporting of the serious adverse event by the Sponsor to the Regulatory authorities:

Reporting requirements for the Sponsors to the Regulatory include time frames as follows:

- Adverse experiences that are associated with the use of the drug and that are both Serious and Unexpected, Unexpected fatal or life-threatening experience associated with use of the drug, to be reported within 24 hours of the occurrence;
- Any adverse experience with a licensed product that is serious and unexpected, whether domestic or export, to be reported by the license holder within 24 hours of the occurrence, by the licensed manufacturer.

- The time lines for reporting of SAE- death and other than death events by the Sponsor (after due analysis) to the Licensing authority (DCGI) as per 122 DAC of New Drugs and Clinical Trial Rules.2019 is within 10 days of occurrence of SAE and reporting of death to chairman of the expert committee –at CDSCO office within 10 calendar days of the occurrence of SAE.
- As per 122 DAC of New Drugs and Clinical Trial Rules,2019 the Sponsor/representative shall pay the compensation in case of clinical study- related injury or death within 30 days of receiving the order from licensing authority (DCGI). For SAE other than death, the study subject will get the compensation and in case of death, the nominee of the subject will get the compensation.
- In post marketing studies, sponsors must not only report under MedWatch (The FDA's safety information and adverse event reporting program, which provides information about safety issues and provides an online gateway for reporting adverse events) requirements but also be consistent with reporting obligations for IND research that require reporting serious consequence or adverse effects of an already approved and legally marketed drug.

2.3. PI Reporting of the serious adverse event to the Ethics Committee

- It is the responsibility of The Principal Investigator should submit within 24 hours an SAE report or the unexpected adverse event report to the Sponsor, IEC, DCGI by hard copy/ by email.
- The report of SAE of due analysis shall be forwarded by the Investigator to IEC, DCGI, sponsor, and Head of the institution within 30 calendar days of the occurrence of SAE.
- The report should be accompanied by a detailed narrative of the SAE and New Drugs and Clinical Trial Rules.2019
- It should be submitted as per checklist detailed by Licensing Authority.

- IEC will perform Causality Assessment with reasoning for Relatedness/Un-relatedness and will communicate to DCGI within 30 days of Occurrence of SAE (as per CDSC Rules)
- PI also communicates the SAE initial report to the Head of the Institution

2.4. Reporting of the adverse event by the Sponsor to other Investigators:

Sponsors are required to report to another investigator in a multisite trial. The requirements are similar to those for sponsors reporting to the Regulatory. The reporting obligations include the following:

- Adverse events that are serious, unexpected, and associated with the drug, to be reported promptly.
- Any new observations discovered by or reported to the sponsor about the drug (other than the other safety information) as the investigation processed.
- The Ethic Committee shall forward its report of death and/or any other SAE after due analysis on SAE with its opinion on the financial compensation (if any) to be paid by the Sponsor to DCGI office, and the report of death to the Chairperson of expert committee – at CDSCO office within 30 calendar days.

2.5. Reporting of the Serious Adverse Event (SAE) by the Investigator to DCGI/CDSCO through the SUGAM Portal

a) All SAEs occurring in clinical studies should be reported as per the details provided in New Drugs and Clinical Trial Rules.2019 within the applicable timeline to, The Drugs Controller General (India)

Directorate General of Health Services Central Drugs Standard Control Organization (CDSCO) FDA, Bhawan, Kotla Road, New Delhi – 110 002

b) Pharmaceutical company/the Sponsor/CRO (Investigator in investigator-initiated studies) is responsible for reporting SAEs within the applicable timelines.

c) Every report (both initial as well as follow-up reports) should be submitted along with a covering letter.

d) Covering letter should be prepared using the template as guide, and printed on the company/CRO's letter head, attached is the template of covering letter.

e) Instructions are provided in the template as highlighted text in *"Italics"*. Delete all instructions from the final letter.

f) All the sections of the covering letter should be completed. When some information is not available at the time of report e.g. causality assessment by medical monitor of Sponsor/CRO, compensation provided for study related injury or death, the same has to be provided as a follow-up report.

g) All the clinical trial-related SAEs to be uploaded through CDSCO online sugam portal

h) Covering letter of every report arising from the clinical trials (CT) has to capture, (at the stipulated box provided in the template) as per the format.

   i. DCGI CT file number
   ii. Complete address of Sponsor and CRO (if any) including phone & e-mail address
   iii. Phase of clinical trial
   iv. Category of the clinical trial as per the codes mentioned below. Mark the appropriate Code from this list provided in the covering letter using below details.
   v. Protocol or Study No./Code/ID and the study title.
   vi. Adverse event term/diagnosis (Whenever possible provide a 'preferred' term)
   vii. A brief narrative of the event, not exceeding 10 lines. A detailed narrative may be enclosed, if available.

Code	SAEs occurring in clinical trial
CT-1-IND	New Drug - Investigational New Drug (IND) study (where IND is filed in India and is an NCE)

CT- 2- Reg	New Drug –Local Clinical Trial– For product approval in India
CT- 3- GCT	New Drug –Global CTs
CT- 4rDNA	Biological –Recombinant products (Global CTs, India IND and study for product approval)
CT- 5- Vac	Biological –Vaccines (Global CTs, India IND and study for product approval)
CT- 6- Oth	Biological – Others (e.g. stem cell studies)
CT- 7- Dev	Device study (Global CTs, India IND and study for product approval)
CT- 8- Oth	Others

viii. Unexpected SAEs have to be submitted to the office as per Schedule Y of Drugs and Cosmetics Rules, 1945.

ix. Causality assessment by the investigator and the medical monitor of Sponsor / CRO.

x. The assessment report should clearly mention whether the SAE that occurred is related or not related (Situations like unlikely, possibly, suspected, doubtful etc should not be used).

xi. Whether the outcome is fatal

xii. Details of compensations provided for injury or death. In case no compensation has been paid, reason for the same should be submitted. It is pertinent to mention that in case of study related injury or death, complete medical care as well as compensation for the injury or death should be provided.

xiii. Mention whether it is “initial” or “follow- up” report. For follow- ups, clearly mention the follow- up report number e.g. Follow- up #01, Follow- up #02, etc. In case of follow- up reports, mention the date of submission of initial (first) report, as narrative.

xiv. Forms should be completed in legible English, illegible forms, incomplete with respect to critical information and improperly scanned / fax copies would be rejected by DCGI office.

xv. Relevant supportive documents may be enclosed

NOTE: Submission of same SAE in different forms/ format, in different occasions has to be avoided (e.g. submitting CIOMS forms and then later submitting the same event details as per New Drugs and Clinical Trial Rules, 2019

3.0. System of pre- screening for submission of reports of SAEs to CDSCO

i. In order to streamline the submission of reports of SAEs a pre- screening of reports of SAE submitted to CDSCO, this SAE includes death occurring during the clinical study to arrive at the cause of death/injury to the subject, as the case may be and to determine the quantum of compensation, if any to be paid by the Sponsor or his representative whosoever have obtained permission from CDSCO in a time- bound manner.
ii. As per this procedure, each SAE including death will be examined by the CDSCO and decision regarding causality of death and quantum of compensation (if any) will be taken by CDSCO in a time bound manner as per the procedure specified in the New Drugs and Clinical Trial Rules, 2019
iii. As per this New Drugs and CT rules 2019, the investigator shall report all serious and unexpected adverse events to CDSCO, the Sponsor or his representative whosoever had obtained permission from the CDSCO for the conduct of the clinical study and the Ethics committee within 24 hours of their occurrence.
iv. In case of serious adverse event of death, the reports shall be examined by an Independent expert committee constituted by DCG(I) to determine if the cause of death is due to following reasons, which are considered as clinical study related death and gives recommendation to CDSCO. In case of clinical study related death, the committee shall also recommend the quantum of compensation to be paid by the sponsor or his representative, to CDSCO.
    a) Adverse effect of Investigational product (s)
    b) Violation of the approved protocol, scientific misconduct or negligence by the Sponsor or his representative or the investigator;

c) Failure of the investigational product to provide intend therapeutic effect;

d) Use of placebo in a placebo–controlled study

e) Adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol;

f) For injury to a child in- utero because of the participation of parent in clinical study.

g) Any clinical study procedures involved in the study.

v. CDSCO shall consider the recommendations of the expert committee and shall determine the cause of the death and also the quantum of compensation in case of clinical studies related death within three months of receiving the report of SAE of death.

vi. In cases of serious adverse event other than death, CDSCO shall determine the cause of injury, if any, due to any of the reasons mentioned above as in the case of death, which is considered as clinical study related injury.

Note: CDSCO has option to constitute as independent Expert Committee, wherever considered necessary, to examine such serious adverse event. In case of clinical study related injury, CDSCO shall also determine the quantum of compensation within three (3) months of receiving of the SAE)

vii. In case of clinical study related injury or death, the Sponsor or his representative concerned shall pay the compensation as per the order of CDSCO within thirty (30) days of the receipt of such order.

viii. As per this procedure the preliminary scrutiny of the SAE reports will be done by CDSCO Officer (s) based on the laid down checklist attached as Annexure - 06. During the preliminary examination, the CDSCO Officer(s) will scrutinize the SAE report to ensure that it contains all the required administrative as well as technical information in

proper manner as per the checklist. CDSCO will only accept the SAE reports for further examination if it is submitted in accordance with the format and the checklist.

ix. Once the report of SAE is accepted by the CDSCO, the information in the report will be reviewed by CDSCO as per the specified procedures:

a) The Sponsor or his representative conducting clinical studies in India will have to prepare the SAE reports for submission to CDSCO as per New Drugs and CT rules, 2019

b) The SAE reports must be submitted with proper binding, indexing and page number.

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

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

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

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

d) Text and tables should be prepared using margins that allow the document to be printed clearly without losing any information and the left-hand margin should be sufficiently large so that information is not obscured by the methods of binding. The documents printed on both sides of a page, can be submitted. However care should be taken that the information is not obscured when the page is placed in a binder.

e) While submitting reply to a query, the applicant should always enclose with the reply, a copy of query letter issued by CDSCO.

VI) RFERENCES:

- Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants- 2011
- WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects 2013
- National Ethical guidelines for Biomedical and health research involving research participants Guidelines- ICMR- 2017
- New Drugs and Clinical Trial Rules, 2019

SOP-V. SOP- **Archival of study documents**

Effective date: 01-Apr-2022 to 31-Mar-2025

Prepared By:

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Reviewed By:

Dr.Shimpa Sharma Member-secretary	Signature with date

Approved By:

Dr.Rakesh Kumar Sharma Dean, Dr.D.Y.Patil Medical College, Kolhapur	Signature with date

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I. PURPOSE:

The purpose of this Standard Operating Procedure (SOP) is to describe the standard procedures to be followed when archiving essential paper/electronic documents related to clinical research/trial sponsored and conducted at Dr. D.Y.Patil Medical College and research institute, Kolhapur

All trial data must be kept so that the data can be accessed after the trial is finished. This may be necessary for the event of unexpected side effects after the trial drug has been approved. It is the responsibility of the Sponsor, and the Principal Investigator/ Institution to keep these records.

II. INTRODUCTION

Archiving is the act of storing and preserving non-active records with an enduring value. the archivist coordinates and ensures quality storage and easy retrieval of the records.

As specified in GCP, the sponsor as well as the investigator/institution (i.e. investigational site) should maintain essential trial documents in accordance with applicable regulatory requirements. Essential study documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 5-10 years (total 15 Years) have elapsed since the formal discontinuation of clinical development of the investigational product. However, these documents should be retained even longer if required by applicable regulatory requirements or else agreed with the sponsor.

III. SCOPE:

This SOP Will applies to all Clinical trials conducted at Dr.D.Y.Patil Medical College and Research Institute, Kolhapur

IV. RESPONSIBILITY:

- Archivist or designated personnel are responsible to follow this SOP during archival retrieval and re-archival of documents/data.
- Relevant department personnel have to follow this SOP while submitting documents for archival / re-archival and requesting retrieval of documents/data.
- It is the responsibility of the Dr.D.Y.Patil Medical College and Research Institute, Kolhapur to conduct a periodic audit to assure the implementation of this SOP.

V. DEFINATION

- **Archival:** The procedure of preserving documents in any media for longer storage, in a safe environment with controlled access.
- **Retrieval:** The procedure of getting the documents from the archives for reference, regulatory requirements etc.
- **Re-archival:** The procedure of re-archiving the documents after the purpose of retrieval is completed.
- **Clinical Trial** - Any investigation in human subjects, other than a non-interventional trial intended to discover or verify the clinical, pharmacological or other Pharmacodynamic effects of one or more medicinal product or to identify any adverse reactions to one or more such products and to study absorption, distribution metabolism and excretion in one of more such products with the object of ascertaining the safety or efficacy of those products.
- **International Council for Harmonisation (ICH)** - Produced a series of guidelines in 1996, E6 being the guideline on Good Clinical Practice, otherwise known as ICH-GCP. Formerly known as International Conference on Harmonisation.
- **Investigator Site File (ISF)** - A standard filing system which contains all essential documents held by Principal investigator(s) conducting a trial. Which individually

and collectively permit the evaluation of the conduct of a trial and the quality of the data produced.

- **Principal Investigator (PI):** A Registered Physician, Dentist who has responsibility for the conduct of the trial at a host site.
- **Essential Documents:** Essential documents are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. Essential documents include the Trial Master File, source documents and Case Report Forms (CRFs).
- **Trial Master File:** The Trial Master File is a file that consists of essential documents, which enable both the conduct of a clinical trial and the quality of the data produced to be evaluated. Those documents shall show whether the investigator and the sponsor have complied with the principles of Good Clinical Practice and with the applicable regulatory requirements.
- **Source Documents:** Source documents are original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).
- **Case Report Forms (CRFs):** A printed, optical or electronic document designed to record all of the protocol required information on each trial subject.

VI. PROCEDURE:

i. Archival Room Maintenance and Access control

- õ Access to the archival room shall be controlled and tracked.
- õ Access to archives is restricted to archivists and Administration. Entry of other individuals Third Party employees and external personnel such as Auditors / Clients) into the archival

facility shall be escorted by the archivist during visit. Entry and exit details shall be captured in the logbook as per Annexure 01 – Entry and Exit of Archives.

- õ Archival room is provided with the CCTV Camera, fire extinguisher, Heat and smoke detector.
- õ The temperature of 23(+/-) 4oC and humidity 30- 70%RH shall be maintained in archival room.
- õ Pest control activity shall be performed quarterly or as whenever required
- õ The archivist shall perform a quality check of the archives once in 06 months by visual audit for any signs of deterioration.
- õ The minimum signs of deterioration for visual evaluation include the following but are not limited to:
  - Presence of Paper Mites
  - Presence of Dust in the storage cabinets
  - Presence of Rodents/insects Excreta
  - Presence of any growth of molds
  - Presence of any self- deterioration of paper documents/files
- For any deterioration noticed, ensure immediate remedial actions are taken.

ii. Archival period: All essential documents relating to clinical study including monitoring documents, projects files and audit documents shall be archived in accordance with the requirements of the applicable regulations/guidelines as follows:

- o As defined in protocol or/ and as per the contract agreement with the sponsor
- o Until at least 2 years after the last approval of a marketing application in a region where the ICH guidelines apply
- o Until there are no pending or contemplating marketing applications in an ICH region.
- o Documents relating to clinical study documents shall be archived for a minimum period of 10 to 15 years (or) in accordance with Regulatory guidelines and

Dr.D.Y.Patil Medical College and Research Institute, Kolhapur which shall be decided by the management team as per requirement.

iii. Location of Archival Documents:

- Archived material shall be stored in a legible condition at Dr.D.Y.Patil Medical College and Research Institute, Kolhapur

VII. Frequency of archival:

i. Study documents:

- During the conduct of a study, study documents and data can be retained in the Archival room at Dr.D.Y.Patil Medical College and Research Institute, Kolhapur
- and stored in the project file and /or e-directory, or otherwise as specified in the contract/work order with the sponsor.
- Once the trial is completed, project documents shall be returned to the client or archived according to the terms and conditions as per regulations/site policies.
- Study documents shall be archived after the completion of the study and within 30 days. The Study completion letter along with study progress to submit to the IEC

ii. Non-Study related documents:

Superseded SOPs shall be archived within 10 working days from the date they become obsolete.

iii. Archival of paper documents:

- The respective department head/designee is responsible for notifying the archivist in writing, of the intent to archive study documents.

- All records related to the project shall be retained in a manner that shall preserve security, integrity, and authenticity.

- The contents in the files shall be verified against the index given in the respective files by the archivist before archival.

- Upon completion of the contracted archival period, the sponsor shall be informed/intimated in writing. If the archival period is extended by the sponsor
- While archiving do not compile all versions of single SOPs/Work Procedures of different departments together.

- If the responsibility of electronic archival is not delegated Dr.D.Y.Patil Medical College and Research Institute, Kolhapur, the protocol-specific electronic data, along with details of e-Data, shall be returned to the sponsor.

iv. Disposition of archived data/documents:

- Under circumstances, shall any archived material be removed/ destroyed by the Clinical service's administrators of Dr.D.Y.Patil Medical College and Research Institute, Kolhapur without intimation from the sponsor or any other specified in the contract with the sponsor.
- Processes for identifying materials that have reached the end of their retention period
- Upon completion of the contracted archival period, the sponsor shall be informed/intimated in writing. If the archival period is not extended by the sponsor then the study documents shall be returned to the sponsor and a list of documentation provided to the sponsor shall be created. A sponsor acknowledgment copy of this shall be retained.
- If required, disposition of study documents/data shall be outsourced to an external vendor by Dr.D.Y.Patil Medical College and Research Institute, Kolhapur

VIII. References:

1. 21 CFR 312.55- Informing Investigators
2. 21 CFR 312.57- Record Keeping and Record Retention
3. 21 CFR 312.58- Inspection of Sponsor records and Reports
4. 21 CFR 312.62- Investigator Record Keeping and Record retention
5. 21 CFR 312.64- Investigator Reports
6. Appendix V- CDSCO guideline: Essential Documents
7. ICH Guidelines for GCP (E6) Section 4.4- communication with IRB/IEC
8. ICH Guidelines for GCP (E6) Section 4.9- Records and reports
9. ICH Guidelines for GCP (E6) Section 5.22- Clinical Tail/Study Reports

SOP-VI. SOP- **Investigational Medicinal Products Management**

Effective date: 01-Apr-2022 to 31-Mar-2025

Prepared By:

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Reviewed By:

Dr.Shimpa Sharma Member-secretary	Signature with date

Approved By:

Dr.Rakesh Kumar Sharma Dean, Dr.D.Y.Patil Medical College, Kolhapur	Signature with date

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Objectives: The Investigator may assign an appropriate person (pharmacist/nurse) to be responsible for investigational product storage and accountability at the trial site.

1. GOALS OF INVESTIGATIONAL PRODUCT (IP) MANAGEMENT

1.1.The goals of IP management for this clinical trial include the following:

a) To ensure the protection of the subject and traceability;

b) To enable identification of the product and the trial;

c) To facilitate proper use and storage of the product;

d) To ensure the reliability and robustness of data generated in the trial.

e) To ensure to maintain the Temperature of IMPs

2. Communications:

a) Periodic GCP/Protocol Training will be conducted for the site Research pharmacists by the Sponsors/CROs/Site

b) The purposes of these GCP/Protocol training are to keep abreast of new information and protocol changes, to follow up on action items, to problem solve, to coordinate and collaborate on activities, to build relationships, and to review the results of pharmacy audits.

3. ROLES AND RESPONSIBILITIES:

- ROLES AND RESPONSIBILITIES OF SITE

3.a.1. The following Pharmacist will be responsible for IP management:

a) IP Shipment and receipt

b) IP Storage

c) IP Repackaging and relabeling

d) IP Dispensing and Accountability

e) IP Return and Destruction

3.a.2. The roles and responsibilities of the Pharmacist/study staff involved in IP management for this clinical trial will be documented in a Signed Signature Sheet. Study staff/Pharmacists will be trained on IP management procedures.

3.a.2.1. Training will be documented and maintained in the Investigator Site Files.

➢ ROLES AND RESPONSIBILITIES OF SPONSOR

a) This clinical trial will be monitored by the Sponsor monitor.

(For sites involved in IP repackaging and relabeling, describe that there will be two separate monitors:

a) The blinded monitor will be responsible for monitoring all aspects of the clinical trial except IP management. [to be intimated to site pharmacist prior to one week of the Monitoring]

b) The unblinded monitor will be responsible for monitoring the IP management of this clinical trial). [to be intimated to the site pharmacist prior to one week of the Monitoring]

4. Pharmacy Procedures:

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 by /Sponsor and in accordance with the protocol and applicable regulatory requirement(s).

Maintain 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 instructions properly (compliance).

Return any unused product to / Sponsor at the end of the trial.

SOP-VII. SOP- **Screening and Enrollment of study participants**

Effective date: 01-Apr-2022 to 31-Mar-2025

Prepared By:

Dr.Rajesh Jagannath Khalyalappa Department of Medicine, Dr.D.Y.Patil Medical College, Kolhapur	Signature with date

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I) OBJECTIVE: This SOP gives the procedure for screening and enrollment of subjects in all clinical trials at Dr.D.Y.Patil Medical College, Hospital and Research Institute, Kolhapur

II) SCOPE: This SOP is applicable for all clinical studies conducted in the facility.

III) PROCEDURE:

1) It is important that the principal investigator resolves all questions from his/her staff concerning the interpretation of Exclusion/Inclusion criteria.
2) The investigator should be able to dedicate time to the recruitment of each subject is likely to be longer than the time required for a normal consultation.
3) The Clinical Investigator/Co-investigator will inform the subject (s) by word of mouth about the recruitment of subjects for the study.
4) The Clinical Investigator/Co-investigator will schedule the screening dates and will inform the subject (s).
5) The Study Coordinator/designated person will issue the Ethics Committee approved 'Inform Consent Form' to the subjects who have come for the screening procedure.
6) The Designated person will give the information of the screening and the study-related activity to the subjects.
7) Clinical Investigator/Co-investigator/Medical Officer will request the interesting subjects and the subject's Legally Acceptable Representative (LAR) to sign the Ethics Committee approved 'Informed Consent Form" in the language best understood by them.
8) If the subject / Legally Acceptable Representative (LAR) is unable to read, then an impartial witness present during the presentation of the screening and study-related activities will explain the contents of the Informed Consent Form in the best language understood by the subject. After the subject consent for participation in the study the

subject and /or the LAR will sign /put thumb impression on the consent form and then the witness will sign and date the 'Informed Consent Form' as per 'Standard Operating Procedure for Obtaining Informed Consent from Subject'.

9) In case the subject requires more than the allotted time to inquire about the details of the study /drug product/or to consult his family Physician to decide about the participation in the Clinical trials, then the Investigator shall permit him/her to leave the study center and will ask him to return if he/she is willing to participate in the particular study.

10) The subject who is found eligible for participation in the study will be given a unique Screening identification number for identification of subject.

11) The responsible Person will measure the height, weight, and calculate the BMI of subject as per the BMI. The details of the demographic data will be recorded in the Screening Form of the CRF designed for the study.

12) Investigator/designated person will take the medical history, will conduct the physical examination (General and Systemic examination) and the vital measurement and record the details in the 'Screening Form' of the CRF.

13) Technician/designated person will take the 12 lead ECG of the subjects. The Technician/designated person will sign and date the ECG print and will attach the same to the respective subject's 'Screening form' of the CRF.

14) Investigator/designated person will review the ECG of the respective subject and will put the appropriate comment on the same after interpretation.

15) During the entire process of screening if the subject is found to be ineligible at any point of time, then the subject will not be considered for further screening procedure and will be excluded at that stage.

16) If the ECG of the subject is within normal limits then he/she will be sent for collection of blood and urine samples for Clinical Laboratory Investigations.

17) The Laboratory Technician (pathology)/Phlebotomist/Nursing staff will request the subject to collect the urine sample and will collect the blood sample after verifying the screening identification number of the subject from the 'Screening form', and on the labeled container/vial/vacationers used for collection of the respective sample and will make appropriate entry of the collection in the 'Test Requisition form' and the 'Screening form'. The biological samples will be then transferred to the Clinical Pathological Laboratory.

18) In case the Clinical Laboratory Investigation has to be done in an outsourced facility then the Study Coordinator/designated person will give the details of subject 's identification (screening identification number, initial, gender and age) and other required test information(s) to the respective Clinical laboratory person in the 'Test requisition form'.

19) After receiving Clinical Laboratory Investigation reports the Investigator/ designated person will review the reports and if any significant observations then it will be recorded in the clinical investigation details of the 'Screening form' of the respective subject. The Clinical Laboratory Investigation report will be attached to the 'Screening form' of the CRF of the respective subject.

20) The Investigator/designated person will review the complete screening record forms for the health status of the subject.

21) The X-ray has to be done for the subjects who are found fit in all the above procedures to avoid unnecessary exposure to radiation hazards.

22) The Investigator/designated person will record the observations reported by the radiologist in the 'Screening Form'. The X-ray film will be kept along with the screening documents and the report will be attached to the respective subject's 'Screening form'.

23) Study coordinator will compile the screening documents in the following sequence:

a) Screening Consent Form

b) Screening form (including the Demographic profile, medical history of subject s, Vital Sign and physical examination form, ECG and Clinical Investigation details form)

c) Clinical Laboratory Report(s), X-Ray reports

d) Other Investigation Report (if any)

1.0 Study Coordinator/designated person shall inform the eligibility of the subject to the subject or the LAR of the subject.

2.0 Laboratory Technician (pathology)/Phlebotomist/Nursing staff will request the subject to collect urine in labeled container and will perform the 'Urine Screen for Drugs of abuse' test for Urine Screen for Drug of Abuse and Serum Pregnancy test (for female subjects). The results will be recorded in the respective Pre-Enrollment Day Activity format of the subject. If the Test is found to be negative then the subject will be sent for further procedures.

3.0 If any additional test has to perform on this pre-enrollment day, then it will be performed as per the requirements specified in the Study protocol.

4.0 The Clinical laboratory Investigation report obtained from the in-house/ outsourced laboratory will be reviewed by the Investigator/designated person and the comments/discrepancy will be noted and recorded in the 'Pre-enrollment day activity' format of the respective subject. The Clinical Laboratory Investigation reports will be attached to this format.

5.0 After enrollment of the subject in the study coordinator/designated person will issue a Subject identification number/Subject number (ID card) and will be checked-in to the clinical facility.

6.0 The Study coordinator/responsible person will prepare the list of subjects enrolled in the format for 'Screening and Enrollment Log'

7.0 Randomization Procedures and Unblinding

- The Investigator must follow the randomization procedures, if any In the case of a randomized, Controlled, double- blinded trial, the code is usually prepared in the form of numbered envelopes, each containing the identification of the corresponding treatment in order to enable the Investigator to open the code when needed, without identifying other patients' treatment
- Ensure that the code is broken only in accordance with the Protocol and mainly for a medical reason(s).
- Premature unblinding must be reported to the Clinical Monitor immediately and should be documented in the File. The reason for premature unblinding of the investigational product should be given, e.g. due to a serious adverse event.
- At the end of the trial, the Investigator must return all the unbroken codes to the Clinical Monitor to prove that the study was blinded throughout

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(Institution Deemed to be University) KOLHAPUR

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