STANDARD OPERATING PROCEDURES FOR GOOD CLINICAL PRACTICE
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STANDARD OPERATING PROCEDURES FOR GOOD CLINICAL PRACTICE

INTRODUCTION

Adherence to the principles of good clinical practice is universally recognized as a critical requirement to the conduct of human subjects’ research. The Food and Drug Administration (FDA) regulations and guidance is intended to assist clinical investigators, sponsors and IRBs’ in the assurance that the rights, safety, well-being and confidentiality of study participants are protected. For researchers, complying with Good Clinical Practices (GCPs) often means creating, and adopting SOP’s into every aspect of the investigational site’s research.

There are two broad categories that can define clinical research studies: trials often with formal controlled protocols designed to test ways to prevent, diagnose or treat disease and observational studies with no direct intervention and participants are allocated treatment based on clinical decision. Whatever method is used following good clinical practice and operating procedures is imperative for the protection of the participants and for the interpretation of the results.

The purpose of these documents is to establish internal procedures for the identification and evaluation of consensus standards in research practice. These SOPs describe the processes that are used by the research program. The SOPs that follow are intended to complement existing processes and procedures. These are generic and should be viewed as recommendations.

The basic procedures are described step-by-step for a given topic. These represent a typical listing of what operations are ordinarily carried out in conjunction with that particular topic.

Following the SOP for most topics are the attachments. These are the site-specific forms and checklists that are not part of the official SOP document. These attachments describe the details for carrying out the procedures. Attachments can be changed without changing the text of the SOP.
## ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
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<td>PHI</td>
<td>Personal Health Information</td>
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<td>PI</td>
<td>Principal Investigator</td>
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<td>SAE</td>
<td>Serious Adverse Event</td>
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<td>SOP</td>
<td>Standard Operating Procedure</td>
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GLOSSARY

**Adverse Event (AE):** An AE is any untoward medical occurrence in a patient or clinical investigation subject enrolled in a study and/or 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.

**Audit Trail:** Documentation that allows reconstruction of the course of events also includes a secure, computer generated, time-stamped electronic record that allows reconstruction of the course of events relating to the creation, modification, and deletion of an electronic record.

**Audit:** A systematic and independent examination of research-related activities and documents to determine whether the evaluated research-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor’s standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s).

- **Internal audits** work within an organization and report to an audit committee or management. An internal audit is designed to look at the key risks facing the business and how the business is managing those risks effectively.

- **External audits** are independent of the organization audited. They provide experienced opinions on the truthfulness of the financial statements or data collected and perform work on a test basis to monitor systems.

**Blinding/Masking:** A procedure in which one or more parties to the research are kept unaware of the treatment assignment(s). Single blinding usually refers to the subject(s) being unaware, and double blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

**Case Report Form (CRF):** A printed, optical, or electronic document designed to record all of the protocol-required information to be reported to the sponsor on each study subject.

**Clinical Trial/Study Report:** A written description of a trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report.

**Clinical trial/study:** Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study
absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

**Compliance:** Adherence to all the research-related requirements, good clinical practice (GCP) requirements, and the applicable regulatory requirements.

**Confidentiality:** Prevention of disclosure, to other than authorized individuals, of a sponsor’s proprietary information or of a subject’s identity.

**Contract Research Organization (CRO):** A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor’s research-related duties and functions.

**Contract:** A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract.

**Digital Signature:** means an electronic signature based upon cryptographic methods of originator authentication, computed by using a set of rules and a set of parameters such that the identity of the signer and the integrity of the data can be verified.

**Direct Access:** Permission to examine, analyze, verify, and reproduce any records and reports that are important to evaluation of a clinical trial/research studies. Any party (e.g., domestic and foreign regulatory authorities, sponsors, monitors, and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects’ identities and sponsor’s proprietary information.

**Direct Entry:** means recording data where an electronic record is the original capture of the data. Examples are the keying by an individual of original observations into the system, or automatic recording by the system of the output of a balance that measures subject’s body weight. In these cases, the electronic document is the source document.

**Disability:** A substantial disruption of a person’s ability to conduct normal life functions.

**Documentation:** All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records; and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting research, and the actions taken.

**Electronic Case Report Form (e-CRF):** means an auditable electronic record designed to record information required by the clinical trial/research protocols to be reported on each study subject.

**Electronic Patient Diary:** means an electronic record into which a subject participating in a clinical trial/research directly enters observations or directly responds to an evaluation checklist.
**Electronic Record:** means any combination of text, graphics, data, audio, pictorial, or other information representation in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system.

**Electronic Signature:** means a computer data compilation of any symbol or series of symbols executed, adopted, or authorized by an individual to be the legally binding equivalent of the individual’s handwritten signature.

**Essential Documents:** Documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.

**Good Clinical Practice (GCP):** A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials/research that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of study subjects are protected.

**Impartial witness:** A person, who is independent of the research, who cannot be unfairly influenced by people involved with the research, who attends the informed consent process if the subject or the subject’s legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.

**Informed Consent:** A process by which a subject voluntarily confirms his or her willingness to participate in research, after having been informed of all aspects of the research 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.**

**Inspection:** The act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial/research and that may be located at the site of the research, at the sponsor’s and/or contract research organization’s (CRO’s) facilities, or at other establishments deemed appropriate by the regulatory authority(ies).

**Institutional Review Board (IRB):** An independent body constituted of medical, scientific, and nonscientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in research by, among other things, reviewing, approving, and providing continuing review of research, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the study subjects.

**Investigational Product:** A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial/research, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.
Investigator: A person responsible for the conduct of the clinical trial/research at a site. If research is conducted by a team of individuals at a site, the investigator is the responsible leader of the team and may be called the principal investigator.

Investigator’s Brochure (IB): A compilation of the clinical and nonclinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects.

Legally acceptable representative: An individual or other body authorized under applicable law to consent, on behalf of a prospective subject, to the subject’s participation in the clinical trial/research study.

Life-threatening adverse drug experience: Any adverse drug experience that places the patient, in the view of the investigator, at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction that, had it occurred in a more severe form, might have caused death.

Monitoring: The act of overseeing the progress of a clinical trial/research, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), GCP, and the applicable regulatory requirement(s).

Personal Health Information: Information that is created or received by a health care provider, health plan, employer, or health care clearinghouse; and relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual; and identifies the individual; or when there is a reasonable basis to believe the information can be used to identify the individual. (Under HIPAA regulations at 45 CFR 164, PHI (Protected Health Information) also includes: (i) Transmitted by electronic media; (ii) Maintained in any medium described in the definition of electronic media at §162.103, or (iii) Transmitted or maintained in any other form or medium.)

Predicate Rule: means an FDA regulation that requires the submission to and/or inspection by FDA, of certain data and information relevant to FDA-regulated investigational and/or marketed products. Examples include clinical trial data to support a New Drug Application or device Premarket Approval application.

Protocol Amendment: A written description of a change(s) to or formal clarification of a protocol.

Protocol: A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guideline, the term protocol refers to protocol and protocol amendments.
Quality Assurance (QA): All those planned and systematic actions that are established to ensure that the research is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement(s).

Quality Control (QC): The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the research-related activities have been fulfilled.

Randomization: The process of assigning study subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

Serious adverse drug experience (ADE): Any experience that results in death, in a life-threatening ADE, inpatient hospitalization or prolongation of hospitalization, a persistent or significant disability or incapacity, or congenital anomaly.

Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (Serious ADR): 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 or requires medical or surgical interventions to prevent any of the above outcomes.

Source Data: All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial/research necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).

Source Documents: Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects’ diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial or research study).

Sponsor: An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial/research study.

Standard Operating Procedures (SOPs): Detailed explanation of how a policy is to be implemented to achieve uniformity of the performance of a specific function.

Sub-investigator: Any individual member of the clinical trial/research team designated and supervised by the investigator at a site to perform critical trial/research-related procedures and/or to make important trial/research-related decisions (e.g., associates, residents, research fellows).

Subject/Trial Subject: An individual who participates in a clinical trial/research, either as a recipient of the investigational product(s), as a control.
**Unexpected adverse drug experience:** Any adverse experience the specificity or severity of which is not consistent with the current Investigator Brochure, or if an Investigator Brochure is not required, that is not consistent with the specificity or severity in the risk information described in the general investigational plan or elsewhere in the current application, as amended.

**Vulnerable Subjects:** Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.
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<td>E  Principal Investigator Job Description</td>
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<td>F  Research Nurse/Coordinator Job Description</td>
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<td>G  Data Manager Job Description</td>
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<td>B  Serious Adverse Event Report</td>
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<td>Specimen Shipping Log</td>
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<td>Data Management</td>
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<td>List of Logs Kept for Each Study</td>
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<td>Management of Electronic Records and Signatures</td>
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<td>Guidelines for Safeguarding Personal Health Information</td>
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<td>Fax Log</td>
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STANDARD OPERATING PROCEDURE ON SOPs:
PREPARING, MAINTAINING AND TRAINING

I. INTRODUCTION AND PURPOSE

This Standard Operating Procedure’s (SOP) describes the process needed for producing, revising and approval of SOPs which may include review of methods format and numbering for SOPs. It describes the preparation and maintenance of the written procedures that the research team follows to ensure compliance with all FDA regulations and GCP guidelines for all research and clinical trials conducted at this investigative site. This SOP also describes procedures for training on SOPs and documentation of training.

2. SCOPE

This SOP procedure describes the development, approval, implementation, management and change procedures of the SOPs. It describes the operating policies of the SOPs in the institution and concerns all personnel working in clinical research and especially those working on clinical studies involving human subjects.

3. APPLICABILITY

Well written SOPs with training help maintain process and quality control, reduce system variation, facilitate training, assist with employee orientation and training, refresher and advanced training, work site reminders, cross training, performance appraisal, employee safety, accident prevention, process improvement, quality control, and job description development.

4. RESPONSIBLE PARTIES

It is the responsibility of the principal investigator at this investigative site to approve all SOPs. The principal investigator assumes ultimate accountability for all SOPs. It is the responsibility of all members of the clinical research team involved in supervising, managing, or conducting study-related activities to follow the SOPs. This includes the following:

1. Principal investigator
2. Sub-investigator
3. Research manager
4. Research nurse/coordinator
5. Study pharmacist
6. Data manager
7. Support staff
5. REFERENCES TO OTHER APPLICABLE SOPs

All SOPs are applicable to this SOP.

6. ATTACHMENT A

Training Compliance Form

7. PROCEDURES
   A. SOP formatting
      a. The header section of each page contains the Institution’s name, title of the SOP, the SOP number, original version date, effective date and revisions.
      b. The footer section of each page contains the Institutional name, page number, version number and date
      c. The font of the SOP will be Times New Roman, 11 point.
      d. The text section is numbered using a standard format.
      e. Each SOP may contain the following sections. Additional sections can be added as necessary.

1. Purpose: defines the general area and how it is used
2. Scope: will describe specific tasks to be covered
3. Applicability
4. Attachments when relevant
5. Responsible parties
6. Process Overview
7. Procedures: provides step by step instructions
8. List of Attached Forms: lists forms and documents related and that may work in conjunction with each SOP
B. Revision, Implementation and Monitoring of SOP
   a. Talk with employees to gain agreement that procedures and expectations are appropriate and achievable.
   b. Use the team and other experts to address opportunities, problems and concerns.
   c. Review for accuracy, completeness and appropriateness.
   d. Have employees check the written procedures against actual practices before implementation.
   e. Principle investigator should approve all SOPs and designate an effective date.
   f. Distribute the new SOP, inform and train employees on the written SOPs and any new information.

C. Monitor SOPs regularly, and make revisions appropriately.
   a. SOPs should be reviewed annually to ensure regulations are up to date.
   b. All SOPs will be reviewed at least once every 3 years but preferably on an annual basis to ensure compliance to applicable regulations, policies and procedures.
   c. If determined that revisions are needed, follow the procedure described above.
   d. Previous versions should be retained.
   e. Ensure that SOP is followed consistently over time.

D. All staff should have SOP training within a specified period of time.
   a. Training should be documented on the Training Compliance Form.
   b. SOP should be accessible to staff.
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<thead>
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<th>SOP #</th>
<th>Standard Operating Procedure Title</th>
<th>Initials</th>
<th>Date Reviewed</th>
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Reviewed by: _____________________________  ____/____/____
1.2

STANDARD OPERATING PROCEDURE FOR RESPONSIBILITIES OF THE RESEARCH TEAM

1. INTRODUCTION AND PURPOSE

The principal investigator (PI) is the individual of record who assumes the authority and responsibility for the conduct of a clinical study. By signing Form FDA 1572, the PI agrees to comply with the conditions required by the FDA for use of investigational articles. The PI has the authority to delegate responsibility to individual members of the research team; however, the PI is ultimately responsible for the overall conduct of the study.

2. SCOPE

This standard operating procedure (SOP) defines the responsibilities of the research team for conducting clinical studies at this investigative site. It identifies administrative accountability as well as general responsibilities of the research team and of individual team members for fulfilling regulatory and clinical requirements.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.53 Selecting investigators and monitors
21 CFR 312.60 General responsibilities of investigators
21 CFR 312.61 Control of the investigational drug
21 CFR 312.62 Investigator recordkeeping and record retention
21 CFR 312.64 Investigator reports
21 CFR 312.66 Assurance of IRB review
21 CFR 312.68 Inspection of investigator's records and reports
21 CFR 312.69 Handling of controlled substances
21 CFR 54 Financial Disclosure by Clinical Investigators
May 1997 International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline.
4. REFERENCES TO OTHER APPLICABLE SOPs

All SOPs are applicable to this SOP.

5. ATTACHMENTS

A. Form FDA 1572
B. Delegation of Authority Form
C. Research Nurse/Coordinator Job Description
D. Data Manager Job Description
E. Research Assistant Job Description
F. Study Pharmacist Job Description
G. Orientation Checklist
H. Employee Evaluation Form
I. Criteria for Review

6. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in supervising, managing, or conducting study-related activities. This includes the following:

- Principal investigator
- Sub-investigator
- Research nurse/coordinator
- Research manager
- Data manager
- Study pharmacist
- Technician
- Support staff

7. PROCESS OVERVIEW

A. Administrative responsibilities
B. General responsibilities of the research team
C. Individual responsibilities within the research team
8. PROCEDURES

A. Administrative responsibilities

PI
Research manager
Research nurse/coordinator

- Participate as appropriate in the hiring and training of individuals recruited as members of the research team.
- Assign trained research nurse/coordinators to manage each clinical study planned or ongoing at this site.
- Manage the business aspects of studies, including developing and negotiating study budgets and contracts.
- Design appropriate recruitment strategies and track study enrollment.
- Communicate with the IRB as appropriate.

B. General responsibilities of the research team

PI
Sub-investigator
Research manager
Research nurse/coordinator
Study pharmacist
Support staff

- Conduct clinical studies according to FDA regulations and guidelines and SOPs of this clinical site and according to the policies and procedures of this institution, if appropriate.
- Ensure that the PI is informed in a timely manner of all study-related activities through: meetings, memos, reports and/or face to face communication.
- Ensure the safety and welfare of study subjects by being knowledgeable about ongoing study protocols and investigational articles.
- All investigators and covered research personnel must comply with federal regulations governing disclosure of personal, professional or financial interests in a research study that may impact upon its conduct, evaluation or outcome.
C. Individual responsibilities within the research team

PI

- Sign Form FDA 1572 to acknowledge responsibilities as defined by the regulations (Attachment A, Form FDA 1572).
- Provide sponsor with required information that either:
  - Attests to the absence of financial interests or arrangements as described in the regulations (CFR 54.4) and reported on Form FDA 3454 that is completed by the sponsor), or
  - Provides the sponsor a complete and accurate disclosing of financial interests and arrangements as described in the regulations (CFR 54.4) and reported on Form FDA 3455 that is completed by the sponsor.
- Supervise members of the research team qualified by their education and training to accept these responsibilities for study-related activities not directly performed by the PI.
- Document the delegation of responsibilities (Attachment D, Delegation of Responsibility Form).
- Ensure the safety and welfare of study subjects by being knowledgeable about ongoing study protocols and investigational articles.
- Participate as appropriate in the hiring and training of individuals recruited as members of the research team.
- Assign trained research nurse/coordinators to manage each clinical study planned or ongoing at this site.
- Ensure that specific sponsor requirements of the PI are fulfilled as requested.
- Meet with sponsors’ representatives as appropriate to discuss planned and ongoing
Research nurse/coordinator
Data manager

- Meet with auditors (internal, sponsor and FDA) at the conclusion of their audits to review findings.
- Develop organizational aids and checklists to facilitate patient recruitment and enrollment as well as the collection of complete and accurate study data.
- Enroll subjects in studies and manage their participation according to ethical, regulatory, and protocol-specific requirements.
- Maintain the regulatory and study files for each research project.
- Participate in quality assurance activities (monitoring visits, internal audits, sponsor audits, FDA audits).

Research team

- Fulfill those job responsibilities specific to that job title according to federal regulations and guidelines as well as the appropriate SOPs (Attachments E, F, G and H for job descriptions and qualifications).
Attachment A
FORM FDA 1572

To retrieve (PDF) format of the above forms go to web site:

http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf

Download this form, or Xerox a copy of the form provided as an attachment in the SOP printed document.
Attachment B
Form FDA 3454

To retrieve (PDF) format of the above forms go to web site:

http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048304.pdf

Download this form, or Xerox a copy of the form provided as an attachment in the SOP printed document.
Attachment C
Form FDA 3455

To retrieve (PDF) format of the above forms go to web site:

http://www.fda.gov/downloads/aboutfda/ReportsManuals/Forms/Forms/UCM048310.pdf

Download this form, or Xerox a copy of the form provided as an attachment in the SOP printed document.
Attachment D

**DELEGATION of RESPONSIBILITY FORM**

I, ____________________ MD, located at ___________________________

am Principal Investigator for Protocol # ____________________________

entitled ____________________________

________________________________________________________________________

I have ensured that the individuals listed below are properly qualified and have received appropriate training. Based upon this, I have delegated the following responsibilities to the individuals named below, and assert that these duties will be performed under my direct supervision:

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<thead>
<tr>
<th>RESPONSIBILITY</th>
<th>PERSONNEL</th>
<th>DATE</th>
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<tbody>
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<td>Administration</td>
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<td>Contract negotiations</td>
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<td>IRB submissions &amp; communications</td>
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<td>Patient recruitment activities</td>
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<td>Regulatory files creation and maintenance</td>
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<td>Data management/CRF completion</td>
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<td>Adverse event reports</td>
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<td>Organizational tools</td>
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<td>Office staff training</td>
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<td>Storing, dispensing, accounting for study drug</td>
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<td>Subject Management</td>
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<td>Screening subjects for eligibility</td>
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<td>Obtaining informed consent</td>
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<td>Monitoring patient compliance</td>
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<td>Subject enrollment and follow-up</td>
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<td>Appointment scheduling</td>
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____________________________________  ______________________  
Signature                                 Date
JOB TITLE: PRINCIPAL INVESTIGATOR

PURPOSE: PROMOTES GOOD CLINICAL PRACTICES IN THE CONDUCT OF CLINICAL INVESTIGATIONS

Assuring adherence to protocol requirements, protecting the rights and welfare of subjects, assuring the integrity of data generated at the site and directing the conduct of the clinical investigation according to federal and state regulations and guidance documents.

ESSENTIAL JOB RESULT:

1. PROVIDES INVESTIGATOR QUALIFICATIONS AND AGREEMENTS

   o maintaining a current, up-to-date curriculum vitae
   o maintaining current licensure to practice
   o providing the sponsor and IRB with documentation of credentials as requested
   o demonstrating the proper education, training and experience to conduct the clinical investigation
   o assuming responsibility for the conduct of the clinical investigation
   o signing the Form FDA 1572 as appropriate
   o signing the protocol as required
   o signing sponsor contract(s) as appropriate
   o documenting the financial aspects of the trial
   o disclosing conflicts of interest as described in the regulations

2. ASSURES PROTOCOL COMPLIANCE

   o possessing a thorough understanding of the requirements of each protocol
   o determining that inclusion/exclusion criteria are applicable to the study population
   o assuring recruitment goals are reasonable and attainable
   o assessing overall protocol feasibility
   o following the trial’s randomization procedures
   o not implementing any protocol deviation or changes without agreement by the sponsor and prior review and approval by the IRB (except to eliminate immediate hazards to the subject)
   o reviewing the inclusion/exclusion criteria, schedule of visits, end point criteria and investigational article use with the research team
JOB TITLE: PRINCIPAL INVESTIGATOR

ESSENTIAL JOB RESULTS:

3. ASSURES INITIAL AND ONGOING REVIEW BY THE IRB
   - providing the IRB with adequate information to initially review the study (i.e., protocol, investigator’s brochure, informed consent form, recruitment advertisements and any written information to be given to subject(s))
   - providing the IRB with documents for ongoing review (i.e., amendments to the protocol, adverse events, deviations or new information)
   - securing written IRB approval prior to initiating the study or instituting any changes to the protocol as approved
   - providing written summaries of the study status to the IRB annually, or as requested
   - providing written information of premature termination or suspension of a trial
   - providing the IRB with all documents subject to their review

4. DETERMINES ADEQUATE RESOURCES ARE AVAILABLE TO CONDUCT THE STUDY
   - having adequate number of qualified staff to conduct the study
   - having adequate facilities to conduct the study
   - assuring he/she has adequate time to conduct and supervise the study

5. MANAGES THE MEDICAL CARE OF SUBJECTS
   - assuring that a qualified physician (PI or sub-investigator) is responsible for all trial-related medical decisions
   - assessing subject compliance with the test article and follow-up visits
   - assessing subject’s response to therapy
   - evaluating for adverse experiences
   - ensuring that medical care is provided to a subject for any adverse event(s)
   - informing a subject when medical care is needed to treat an intercurrent illness(es)
   - informing the subject’s primary physician about their participation in the trial

6. PROTECTS THE RIGHTS AND WELFARE OF SUBJECTS
   - reporting all serious adverse events immediately to the sponsor and IRB
   - assuring that the informed consent form contains all the elements required by CFR 56 and 45
obtaining a signed and dated informed consent from the subject or subject’s legal representative prior to initiating any study-related procedures
informing the subject or legal representative about all aspects of the clinical trial
providing new information about the study or test article(s)
ensuring subject confidentiality
providing the subject or subject’s legal representative with a copy of the signed and dated informed consent form
assuring that the informed consent form is in language that is understandable to the subject
securing a witness to the informed consent process when the subject or legal representative is unable to read
allowing ample time and opportunity for the consent process and answering questions about the trial to the satisfaction of the subject or legal representative
securing consent/assent from minors and mentally impaired subjects as appropriate
following emergency use guidelines for waiver of consent in emergency situations as directed by the federal regulations and IRB policy and procedures

7. ASSURES VALIDITY OF THE DATA REPORTED TO THE SPONSOR

ensuring the accuracy, completeness, legibility and timeliness of case report forms
ensuring that case report forms accurately reflect source documents
explaining any discrepancies between source documents and case report forms
endorsing changes or corrections to a case report form

8. ASSURES DOCUMENTATION OF STUDY-RELATED PROCEDURES, PROCESSES AND EVENTS

documenting deviations from the approved protocol
documenting and explaining premature un-blinding of the investigational product(s)
documenting that informed consent has been obtained from the subject or legal representative
ascertaining the reason for a patient’s premature study withdrawal
documenting adverse experiences
complying with written procedures to document changes to data and/or case report forms
maintaining trial documents as required by the regulations and sponsor for the appropriate timeframe and under secure conditions
providing study reports as requested by the sponsor, IRB and regulatory authority(ies)
JOB TITLE: PRINCIPAL INVESTIGATOR

ESSENTIAL JOB RESULTS:

9. ASSURES THE PROPER USE AND STORAGE OF INVESTIGATIONAL AGENTS
   ○ being thoroughly familiar with the use of the investigational product(s)
   ○ reading the current investigator’s brochure, product insert, or other source information
   ○ assuming responsibility for the investigational product at the study site
   ○ ensuring the proper use and storage of the investigational product(s) at the site
   ○ reviewing the proper use of the study article(s) by the subject(s)

10. DIRECTS SITE OPERATIONS
    ○ communicating effectively with subjects, research team, IRB and sponsor
    ○ meeting regularly with the research team to discuss subject participation and protocol progress
    ○ assuring that all research staff are informed about the protocol and investigational products
    ○ being knowledgeable about regulatory requirements and GCP standards
    ○ preparing for and attending investigator and start-up meetings
    ○ participating in monitoring visits and audits as appropriate
    ○ permitting monitoring and auditing by the sponsor and appropriate regulatory authorities
    ○ making available to monitors, auditors, IRB and regulatory authority(ies) all requested trial-related records
    ○ delegating authority at the site appropriately
    ○ assuring that all research staff are informed about their trial-related duties and functions
    ○ maintaining a list of qualified persons and their corresponding trial-related delegated duties

11. MAINTAINS PROFESSIONAL AND TECHNICAL KNOWLEDGE
    ○ attending educational workshops
    ○ reviewing professional publications
    ○ participating in professional societies
# RESEARCH NURSE/COORDINATOR
## JOB DESCRIPTION

### GENERAL DESCRIPTION
The primary responsibility of the research nurse/coordinator is to manage all aspects of conducting clinical trials/research studies. The research coordinator is required to have an in-depth knowledge of protocol requirements and good clinical practices as set forth by federal regulations. As the primary resource for the protocols, the research nurse/coordinator will act as liaison between the investigators, primary care providers, the institutional review board (IRB), and the sponsor. Along with the investigator, the research nurse/coordinator will screen, enroll and follow study subjects, ensuring protocol compliance and close monitoring while the subjects are on study. In addition, the nurse/coordinator is responsible for all data and source documentation, adverse experience reporting, and maintenance of complete regulatory files.

### QUALIFICATIONS
Registered nurse with a current license to practice, and at least two (2) years of clinical experience; or baccalaureate in a health-related field and at least four (4) years of clinical research-related experience, certification preferred, or two (2) years clinical research-related experience and a Masters degree in a related field.

### CRITERIA FOR EVALUATION
A. Sound conduct of the clinical trial, including but not limited to recruitment, screening, enrollment, and follow-up of eligible subjects according to protocol requirements (e.g., subject follow-up, case report form completion, and reporting of adverse drug experiences).

B. Maintenance of accurate and complete documentation, including not but limited to regulatory documents, signed informed consent forms, relevant IRB approvals, source documentation, drug dispensing logs, subject logs, and study-related communications.

C. Organizational management of all aspects of the trial, including but not limited to timeliness in completing case report forms (CRFs), data entry, reporting adverse drug experiences (ADEs), managing case load and managing study files.

D. Communication of all protocol-related issues/problems to the appropriate management staff, including but not limited to questions regarding the conduct of the clinical trial, concerns regarding possible AEs or subject compliance.

E. Professional conduct in the presence of subjects, research staff, sponsors, monitors, etc.
SPECIFIC RESPONSIBILITIES INCLUDE BUT ARE NOT LIMITED TO THE FOLLOWING:

A. Develop enrollment/follow-up mechanisms
   • Possess a sound and in-depth understanding of each protocol that has been assigned as a primary responsibility.
   • Review with the principal investigator the inclusion/exclusion criteria, overall structure, and requirements of each protocol.
   • Review the protocol summary sheet and the informed consent form for accuracy and clarity.
   • Develop draft protocol follow-up worksheets and then review the worksheets for accuracy and clarity.
   • Develop a mechanism for subject recruitment and ongoing communications with primary care physicians and nursing staff, as appropriate.
   • Prepare IRB applications and ongoing amendments, as directed.

B. Enrollment and follow-up of study subjects

   1. Screening and enrollment procedures
      • Review the study design and inclusion/exclusion criteria with the subject’s primary physician.
      • Review and verify all relevant source documentation in the subject's medical record to confirm study eligibility.
      • Review the protocol, informed consent form, and follow-up procedures with potential study subjects.
      • Ensure the current approved informed consent is signed before subjects are screened and enrolled.
      • Ensure that the randomization procedure is followed as per protocol guidelines.
      • Document protocol exemptions and deviations, as appropriate.

   2. Subject follow-up procedures
      • Ensure adherence to protocol requirements.
      • Schedule subjects for follow-up visits.
      • Assess subject response to therapy and evaluate for adverse events.
      • Review laboratory data and communicate abnormal values to the primary care provider and investigator.
      • Assess and document subject compliance with medications and visits.
      • Communicate with pharmacy staff to assure timely and accurate study drug distribution.
      • Administer study drug therapy as needed and maintain the study drug dispensing log if the pharmacy is not involved in the study (as legally appropriate).
• Maintain copies of all documentation written for study drug supplies, as appropriate.
• Ensure appropriate specimen collection.
• Attend study-related meetings as appropriate.
• Communicate regularly with the principal investigator about study-related issues.

3. Case report form (CRF) preparation and study documentation

• Ensure timely and accurate CRF completion for each study subject.
• Key data for remote data entry or provide completed CRFs on a timely basis.
• Review keyed data for accuracy as needed.
• Maintain source documentation for all CRF entries, including clinic chart visit notes, lab data, and procedure reports.
• Provide auditors with completed CRFs, medical records, lab data and other source documents for review.
• Correct and edit CRFs, as appropriate.

4. Adverse experience monitoring and reporting responsibilities

• Assess and record all AEs as outlined in protocol.
• Report all serious AEs to the principal investigator, sponsor’s monitor, primary care physician, and IRB as outlined in the protocol.

5. Regulatory documentation

• Maintain copies of all required regulatory documents.
• Prepare IRB submissions, protocol revisions, and renewals as needed, and maintain copies of all IRB communications.

6. Sponsor and/or FDA audits

• Ensure that all required documentation is complete and appropriately filed.
• Provide all required documentation to auditors.
• Make all appropriate corrections as requested by auditors.
7. Study close-out

- Ensure that all study documentation (regulatory, IRB communications, patient and drug logs, etc.) is appropriately filed.
- Ensure that all CRFs are complete and that all forms have been forwarded to the sponsor or entered into the computer, as appropriate.
- Store all files in a permanent and safe location.
- Notify the IRB of the study's completion, according to IRB procedure.

8. Management of ancillary staff

- Train and supervise support staff (e.g., research assistants, clerical staff and volunteers).
GENERAL DESCRIPTION
The primary responsibility of this individual is to enter data on to case report forms (CRFs), and/or to key data using remote data entry. The data manager is responsible for collecting all source documentation and worksheets prepared by all members of the research team and then transcribing the data on to the appropriate collection tool for submission to the sponsor.

QUALIFICATIONS
Medical assistant with at least six (6) months of clinical experience, certification preferred; or a research assistant with at least six (6) months of clinical experience.

CRITERIA FOR EVALUATION
A. Completeness and accuracy in performing assigned work, including but not limited recording of clinical data, both computer entry or data transcription.

B. Organization in performing assigned work, including but not limited to timeliness in completing projects, neatness of work performed, and success in managing multiple tasks.

C. Communication of all data entry related questions or problems to the research coordinator.

D. Professional conduct in the presence of subjects, research staff, sponsors, monitors, etc.

SPECIFIC RESPONSIBILITIES INCLUDE BUT ARE NOT LIMITED TO THE FOLLOWING:

• Source document collection
• File and pull study records
• Medical record retrieval and review
• Case report form completion
• Review data for accuracy and completeness
• Clarify data with research staff as necessary
• Enter data into the computer
• Correct/revise data as appropriate
• Maintain back-up system for computerized data
Attachment H

RESEARCH ASSISTANT
JOB DESCRIPTION

GENERAL DESCRIPTION
The primary responsibility of this individual is to assist the research nurse or coordinator in conducting clinical trials. The research assistant is responsible for screening and recruitment of patients, collecting, processing, storing and handling clinical specimens, scheduling study patients for follow-up, and collecting, recording, and filing clinical data.

QUALIFICATIONS
Medical assistant with at least six (6) months of clinical experience, certification preferred; or a laboratory technician with at least six (6) months of clinical experience.

CRITERIA FOR EVALUATION
A. Completeness and accuracy in performing assigned work, including but not limited to recording of clinical data, sample collection and processing.

B. Organization in performing assigned work, including but not limited to timeliness in completing projects, neatness of work performed, and success in managing multiple tasks.

C. Communication of all protocol-related questions or problems to the research coordinator.

D. Professional conduct in the presence of subjects, research staff, sponsors, monitors, etc.

SPECIFIC RESPONSIBILITIES INCLUDE BUT ARE NOT LIMITED TO THE FOLLOWING:

• Clinical data collection such as vital signs, EKG recording, subject weights
• Case report form documentation
• Medical record retrieval and review
• Subject interviews
• Phlebotomy
• Specimen collection, processing, storage, and shipment
• Source document collection
• Filing and pulling study records
• Transporting clinical specimens to the laboratory
• Appointment scheduling
• Answering and triage research office calls
Attachment I

ORIENTATION CHECKLIST

Employee: ________________________________________________

Date of employment: ____/____/____

A. Overview of the protocol
   - Study design
   - Protocol specifications
   - Amendments

B. Consent forms
   - Regulatory requirements
   - Process of obtaining consent
   - Documentation
   - Amendment process

C. Study initiation, management and close-out
   - Regulatory documentation and files management
   - Site initiation
   - Protocol worksheet development and usage
   - Source documentation
   - Case report form completion
   - Study drug supply, storage, logs
   - Patient logs
   - Sponsor communications

D. Adverse experience reporting
   - FDA regulatory requirements
   - IRB reporting requirements

E. Institutional/site policies
   - Employee handbook
   - Phlebotomy
   - Specimen handling and safety precautions

_________________________________________  _____________
Signature of Employee                              Date
EMPLOYEE EVALUATION FORM

Name: ________________________________

Job title: ________________________________

Date of employment: ____/____/____

Date of evaluation: ____/____/____

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<tr>
<th>A. GENERAL</th>
<th>1</th>
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| B. JOB KNOWLEDGE            |   |   |   |   |   | NA |          |
| Protocol requirements       |   |   |   |   |   | NA |          |
| Regulatory responsibilities |   |   |   |   |   | NA |          |

| C. INITIATIVE               |   |   |   |   |   | NA |          |
| Protocol set-up             |   |   |   |   |   | NA |          |
| Subject recruitment         |   |   |   |   |   | NA |          |
| Ongoing management          |   |   |   |   |   | NA |          |

| D. PROTOCOL COMPLIANCE      |   |   |   |   |   | NA |          |
| Subject enrollment          |   |   |   |   |   | NA |          |
| Subject follow-up           |   |   |   |   |   | NA |          |
| Accuracy of CRFs            |   |   |   |   |   | NA |          |
| AE reporting                |   |   |   |   |   | NA |          |
| Study drug dispensing       |   |   |   |   |   | NA |          |

1 – Not acceptable
2 – Needs improvement
3 – Average
4 – Very good
5 – Superior
NA – Not applicable
EMPLOYEE EVALUATION FORM

Name: ____________________________________________

Date of evaluation: ____/____/____

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<th>E. COMMUNICATIONS</th>
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<tr>
<td>Maintains regular contact with PI</td>
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<td>Notifies IRB appropriately</td>
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<tr>
<td>Refers study related questions to management staff</td>
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<tr>
<td>Accurately communicates study progress to PI and CRA</td>
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<table>
<thead>
<tr>
<th>F. MAINTENANCE OF DOCUMENTATION</th>
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<tbody>
<tr>
<td>Regulatory documents</td>
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<td>Communication with the IRB</td>
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<td>Source documentation</td>
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<td>Study drug logs</td>
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<td>Subject logs</td>
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<td>Communications</td>
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<th>G. ORGANIZATIONAL MANAGEMENT</th>
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<tr>
<td>Timeliness in recording data</td>
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<td>Timeliness in AE reporting</td>
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<td>Case load management</td>
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<td>Organization of study files</td>
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<th>H. PROFESSIONAL CONDUCT</th>
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<td>Define as appropriate</td>
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<thead>
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<th>I. SUPERVISION OF ANCILLARY STAFF</th>
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<td>If applicable</td>
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</table>

<table>
<thead>
<tr>
<th>1 – Not acceptable</th>
<th>2 – Needs improvement</th>
<th>3 – Average</th>
<th>4 – Very good</th>
<th>5 – Superior</th>
<th>NA – Not applicable</th>
</tr>
</thead>
</table>
EMPLOYEE EVALUATION FORM

Name: ____________________________________________

Date of evaluation: ____/____/____

1. What are the employee’s strengths?
   ........................................................................
   ........................................................................
   ........................................................................
   ........................................................................
   ........................................................................
   ........................................................................
   ........................................................................

2. What are the employee’s areas for improvement?
   ........................................................................
   ........................................................................
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3. What are the employee's goals and objectives for the next evaluation period?
   ........................................................................
   ........................................................................
   ........................................................................
   ........................................................................
   ........................................................................
   ........................................................................
   ........................................................................
   ........................................................................

Signature of Supervisor ___________________________ Date: ____/____/____
EMPLOYEE CERTIFICATION

☐ I certify that I have seen my complete evaluation form and that my supervisor has discussed this evaluation with me.

☐ I understand and agree with this evaluation.

☐ I have offered a written, dated response that differs from my supervisor’s evaluation.

_________________________________________  ______/_____/_____
Signature of Employee                      Date
Attachment K

CRITERIA for REVIEW

1. Not acceptable
Work performance does not meet the standards of this organization.

2. Needs improvement
Able to complete responsibilities only under continued supervision. Amount and quality of work are below this organization's required levels. Overall contributions and performance do not consistently meet this organization's standards. Interim performance reviews with improvement in performance are required.

3. Average
Able to work independently, but needs some supervision. Performance meets and sometimes exceeds this organization's standards for the job. The amount and quality of work are satisfactory. The employee consistently contributes to the achievement of this organization's business goals.

4. Very good
Able to work independently with little supervision. With some direction, takes initiative to perform beyond the requirements of the position. Consistently produces very good results that contribute to the achievement of business goals. Amount and quality of work are better than average.

5. Superior
Performs independently, using good judgment, with minimal supervision. Shows excellent leadership skills in decision-making, planning and executing responsibilities. Consistently makes significant contributions to business goals. Amount and quality of work are excellent.
1.3

STANDARD OPERATING PROCEDURE FOR
TRAINING AND EDUCATION

I. INTRODUCTION AND PURPOSE

Research studies will be conducted according to FDA regulations and Good Clinical Practice guidelines to protect the safety and welfare of study subjects that must be ensured by a research team knowledgeable about ongoing study protocols and investigational articles.

Investigators and all key members of the research team who are working in or overseeing programs that conduct research on human subjects will receive initial and ongoing training regarding the responsible conduct of research.

2. SCOPE

This standard operating procedure (SOP) describes the process and documentation required by this institution for the initial and ongoing education of the principal investigator and research staff in Good Clinical Practices (GCPs) and the ethical conduct of research conducted at this research site.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.60 General responsibilities of investigators
45 CFR 46 Protection of Human Subjects
21 CFR 812 Subpart E Responsibilities of Investigators
May 1997 ICH Good Clinical Practice: Consolidated Guideline (E6 4.2.4)
Feb 5, 2010 FDA Internal Compliance Program Guidance Manual for Clinical Investigators: 7348.811
Aug 25, 2000 NIH Notice OD-00-029: Required Education in the Protection of Human Research Participants
Sept. 12, 2001 Clarification on June 5, 2000 Notice (OD-00-39)
4. REFERENCES TO OTHER APPLICABLE SOPS

All SOPs are applicable to this SOP.

5. ATTACHMENTS

A. Educational Program Compliance Form

6. RESPONSIBILITY

This SOP applies to the principal investigator and educational staff at this research site who participate in the hiring, orientation and ongoing training of investigators and research staff involved in supervising, managing, or conducting study-related activities at this institution.

This includes the following:

Principal investigator
Sub-investigator
Administrators
Research manager
Research nurse/coordinator
Pharmacist

7. PROCESS OVERVIEW

A. Process for education and documentation by research staff
8. PROCEDURES

A. Process for education and documentation by research staff

PI

- Ensure that all members of the research team are provided access to this organization/site’s educational program.

Research manager

- Determine that each member of the research team provides appropriate documentation that he/she has fulfilled the education and training requirement.
- Maintain a record of initial and ongoing educational activities and certification for all research staff at the investigative site.
EDUCATIONAL PROGRAM COMPLIANCE FORM

Form for ____________________________________________________________ (Research Site)

<table>
<thead>
<tr>
<th>Date</th>
<th>Name</th>
<th>Educational Program Title</th>
<th>Date of Certificate</th>
</tr>
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<tr>
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</tbody>
</table>

Reviewed by: _________________________________  Date  ___/___/___
2.1

STANDARD OPERATING PROCEDURE
FOR ASSESSING PROTOCOL FEASIBILITY

I. INTRODUCTION AND PURPOSE

A clinical protocol that meets scientific and ethical standards is a fundamental requirement of clinical investigations. The site must determine the scientific, ethical and financial merits of conducting the study. The sponsor must compensate the site for the resources necessary to perform all study-related procedures according to the requirements of good clinical practice (GCP). This standard operating procedure (SOP) describes the steps for fulfilling the regulatory, medical, and ethical requirements for assessing the feasibility of implementing a protocol at this investigative site.

2. SCOPE

This SOP applies to the activities involved in assessing protocols for studies conducted at this investigative site subject to investigational new drug (IND) regulations for drugs and biologics during all investigational phases of development, investigator initiated research and observational studies.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.109 IRB review of research
21 CFR 56.111 Criteria for IRB approval of research
21 CFR 312.21 Phases of an investigation
21 CFR 312.23 IND content and format
21 CFR 312.60 General responsibilities of investigators
Feb 5, 1998 International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline

4. ATTACHMENTS

A. Protocol Assessment Checklist
B. Subject Expenses Worksheet
C. Employee Salary Expenses Worksheet
<table>
<thead>
<tr>
<th>Department of OB/GYN</th>
<th>Approved By:</th>
</tr>
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<tr>
<td>Standard Operating Procedures for</td>
<td>SOP No. 2.1</td>
</tr>
<tr>
<td>Assessing Protocol Feasibility</td>
<td>Original Version Date:</td>
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<td></td>
<td>Effective Date:</td>
</tr>
<tr>
<td>Revisions:</td>
<td>Page 1 of 2</td>
</tr>
</tbody>
</table>

D. Budget Worksheet
5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in conducting clinical trials at this research site. This includes the following:

- Principal investigator
- Sub-investigator
- Research manager
- Research nurse/coordinator
- Data manager
- Support staff

6. PROCESS OVERVIEW

A. Based upon the established review process, evaluate the feasibility of carrying out the protocol at this investigative site.

7. PROCEDURES

A. Evaluate the protocol and the investigational article, assess the potential impact upon subjects, and review the budget.

PI
Sub-investigators
Research manager
Research nurse/coordinator
Study pharmacist
Data manager

- Based upon the established review process, determine the scientific, ethical and financial merits of conducting the study at this investigational site.

- Distribute the protocol and assessment tools to key research team members for their assessment (Attachment A, Protocol Assessment Checklist and Attachments B, C and D for budget calculations).

- Review comments from research team and determine feasibility by face to face meetings, emails, telephone, or memos.
Attachment A

PROTOCOL ASSESSMENT CHECKLIST

Protocol title: 

Study article(s): 

Phase: 

1. General

Is the number of patients to be enrolled realistic for this site? ☐ Yes ☐ No

Is the enrollment period realistic for this site? ☐ Yes ☐ No

Are the inclusion/exclusion criteria too restrictive? ☐ Yes ☐ No

Will our IRB have problems with any aspects of this protocol? ☐ Yes ☐ No

Comments: __________________________________________________________________________

____________________________________________________________________________________

____________________________________________________________________________________

____________________________________________________________________________________

2. Procedures/clinical assessments

Are frequent observations/procedures required? ☐ Yes ☐ No

Is the visit schedule flexible? ☐ Yes ☐ No

Are there multiple follow-up visits required? ☐ Yes ☐ No

Are procedures/clinical assessments difficult? ☐ Yes ☐ No

Is additional staffing/specialist involvement needed? ☐ Yes ☐ No

Comments: __________________________________________________________________________

____________________________________________________________________________________

____________________________________________________________________________________

____________________________________________________________________________________
3. Study population

Subject health status

- Acute and life-threatening
  - Yes
  - No
- Chronic and life-threatening
  - Yes
  - No
- Healthy
  - Yes
  - No

Subject population

- Adults capable of giving consent
  - Yes
  - No
- Impaired adults
  - Yes
  - No
- Minors
  - Yes
  - No

Comments: ____________________________________________
____________________________________________________
____________________________________________________

4. Case report forms

- Is concomitant medication documentation detailed?
  - Yes
  - No
- Is adverse event documentation complex?
  - Yes
  - No
- Are diaries detailed?
  - Yes
  - No
- Do the diaries need to be transcribed?
  - Yes
  - No
- Is the study article dispensing/accountability complicated?
  - Yes
  - No

Comments: ____________________________________________
____________________________________________________
____________________________________________________
____________________________________________________
____________________________________________________
5. Other considerations

Will our patient population benefit from the study? □ Yes □ No

Is this study desirable to do from a scientific standpoint? □ Yes □ No

Comments: ______________________________________________________

______________________________________________________________

______________________________________________________________

______________________________________________________________

______________________________________________________________

______________________________________________________________

Do you recommend that the study be conducted at this site? □ Yes □ No

Comments: ______________________________________________________

______________________________________________________________

______________________________________________________________

______________________________________________________________

______________________________________________________________

______________________________________________________________

_______________________________  __/____/____
Signature                              Date
## SUBJECT EXPENSES WORKSHEET

**Protocol title:**

<table>
<thead>
<tr>
<th>Procedures, Tests, and Labs</th>
<th>Cost per subject</th>
<th>Screening</th>
<th>Day</th>
<th>Day</th>
<th>Day</th>
<th>Day</th>
<th>Termi-nation</th>
<th>Total #</th>
<th>Total Cost</th>
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<tr>
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<td><strong>Salary or Fee</strong></td>
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<td>Research nurse/coordinator</td>
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Attachment C

EMPLOYEE SALARY EXPENSES WORKSHEET

Protocol Title:  
Position:  

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Time required (Record in minutes.)</th>
<th>Frequency</th>
<th>Number of subjects</th>
<th>Total time required</th>
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<tbody>
<tr>
<td>Recruitment</td>
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<tr>
<td>Screening</td>
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<tr>
<td>Consent (including explaining the study, answering questions)</td>
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<tr>
<td>Per visit activities</td>
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<tr>
<td>Vital signs</td>
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<tr>
<td>Lab processing</td>
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<tr>
<td>Interview (AE assessment, concomitant meds, diary)</td>
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<tr>
<td>Prep, assist/perform assessments and procedures</td>
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<tr>
<td>Study article dispensing and accounting</td>
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<tr>
<td>Instructing and scheduling subject next visit</td>
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<td>CRF completion</td>
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<td>Monitor visits and CRF clarifications</td>
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<td>SAE forms</td>
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<tr>
<td>Communication between sponsor and site</td>
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<td>TOTAL</td>
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</tbody>
</table>

Employee hourly rate  
Hours required  
Total base salary  
Per cent fringe benefits  
Project cost
Protocol title: ____________________________________________

1. Direct expenses (from Subject Expenses Worksheet)

Enrolled subjects: Cost per subject x No. of subjects = Total

Screened/dropped: Cost per subject x No. of subjects = Total

Subtotal direct expenses (A)

2. Other expenses

New equipment

IRB fee

Other

Subtotal other expenses (B)

3. Indirect expenses

Direct costs x % overhead (C)

TOTAL PROJECT COST (A+B+C)
2.2

STANDARD OPERATING PROCEDURE FOR PRESTUDY SITE VISIT

I. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) describes the processes followed at this investigative site when the sponsor of a study conducts a pre-study site visit to:
• Meet with study personnel and review their qualifications for the study,
• Assess the facilities of the research site for implementing the study,
• Evaluate the possibility of collaborating on the study.

2. SCOPE

This SOP applies to the procedures for conducting the pre-study site visit for all clinical studies subject to investigational new drug (IND) regulations for drugs and biologics during all investigational phases of development. It describes the steps followed by this clinical research site.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.50 General responsibilities of sponsors
21 CFR 312.52 Transfer of obligations to a contract research organization
21 CFR 312.53 Selecting investigators and monitors
21 CFR 312.60 General responsibilities of investigators
21 CFR 312.66 Assurance of IRB review
21 CFR 312.68 Inspection of investigator's records and reports
August 2011 Guidance for Industry Oversight of Clinical Investigations

4. ATTACHMENTS

A. Agenda for Pre-study Site Visit
B. Checklist of Activities Associated with the Pre-study Site Visit
C. Pre-study Site Visit Follow-up

5. RESPONSIBILITY
This SOP applies to those members of the clinical research team involved in arranging, managing, or participating in the pre-study site visit. This includes the following:

- Principal investigator
- Sub-investigator
- Research nurse/coordinator
- Data manager
- Study pharmacist
- Support staff

6. PROCESS OVERVIEW

A. Preparing for the pre-study site visit
B. Conducting the pre-study site visit
C. Following-up after the pre-study site visit

7. PROCEDURES

A. Preparing for the pre-study site visit

- Identify key clinical research personnel likely to be involved in conducting the study under consideration.

- Ensure that the sponsor's Confidentiality Agreement (if applicable) has been signed by the principal investigator and returned promptly to the sponsor.

- Ensure that the site has received critical study documents, such as the protocol, the investigator brochure, and CRFs (if available), sample budget worksheet, and a draft contract.

- Review the protocol and other study-related materials to assess the feasibility of conducting the study at this site.

- Consider personnel resources, patient availability,
nurse/coordinator potential benefits to patients, ease of implementing the study.

Study pharmacist

Data manager • Determine if the sponsor has any areas of special interest that require advance scheduling, such as:
  Visiting the treatment site (clinic or hospital), pharmacy, central laboratory, medical records department;
  Seeing any specialized equipment needed to implement the study;
  Meeting briefly with ancillary personnel involved in any specialized data collection;
  Visiting any ancillary facilities.

Support staff • If not on file, obtain copies of current Curricula Vitae and resumes from key site personnel.
• Provide photocopies to the sponsor.

B. Conducting the pre-study site visit

PI • Meet with sponsor/CRO representatives to review protocol, investigator’s brochure, communication plan for sponsor/CRO and clinical site.

Sub-investigator • Tour the areas of the research facility with sponsor representatives, where the clinical trial will be conducted.

Research nurse coordinator

Key study personnel • (See Attachment B, Checklist of Activities Associated with the Pre-study Site Visit)

C. Following up after the pre-study site visit
<table>
<thead>
<tr>
<th>Department of OB/GYN</th>
<th>Approved By:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Operating Procedures for Pre-study Site Visit</td>
<td>SOP No. 2.2</td>
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<td>Original Version Date:</td>
<td>Effective Date:</td>
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<tr>
<td>Revisions:</td>
<td>Page 1 of 4</td>
</tr>
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Research nurse/coordinator

- Complete the checklist to document the pre-study site visit (Attachment C, Pre-study Site Visit Follow-Up)
## AGENDA FOR PRESTUDY SITE VISIT

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 minutes</td>
<td>Welcome and introductions</td>
<td>PI, All</td>
</tr>
<tr>
<td>30 minutes</td>
<td>Tour of facilities</td>
<td>Research nurse/ coordinator</td>
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<tr>
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<td></td>
<td>Sponsor personnel</td>
</tr>
<tr>
<td>30 minutes</td>
<td>Review of protocol and CRFs</td>
<td>All</td>
</tr>
<tr>
<td>15 minutes</td>
<td>Site qualifications</td>
<td>Research nurse/ coordinator, other site personnel, as appropriate</td>
</tr>
<tr>
<td>15 minutes</td>
<td>Time line for the study</td>
<td>Sponsor personnel</td>
</tr>
<tr>
<td>5 minutes</td>
<td>Review of action items</td>
<td>PI, Sponsor</td>
</tr>
<tr>
<td>5 minutes</td>
<td>Summary</td>
<td>PI</td>
</tr>
</tbody>
</table>
Attachment B

CHECKLIST FOR PRESTUDY SITE VISIT ACTIVITIES

1. Before the pre-study site visit

☐ Request from the sponsor several potential meeting dates and times to accommodate as many key personnel as possible.

☐ Ensure that these team members will be available and have allocated sufficient time for the Pre-study Site Visit meeting date established with the sponsor.

☐ Ensure that key site personnel receive copies of the protocol, investigator’s brochure, and CRFs for review and comment.

☐ Ensure that the appointment with the sponsor is confirmed. Provide directions to the investigative site. Offer to provide suggestions for hotels and restaurants nearby.

☐ Prepare information on:
  • Dates of regulatory meetings, such as the IRB, for the next 3-6 months
  • An overview of the protocol review process at the site (if it is not straightforward)
  • Grants and contracts office, if applicable
  • Names of key contacts, telephone numbers, and e-mail addresses (if available) for individuals at the site involved in contract review and signoff

☐ Prepare supporting documentation, such as:
  • Current organizational chart and proposed management of the study
  • List of generic clinical trials (overall and completed recently)
  • Copies of any publications by research staff relevant to clinical study under consideration
  • Copies of current medical licenses and laboratory certification (if applicable)
  • Sample source documentation of subject participation in a clinical study
  • Estimate of the number of potential study participants
  • Proposed recruitment strategy, including primary and secondary resources
2. **During the pre-study site visit**

- Ensure that sponsor’s representatives have the opportunity to tour the facilities including:
  - Exam rooms for subject evaluation and treatment
  - Laboratory area
  - Any special testing areas
  - Pharmacy; satellite pharmacy, if appropriate
  - Hospital unit
  - Work areas for research staff
  - Storage areas for study drug
  - Storage areas for supplies
  - Data entry area, if appropriate

- Be prepared to discuss the following:
  - Comments from site personnel's review of the protocol
  - Any requests for site-specific modifications to the protocol
  - Laboratory (central or local)
  - Provision for any specialized procedures
  - Any specialized data entry procedures
  - Storage space required for study drug, specialized equipment, computers, etc.

- Request that the sponsor/CRO provide an overview of the management process for the study at this site including:
  - Sponsor/CRO responsibilities
  - Monitoring plan
  - Overview of data management

- Discuss the following potential concerns:
  - The benefits of the investigational product for the site's patient population
  - Publication policy if the investigative site is interested in publishing the results of the study
  - Availability of qualified, experienced and sufficient site personnel to conduct this study
  - After study initiation, the site training plan for ancillary research and facility personnel involved in the study
Request from the sponsor:

- Information on the anticipated time line for the study
- Information on key dates, such as:
  - Investigators’ meeting and/or
  - Study initiation meeting
  - Study drug availability
  - Indemnification agreement
  - Draft contract for review
  - Sponsor/CRO chain of command and communication plan

Determine if there is any other information that the sponsor requires.

Discuss time line at the site for IRB review and contract and indemnification agreement review and signoff.

3. **After the pre-study site visit**

- Request that the sponsor notify the site in writing if selected to participate in the clinical trial.

- Once the protocol is finalized, prepare the following:
  - The site-specific informed consent form
  - The IRB submission
  - The final budget

- Submit the clinical trial agreement for signoff.

- Track documents identified above at the site/within the institution.

- Plan for the site initiation meeting.
## PRESTUDY SITE VISIT FOLLOW-UP

1. **Date of visit:**  
   ________________________________
   
   **Sponsor of protocol:**  
   ________________________________
   **Protocol number:**  
   ________________________________
   **Protocol title:**  
   ________________________________

2. **Primary sponsor/CRO contact name, address, and telephone:**  
   ________________________________
   ________________________________
   ________________________________

3. **Sponsor CRO/representative(s) present:**  
   ________________________________
   ________________________________
   ________________________________

4. **Site representative(s) present:**  
   ________________________________
   ________________________________
   ________________________________

5. **Summary of meeting:**  
   ________________________________
   ________________________________
   ________________________________
   ________________________________
   ________________________________

6. **Action items:**  
   □ None  
   ________________________________
   ________________________________
   ________________________________
7. Any other follow-up required?  ❑ No    ❑ Yes

8. Outcome:
   ❑ Study placed at this site.
   ❑ Site declined study because _______________________________________
   ❑ Sponsor declined to place study at this site because ____________________

_________________________________        ______/_____/_____
Signature of person completing this form    Date
I. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) describes the processes followed at this investigative site when the sponsor of a potential study conducts a study initiation meeting to:

• Prepare site personnel to implement the protocol according to GCP requirements,
• Review study drug administration and accountability,
• Provide instruction in any specialized procedures such as diagnostic tests and special computer programs,
• Provide direction for CRF completion.

2. SCOPE

This SOP applies to all clinical studies subject to investigational new drug (IND) regulations for drugs and biologics during all investigational phases of development. It describes the steps followed by this clinical research site from the time a study initiation meeting is scheduled by a sponsor until all follow-up activities associated with the meeting have been completed.

3. APPLICABLE REGULATIONS AND GUIDELINES

<table>
<thead>
<tr>
<th>CFR Section</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 CFR 312.50</td>
<td>General responsibilities of sponsors</td>
</tr>
<tr>
<td>21 CFR 312.52</td>
<td>Transfer of obligations to a contract research organization</td>
</tr>
<tr>
<td>21 CFR 312.60</td>
<td>General responsibilities of investigators</td>
</tr>
<tr>
<td>21 CFR 312.66</td>
<td>Assurance of IRB review</td>
</tr>
<tr>
<td>21 CFR 312.68</td>
<td>Inspection of investigator's records and reports</td>
</tr>
</tbody>
</table>
4. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in managing or participating in the site initiation meeting. This includes the following:

- Principal investigator
- Sub-investigator
- Research nurse/coordinator
- Data manager
- Study pharmacist (if complicated study, drug blinding and preparation procedures are required)
- Microbiologist (if this is an infectious disease study)

5. PROCESS OVERVIEW

The study initiation meeting is a meeting arranged and conducted by the sponsor to complete the final orientation of the study personnel to the study procedures and GCP requirements. It occurs after the pre-study site visit when all study arrangements have been concluded or are in process, and the study is about to start.

A. Preparing for the site initiation meeting
B. Participating in the site initiation meeting
C. Following-up after the site initiation meeting

6. PROCEDURES

A. Preparing for the site initiation meeting

- **PI**
  Identify key clinical research personnel likely to be involved in conducting the study under consideration.

- **Research nurse/coordinator**
  Assign study to appropriate clinical research personnel. Ensure that all documentation and materials associated with the study are provided to these individuals assigned to the study.

- **Support staff**

- **Research manager**

- **Research nurse/coordinator**
  Ensure that travel arrangements are in order for those who will be attending the multicenter investigators’ meeting or Arrangements have been made for sponsor personnel to orient the study on-site.
• Research nurse/coordinator
• Support staff

Ensure that any materials needed for the meeting (annotated CRFs, sample study medication) are available.

B. Participating in the site initiation meeting

• Key study personnel attending the meeting

Be prepared to provide sponsor with an update on any study-related issues.

C. Following up after the site initiation meeting

• Research nurse/coordinator

Ensure that the sponsor/CRO sends written documentation summarizing important agreements made during the meeting.

• Research nurse/coordinator
• Support staff

Once the protocol is finalized, prepare the site-specific informed consent form.
Ensure that sponsor/CRO reviews the form prior to IRB submission.
Prepare the following:
• IRB submission
• Final budget
Submit the clinical trial agreement for signoff.
Track documents appropriately.
Create appropriate study files.
File documents as they become available.
STANDARD OPERATING PROCEDURE FOR PROTOCOL START-UP

1. INTRODUCTION AND PURPOSE
   The initiation of a clinical study marks the beginning of subject accrual. Prior to enrolling the first subject, all regulatory and institutional requirements must be met, and preparations for protocol procedures must be complete. In addition, the research staff and others involved in recruitment, selection of subjects and enrollment must receive appropriate training. This standard operating procedure (SOP) describes the steps for fulfilling the regulatory and clinical requirements of starting-up a study.

2. SCOPE
   This SOP describes the steps taken to organize and prepare this clinical site for all clinical studies subject to investigational new drug (IND) regulations for drugs and biologics during all investigational phases of development. It describes the steps followed by this clinical research site from the time a sponsor selects the site for a clinical study until recruitment of subjects begins.

3. APPLICABLE REGULATIONS AND GUIDELINES
   21 CFR 312.68 Inspection of investigator's records and reports
   January 1988 Guidelines for the Monitoring of Clinical Investigations
   May 1997 International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline

4. ATTACHMENTS

   A. Protocol Start-Up Checklist
5. Responsibility

This SOP applies to those members of the clinical research team involved in starting up clinical studies. This includes the following:

- Principal investigator
- Sub-investigator
- Research nurse/coordinator
- Data manager
- Support staff

6. PROCESS OVERVIEW

A. Determine facility readiness
B. Establish site readiness
C. Begin recruitment and screening activities

7. PROCEDURES

A. Determine facility readiness

- PI
- Research manager
- Research nurse/coordinator

Ensure that the contract is executed.
Ensure that a final budget has been negotiated.
Conduct in-service training for referring and support staff (e.g., physicians, nurses, and lab technicians).

B. Establish site readiness

- Research nurse/coordinator
- Data manager
- Support staff

Review regulatory files for completeness.
Establish the receipt of adequate investigational drug supplies.
Inventory supplies of case report forms, central lab supplies.
Develop or utilize sponsor-generated worksheets, checklists.

Review study procedures with assigned research staff (Attachment A, Protocol Start-Up Checklist).

C. Begin recruitment and screening activities

- PI
- Research nurse/coordinator

Notify sponsor of launch date for recruitment and screening activities.

Assemble screening/enrollment materials.

Activate recruitment plan.
### Attachment A

#### PROTOCOL START-UP CHECKLIST

#### Documents required
- Signed Form FDA 1572
- CVs of investigators listed on the Form FDA 1572
- Signed protocol title page
- Investigator’s brochure
- IRB approval letter
- IRB letter of assurance, if applicable
- IRB-approved consent form
- Laboratory certification and range of normal values
- Budget
- Contract

#### Protocol preparation
- Follow-up worksheets
- Patient logs (screening, enrollment and follow-up)
- Protocol summary sheets (purpose, inclusion/exclusion criteria)
- Study drug administration sheets (adverse effects, administration)
- Special lab work requisitions (if required by the institution)
- Randomization table, as appropriate

#### Ancillary staff inservice
- Pharmacy _____________________________ (contact name)
- Nursing _____________________________ (contact name)
- Physicians ___________________________ (contact name)
- Laboratory __________________________ (contact name)

#### Inventory
- Study drug supplies
- Laboratory supplies (central and/or hospital)
- Case report forms
3.1

STANDARD OPERATING PROCEDURE FOR SITE-SPONSOR/CRO COMMUNICATIONS

I. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) describes the various ways of communicating with the sponsor/CRO as all regulatory, medical and ethical requirements are fulfilled, including telephone and written interactions.

2. SCOPE

This SOP applies to communications between this site and sponsors/CROs with regard to any clinical study subject to investigational new drug (IND) regulations for drugs and biologics during all phases of development. These communications serve to protect the safety and well-being of subjects by keeping sponsors/CROs fully apprised of study activities and to ensure that the studies are carried out appropriately.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.32 IND safety reports
21 CFR 312.33 Annual reports
21 CFR 312.44 Termination
21 CFR 50 Protection of Human Subjects
21 CFR 56 Institutional Review Boards
FDA Information Sheets, October 1998
May 1997 International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline

4. ATTACHMENTS

A. Telephone Contact Log
5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in conducting clinical trials/research studies at this research site. This includes the following:

- Principal investigator
- Sub-investigator
- Research nurse/coordinator
- Data manager
- Study pharmacist
- Support staff

6. PROCESS OVERVIEW

A. Communications overall
B. Pre-study communications
C. Communications while the study is ongoing
D. Communications when the study is completed

7. PROCEDURES

A. Communications overall

- Appropriate research team members
  Communicate regularly and appropriately with sponsor/CRO about all study-related issues.
  Document important conversations (Attachment A, Telephone Contact Log).

- Research nurse/coordinator
- Support staff
  Keep originals or photocopies of all relevant documentation, including facsimile confirmations, and file in the study binder with appropriate documents.

B. Pre-study communications

- PI
  Send sponsor/CRO signed confidentiality agreement.
• Research nurse/coordinator
  Notify sponsor/CRO of decision to participate in the study by telephone, fax, letter, electronic mail.
  Send sponsor/CRO signed protocol signature page (if appropriate).

• Research nurse/coordinator
  Submit all pre-study regulatory documents (Attachment A, Protocol Start-Up Checklist in SS-204).
  Send updated/revised documents as necessary.

C. Communications while the study is ongoing

• Research nurse/coordinator
  Inform sponsor/CRO about SAE(s) immediately.

• Research nurse/coordinator
  Inform sponsor/CRO about the study progress through screening/enrollment forms by whatever means (fax, e-mail) requested (Attachment A, Screening/Enrollment Form, SOP 4.2).

• Support staff
  Forward CRFs to sponsor/CRO as requested.
  Respond promptly to data queries as requested (fax, e-mail, remote data entry query resolution procedures).

• Research nurse/coordinator
  Copy sponsor/CRO on IRB communications such as SAEs, IND safety reports, IRB acknowledgment of reports received, amendment approvals, revised informed consent form, continuing approval for study.

D. Communications when the study is completed

• PI
  • Research nurse/coordinator
    Inform sponsor/CRO promptly if notified by FDA of impending inspection.
    Provide copies of all FDA documentation (Form FDA 483, letters) generated as a result of the inspection.
## TELEPHONE CONTACT LOG

<table>
<thead>
<tr>
<th>Date:</th>
<th>Conversation between:</th>
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<td>and _______________</td>
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<td>Summary of discussion:</td>
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3.2

STANDARD OPERATING PROCEDURE FOR INTERACTIONS WITH THE INSTITUTIONAL REVIEW BOARD

I. INTRODUCTION AND PURPOSE

The primary responsibility of the Institutional Review Board (IRB) is to protect the rights and welfare of research subjects. Federal regulations require that the IRB ensure that certain criteria for approval of research are met prior to approving a study. The principal investigator must provide the IRB with the information necessary to permit an informed decision on whether to approve, disapprove, or to require modifications prior to approval.

By signing the Form FDA 1572, the principal investigator ensures that the IRB reviewing the research complies with the regulations. Additionally, the principal investigator agrees to inform the IRB of any changes to the protocol and any materials used to recruit subjects, as well as any additional risks to subjects associated with the investigational article.

This SOP describes how this site communicates with the IRB throughout the research process in order to ensure compliance with the regulations and to protect the safety and well-being of study subjects.

2. SCOPE

This SOP applies to the interactions with the IRB responsible for all research carried out at this site subject to investigational new drug (IND) regulations for drugs and biologics during all phases of development, investigator initiated research and observational studies.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.32 IND safety reports
21 CFR 312.53 Selecting investigators and monitors
21 CFR 312.54 Emergency research
21 CFR 312.66 Assurance of IRB review
21 CFR 50 Protection of Human Subjects
21 CFR 56 Institutional Review Boards
45 CFR 46 Protection of Human Subjects
May 1997 ICH Good Clinical Practice –Consolidated Guidelines
4. ATTACHMENTS

A. Checklist for IRB Submission
B. Serious Adverse Event Report
C. Reporting IND Safety Reports to the IRB
D. Periodic Report to the IRB

5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in communicating with the IRB to ensure appropriate management of all clinical research activity. This includes the following:

1. Principal investigator
2. Sub-investigator
3. Research nurse/coordinator

6. PROCESS OVERVIEW

A. Documenting IRB compliance
B. Communicating with the IRB at study start-up
C. Communicating with the IRB while the study is ongoing
D. Communicating with the IRB when the study is over

7. PROCEDURES

A. Documenting IRB compliance

- PI
- Research nurse/coordinator

Ensure that the IRB is duly constituted and compliant with federal and state regulations. Request a copy of the IRB’s SOPs.

Request a copy of the IRB membership list and the general assurance number (if available).
B. Communicating with the IRB at study start-up

- **PI**
- **Research nurse/coordinator**

Using the IRB online website (https://apps.research.unc.edu/irb/index_auth.cfm) and the appropriate forms, complete the initial IRB submission. Include all attachments as directed, e.g., the protocol, investigator’s brochure, informed consent form and advertisements (Attachment A, IRB Checklist of Application Material).

Submit the package for the next scheduled meeting.

- **Research nurse/coordinator**

Obtain documentation of full IRB approval for the protocol and informed consent form prior to study start. Copy sponsor/CRO on correspondence.

Maintain all documents in the appropriate study files.

C. Communicating with the IRB while the study is ongoing

- **Research nurse/coordinator**

Notify the IRB of any changes to the protocol and/or informed consent and of new information from the sponsor on the test article.

Submit periodic report form for renewal of protocol as requested (Attachment D, Periodic Report to the IRB).

Obtain documentation of IRB approval of amendments and revisions to study-related documents, such as advertisements, prior to implementation except to eliminate apparent hazard to subject safety. Copy sponsor/CRO on correspondence.

- **Research nurse/coordinator**
- **Support staff**

Notify the IRB (919-966-3113) promptly of all serious or alarming events occurring during the approval period for the ongoing study (Attachment B, Serious Adverse Event Report).

Promptly submit to the IRB all IND Safety Reports received from the sponsor (Attachment C, Reporting IND Safety Reports to the IRB).

Report all routine AEs to the IRB as part of the periodic or annual reporting requirements.
Maintain all documents in the appropriate study files.

**D. Communicating with the IRB when the study is over**

Notify the IRB of study closure. Submit required documentation per IRB policy and study protocol.
CHECKLIST FOR IRB SUBMISSION

❑ Study summary

❑ Research protocol

❑ Investigator's brochure (if applicable)

❑ Proposed informed consent form

❑ Proposed patient information (instructions, diaries, etc.)

❑ Up-to-date curriculum vitae of principal investigator

❑ Up-to-date curriculum vitae of sub-investigator(s) or other staff listed on Form FDA 1572

❑ Copy of current medical license for principal investigator and sub-investigators (if applicable)

❑ Other supporting material (e.g., sample of any proposed advertising)

❑ Copy of Form FDA 1572 (if required)
### SERIOUS ADVERSE EVENT REPORT

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Phone (__)</th>
<th>Protocol title</th>
</tr>
</thead>
</table>

1. Subject's birth date ___/___/___  
   Initials ______  
   Sex  F □  M □

2. Study article, if known __________________________  
   Onset ___/___/___  
   Route of administration: ___________  
   Administered from ___/___/___ to ___/___/___

3. Event resulted in  
   - Death ___/___/___  
   - Threat to life  
   - Inpatient or prolongation of hospitalization  
   - Severe or permanent disability  
   - Congenital abnormality  
   - Required medical or surgical intervention to prevent one of the above  
   - None of the above

4. Description of the event  
   ___________________________________________  
   ___________________________________________  
   ___________________________________________  

5. Treatment of the event  
   ___________________________________________  
   ___________________________________________  
   ___________________________________________  
   ___________________________________________

6. Was the event related to the study article?  
   Probably □  
   Possibly □  
   Remotely □  
   Not related □
7. Did the event abate after stopping study article?  
Yes ☐ No ☐
If yes, describe.

8. List concomitant medical problems, treatment, and outcome at the time of this event.

____________________________________________________________________________________
____________________________________________________________________________________
____________________________________________________________________________________
____________________________________________________________________________________

9. Will you be sending follow-up information about this event?  
Yes ☐ No ☐

10. Is a change to the informed consent form required?  
Yes ☐ No ☐
(If yes, attach revised ICF.)

____________________________________________________________________________________
Signature (person reporting adverse event) Date

__/__/
<Date>

<Name>
Chairperson
Institutional Review Board
<Hospital>
&lt;City, State, Zip code&gt;

RE: &lt;Protocol Title&gt;

Dear Chairperson:

Enclosed please find an IND Safety Report #__________, submitted to us by &lt;sponsor&gt; for the above referenced study. The federal regulations require that sponsors notify investigators of immediately reportable adverse events that have occurred worldwide in connection with the investigational drug. I am, in turn, notifying you of this event.

In my opinion, information contained in this IND Safety Report (does/does not) require a change to our approved informed consent form. (Enclose revised consent form when a change is being requested)

If you have any questions, please call.

Sincerely,

&lt;Signature&gt;

Copy: Study file
Attachment D

PERIODIC REPORT to the IRB

Protocol Title: __________________________ Date of Report: ____/____/____

☐ Interim Report

☐ Renew approval for the study

☐ The study has ended

☐ Completed Date ___/___/___
☐ Terminated Date ___/___/___
☐ Not Started
☐ Inactive

If the study is inactive, terminated or never started, please state the reason.

1. Study Summary
   a. Results obtained to date, if any.

   b. Have there been any significant new findings? ☐ Yes ☐ No

   c. Has there been an interim analysis? ☐ Yes ☐ No

   d. Have there been any changes to the approved protocol that have not been reviewed by the IRB? ☐ Yes ☐ No

2. Site Summary
   a. Number of subjects enrolled at this site __________

   b. Number of subjects who withdrew or discontinued participation for a reason other than an adverse event __________
c. Number of subjects who discontinued participation in the study because of an adverse event

__________

d. Number of subjects who experienced a serious adverse event

__________

e. Summarize serious adverse events that occurred in the study.

f. Explain why any subjects terminated their participation prematurely.

3. Have all serious adverse events, whether related to the study article or not, been reported to the IRB? (Please include reports of serious adverse events not reported, including sponsor-generated reports.)

☐ Yes ☐ No

4. Have all subjects signed the approved informed consent form?
   If not, please explain.

☐ Yes ☐ No

5. Have all subjects received a copy of the informed consent form?
   If not, please explain.

☐ Yes ☐ No

I certify that the information on this report and any attachments accompanying this report are correct.

Submitted by: _____________________________ on _____/_____/____

3.3

STANDARD OPERATING PROCEDURE FOR
REGULATORY FILES AND SUBJECT RECORDS

I. INTRODUCTION AND PURPOSE

Federal regulations require documentation of all study-related activities. The regulatory files and subject records, which are periodically reviewed by the sponsor and upon request by the FDA, serve as the site’s record of compliance with good clinical practice (GCP).

This standard operating procedure (SOP) describes the steps for fulfilling all regulatory, and clinical requirements for collecting, filing and storing study-related documents and records.

2. SCOPE

This SOP applies to the activities involved in maintaining the regulatory and subject records for all clinical studies conducted at this investigative site subject to investigational new drug (IND) regulations for drugs and biologics during all phases of development, investigator initiated research and observational studies.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.60 General responsibilities of investigators
21 CFR 312.62 Investigator recordkeeping and record retention
21 CFR 312.68 Inspection of investigator’s records and reports
FDA Information
Sheets, October 1995
May 9 1997 International Conference on Harmonization; Good Clinical Practice:
Consolidated Guideline

4. ATTACHMENTS

A. Regulatory Files Checklist
5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in conducting clinical trials/research studies at this research site. This includes the following:

- Principal investigator
- Sub-investigator
- Research manager
- Research nurse/coordinator
- Data manager
- Support staff

6. PROCESS OVERVIEW

A. Collecting, filing and storing study-related documents and records.

7. PROCEDURES

A. Collecting, filing and storing study-related documents and records

- Research nurse/coordinator
  
  For each study, create a series of file folders or start a binder for documents collected during the study (Attachment A, Regulatory Files Checklist).
  
  Maintain and update the file folders or binder as necessary, adding appropriate documents as they are generated or received.
  
  Retain copies of all original and revised documents (e.g., protocol, investigator’s brochure, informed consent form).

- Research nurse/coordinator
- Support staff
  
  Ensure that subject records and regulatory files are kept confidential and are stored in a secure, limited-access location.
• Research nurse/coordinator

Prior to appointments scheduled by monitors and auditors, review content of regulatory files and subject records for completeness.

Ensure that files are organized and complete following the appointment.

• Research manager
• Research nurse/coordinator

When the study is over, review the contents of regulatory files and subject records for completeness by comparing with the checklists.

Archive regulatory files and subject records.

Label storage boxes clearly and completely.

Document inventory of storage boxes.

Store in a secure location for the required period of time.
REGULATORY FILES CHECKLIST

INVESTIGATOR'S BROCHURE

File the most recent version of the Investigator's Brochure along with all previous versions.

PROTOCOL and CASE REPORT FORMS

File a copy of the complete final protocol for this study. If required by the sponsor, ensure that the protocol title page has been signed and dated by the principal investigator. Retain a complete blank set of all case report forms used for data collection in the study.

PROTOCOL AMENDMENTS

In this file, retain copies of any amendments to the original final protocol made by the sponsor or the investigator. Modifications may be in the form of new pages to be inserted in the protocol, an addendum to the protocol in the form of a letter, or contained in the body of an amended protocol. All three types of modifications should be filed here.

Note that all protocol amendments must be reported to your Institutional Review Board (IRB). Also, protocol amendments that increase the risk to the subject in any way must receive IRB approval prior to implementation.

FORM FDA 1572

A copy of the signed original FDA Form 1572 Statement of Investigator should be filed in this section. The form should list the name of the principal investigator and include any sub-investigators, if applicable. Any changes to the FDA Form 1572 should be submitted to the sponsor and to the IRB.

INVESTIGATOR CVs

Include copies of the current CVs for all personnel listed on the FDA Form 1572.
**IRB CORRESPONDENCE**

File in this section all correspondence between the investigator and the IRB regarding this protocol. Examples of documents to retain are comments from the IRB on the consent form or the protocol, the IRB approval letter(s), advertisements for the study approved by the IRB, yearly renewals of approval, site updates to the IRB, serious adverse event reports, notification to the IRB of IND safety reports, and a letter notifying the IRB of the completion of the study.

**IRB-APPROVED INFORMED CONSENT FORM**

The original approved IRB consent form(s) should be filed in this section, as well as any amended or renewed consent forms.

**LABORATORY CERTIFICATION**

A copy of the most recent certificate issued showing the expiration date.

**RANGE OF NORMAL VALUES for the REFERENCE LABORATORY**

A copy of the range of normal laboratory values used for this study will be filed here. If the units or ranges differ from those previously supplied to the sponsor, these must be submitted to the sponsor and a copy filed in this section. Retain the previous listing and ensure that the revised listing incorporates the effective date of change.

Note that if your certificate has expired and you have not received the updated certificate, include the most recent approval letter in this section. When the updated certificate arrives, attach the approval letter to it. Forward a copy to the sponsor and retain a copy in this section.

**SAE REPORTS and IND SAFETY REPORTS**

All serious adverse events must be reported promptly to the sponsor and to the IRB. File copies of all IND safety reports sent by the sponsor here, as well.

**DRUG ACCOUNTABILITY**

Items to be included in this section are:

1. Sponsor investigational drug shipping inventory
2. Drug dispensing log
3. Return shipment documentation
**MONITORING LOG**

At each visit from the sponsor, the log sheet should be signed and dated by all sponsor personnel and the purpose of the visit noted.

**INCLUSION/EXCLUSION LOG**

Retain a list of all subjects who signed the informed consent form and were screened for entry into the study. A list of the subjects who were enrolled, as well as those who did not meet the entry criteria, must be retained.

**SIGNATURE LIST**

File a list of the signatures of all study site personnel who entered, edited or deleted study data in the source documents and case report forms.

**FINAL STUDY REPORT**

A copy of the final clinical study report provided by the sponsor should be kept in this section.

**SPONSOR CORRESPONDENCE**

File in this section all correspondence between the investigator and sponsor, except for items dealing with protocol changes (which go into the Protocol file) and financial matters (which are filed separately).
3.4

STANDARD OPERATING PROCEDURE
FOR SPONSOR/CRO MONITORING VISITS

I. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) describes the processes followed at this investigative site when the sponsor’s monitor conducts a monitoring visit to:

• Assess adherence to the protocol;
• Review regulatory files for completeness;
• Ensure appropriate study drug storage, dispensing, and accountability;
• Verify data in case report forms (CRFs) with source documentation;
• Meet with the research nurse/coordinator and investigator to discuss progress of the study and any concerns raised as a result of the visit.

2. SCOPE

This SOP applies to the procedures for conducting the monitoring visit for all clinical studies subject to investigational new drug (IND) regulations for drugs and biologics during all investigational phases of development. It describes the steps followed by this clinical research site from the time the monitor schedules a monitoring visit until all follow-up activities associated with the visit have been completed.

3. APPLICABLE REGULATIONS AND GUIDELINES

<table>
<thead>
<tr>
<th>CFR Section</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 CFR 312.50</td>
<td>General responsibilities of sponsors</td>
</tr>
<tr>
<td>21 CFR 312.56</td>
<td>Review of ongoing investigations</td>
</tr>
<tr>
<td>21 CFR 312.59</td>
<td>Disposition of unused supply of investigational drug</td>
</tr>
<tr>
<td>21 CFR 312.60</td>
<td>General responsibilities of investigators</td>
</tr>
<tr>
<td>21 CFR 312.62</td>
<td>Investigator recordkeeping and record retention</td>
</tr>
<tr>
<td>21 CFR 312.64</td>
<td>Investigator reports</td>
</tr>
<tr>
<td>21 CFR 312.66</td>
<td>Assurance of IRB review</td>
</tr>
<tr>
<td>21 CFR 312.68</td>
<td>Inspection of investigator's records and reports</td>
</tr>
</tbody>
</table>

December, 2008 FDA Compliance Program Guidance Manual 7348.811: Clinical Investigators

March, 2011 FDA Compliance Program Guidance Manual 7348.810: Sponsors,
4. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in arranging, managing, participating in or following up after the monitoring visit. This includes the following:

- Principal investigator
- Sub-investigator
- Research manager
- Research nurse/coordinator
- Data manager
- Study pharmacist
- Support staff

5. PROCESS OVERVIEW

A. Scheduling the monitoring visit
B. Preparing for the monitoring visit
C. Managing the monitoring visit
D. Following up after the monitoring visit

6. PROCEDURES

A. Scheduling the monitoring visit

- PI
- Research nurse/coordinator
- Support staff

Work with the study monitor to schedule a mutually convenient date and time to conduct the monitoring visit.
B. Preparing for the monitoring visit

- PI
- Research nurse/coordinator
  
  Ensure that all regulatory documentation and that case report forms are complete and available for review.
  
  Ensure that all data queries received to date have been resolved to the extent possible.

- Research manager
- Research nurse/coordinator
- Support staff
  
  Ensure that the appropriate patient medical records will be available for review at the time of the monitoring visit.
  
  Inform the study pharmacist of the scheduled visit so that study drug storage and drug accountability records can be prepared for review.

C. Managing the monitoring visit

- Research nurse/coordinator
  
  Ensure that the monitor signs the visit monitoring log.
  
  Ensure that the study monitor has all documents required to complete the monitoring visit. Provide the monitor with an update on any study-related issues.

- PI
- Research nurse/coordinator
  
  At the conclusion of the visit, meet with the study monitor to discuss any issues related to:
  - Adherence to the protocol,
  - Review of the regulatory files,
  - Verification of data in the CRFs with the source documentation,
  - Study drug storage, dispensing and accountability requirements for data storage.

- PI
- Research nurse/coordinator
  
  Discuss any payment issues.
D. Following-up after the monitoring visit

- PI
- Research nurse/coordinator

Ensure that all issues identified for resolution or follow-up at the monitoring visit are addressed.
3.5

STANDARD OPERATING PROCEDURE
FOR STUDY TERMINATION VISIT

I. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) describes the processes followed at this investigative site when the sponsor’s monitor conducts a study termination visit to:

- Review all regulatory files for completeness;
- Complete the verification of all data in case report forms (CRFs) with source documentation;
- Meet with the research team to discuss the results of:
  - the final audit of the regulatory files,
  - the final source data verification,
  - the reconciliation of the study drug shipment and receipt records with drug accountability records,
  - the possibility of a quality assurance and/or FDA audit,
  - the requirements for data storage.

II. SCOPE

This SOP applies to the procedures for conducting the study termination visit for all clinical studies subject to investigational new drug (IND) regulations for drugs and biologics during all investigational phases of development, investigator initiated research and observational studies. It describes the steps followed by this clinical research site from the time the monitor schedules the STV until all follow-up activities associated with the visit have been completed.

III. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.50 General responsibilities of sponsors
21 CFR 312.56 Review of ongoing investigations
21 CFR 312.59 Disposition of unused supply of investigational drug
21 CFR 312.60 General responsibilities of investigators
21 CFR 312.62 Investigator recordkeeping and record retention
21 CFR 312.64 Investigator reports
21 CFR 312.66 Assurance of IRB review
21 CFR 312.68 Inspection of investigator's records and reports
4. ATTACHMENTS

A. Study Termination Visit Checklist

5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in arranging, managing, participating in or following up after the study termination visit. This includes the following:

1. Principal investigator
2. Sub-investigator
3. Research manager
4. Research nurse/coordinator
5. Study pharmacist
6. Support staff

6. PROCESS OVERVIEW

A. Scheduling the study termination visit
B. Preparing for the study termination visit
C. Managing the study termination visit
D. Following up after the study termination visit

7. PROCEDURES

A. Scheduling the study termination visit

- PI
- Research nurse/coordinator
- Support staff

As soon as possible after the last patient has completed all scheduled visits associated with the study, arrange a mutually convenient date and time for the study monitor to conduct the study termination visit.

(See Attachment A, Study Termination Visit Checklist.)
B. Preparing for the study termination visit

- **PI**
  - Research manager
  - Research nurse/coordinator
  Ensure that all regulatory documentation and case report forms not previously monitored are complete and available for review.

- Ensure that all data queries received to date have been resolved to the extent possible.

- **Research manager**
  - Research nurse/coordinator
  - Support staff
  Ensure that the appropriate patient medical records will be available for review at the time of the study termination visit.

  Inform the study pharmacist of the scheduled visit so that study drug can be inventoried and drug accountability records can be completed.

C. Managing the study termination visit

- **Research nurse/coordinator**
  Ensure that the study monitor has all documents required to complete the termination visit. Provide the monitor with an update on any study-related issues.

- **PI**
  - Research nurse/coordinator
  At the conclusion of the visit, meet with the study monitor to discuss any issues related to:
    - Final audit of regulatory files,
    - Final source data verification,
    - Study drug reconciliation,
    - The possibility of a quality assurance and/or FDA audit,
    - Requirements for data retention and storage.

- **PI**
  - Research nurse/coordinator
  If data were entered by computer, determine when hard copies of all CRFs will be provided to the site.

  Review with the monitor the sponsor’s requirements for protecting the integrity of the electronic data.

- **PI**
  - Research
  Discuss with the monitor the sponsor’s requirements for patient follow-up for serious adverse events after formal
nurse/coordinator termination from the study.

- PI
- Research nurse/coordinator

Discuss the possibility of:
- Publication of the data,
- Discuss requirements, pro rata, and final payment

D. Following-up after the study termination visit

- Research nurse/coordinator
- Study pharmacist

Ensure that the study drug is either prepared for return to sponsor/CRO or disposed of at the site at the sponsor’s written request.

File copies of study drug packing slips and shipment receipts appropriately.

**OR**

Provide sponsor with documentation of the previously authorized study drug disposal and file site copy appropriately.

If the randomization code on any study drug was broken for any reason, ensure that complete documentation is available.

Ensure return or destruction of all other study-related materials.

Ensure that any equipment on loan is returned.

- Research nurse/coordinator

Inform the IRB that the study is over and submit the final report. Provide sponsor with a copy of the correspondence.

- Research nurse/coordinator
- Data manager

After all data queries have been resolved, check study files for completeness. Arrange for transfer of study documents to secure storage, noting storage location at the site.
<table>
<thead>
<tr>
<th>DATE</th>
<th>DONE BY (name)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>All data queries resolved or designated unresolvable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Regulatory files reviewed for completeness</td>
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<tr>
<td></td>
<td></td>
<td>Study drug returned to sponsor/CRO or destroyed</td>
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<tr>
<td></td>
<td></td>
<td>Any instances of emergency breaking of the blind appropriately documented</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IRB notified that study has terminated</td>
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<tr>
<td></td>
<td></td>
<td>Report submitted to IRB</td>
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<tr>
<td></td>
<td></td>
<td>Sponsor copied on IRB correspondence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>All study-related supplies that are no longer need either returned or destroyed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Final payment received</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Any equipment on loan returned</td>
</tr>
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<td></td>
<td></td>
<td>Study files prepared for long-term storage</td>
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</tbody>
</table>
3.6

STANDARD OPERATING PROCEDURE FOR INVESTIGATIONAL DRUG ACCOUNTABILITY, STORAGE, DISPENSING AND RETURN

I. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) describes the processes at this investigative site for the receipt, storage, dispensing, reconciliation and return or authorized destruction of the investigational drug (study drug).

2. SCOPE

This SOP applies to all procedures related to all clinical studies subject to investigational new drug (IND) regulations for drugs and biologics during all investigational phases of development. It describes the steps followed by this clinical research site from the time the study drug is received on-site until it is either returned to the sponsor or destroyed on-site at the sponsor’s request.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.50 General responsibilities of sponsors
21 CFR 312.56 Review of ongoing investigations
21 CFR 312.59 Disposition of unused supply of investigational drug
21 CFR 312.60 General responsibilities of investigators
21 CFR 312.61 Control of the investigational drug
21 CFR 312.62 Investigator recordkeeping and record retention
21 CFR 312.68 Inspection of investigator's records and reports
21 CFR 312.69 Handling of controlled substances
January 1988 Guidelines for the Monitoring of Clinical Investigations
September 1993 FDA Internal Compliance Program Guidance Manual 7348.811: Clinical Investigators
May 1997 International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline
4. ATTACHMENT

A. Drug Accountability Form

5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in inventorying, storing, dispensing, or arranging for the return/destruction of study drug in connection with all clinical studies carried out at this investigative site. This includes the following:

1. Principal investigator
2. Sub-investigator
3. Research manager
4. Research nurse/coordinator
5. Data manager
6. Study pharmacist
7. Support staff

6. PROCESS OVERVIEW

A. Receipt and inventorying of study drug
B. Storage of study drug
C. Dispensing of study drug
D. Return/destruction of study drug

7. PROCEDURES

A. Receipt and inventorying of study drug

- Study pharmacist
- Research nurse/coordinator
- Support staff

Upon receipt of the study drug, inventory the shipment, ensuring that the information on the packing slips matches exactly with what has been sent to the site, including
  - Amount
  - Lot numbers
  - Quantity per carrier/container (if easily verified)

Promptly bring any discrepancies to the attention of the sponsor.

If the sponsor includes a form in the shipment to acknowledge receipt, obtain the appropriate signature and
forward the form to the sponsor/CRO.

Retain a copy for the regulatory files.

Ensure that any supplies required for the blinding of the study drug are available.

B. Storage

- Clinical research manager
- Investigator
- Research nurse/coordinator
- Study pharmacist

Store study drug in a secure environment with access limited to essential research personnel, according to the storage requirements detailed in the protocol or supplied by the sponsor in a supplementary document. Ensure that study drug is stored at the appropriate temperature, maintaining a storage area temperature log, if appropriate.

Follow any special requirements for controlled substances required at this investigative site in addition to those specified by the regulations.

Ensure that the randomization code, if appropriate, has been received.

C. Dispensing of study drug

- Research nurse/coordinator
- Study pharmacist

Ensure that each time study medication is dispensed, the drug accountability form is completed. Documentation will include:

- Amount (and lot number, if appropriate) dispensed,
- Name of individual dispensing study drug,
- Subject’s number,
- Subject’s initials,
- Date (and time, if appropriate) of dispensing,
- Date and time if appropriate amount of study drug returned,
D. Return/destruction of study drug

- Research nurse/coordinator
- Study pharmacist

At the conclusion of the study, ensure that the all documentation regarding receipt, storage, dispensing, and return of used containers is complete, accurate, and ready for review at the monitor’s termination visit.

Ensure that the study drug is available for the monitor to inventory and prepare for return shipment to the sponsor/CRO.

- Amount of study drug returned.

After use by the study subject, return all used containers/units, if appropriate, to the study pharmacist. If any containers/units are missing, document the reasons.

Note any discrepancies between amounts used by subjects and amounts expected to be returned and document the reasons.

- Study pharmacist
- Research nurse/coordinator
- PI
- Research manager
- Research nurse/coordinator
- Study pharmacist

Ensure that study drug supplies are adequate and within an appropriate expiration date.

Alert the monitor when additional supplies will be required.

If emergency breaking of the study drug blind is medically necessary, document all circumstances appropriately.
- Research nurse
- Study pharmacist

Destruction of study drug at this site, upon written authorization from the sponsor to do so, may be undertaken so long as such procedures are permitted by this site’s OSHA and biohazard materials policies.

Provide the sponsor with written documentation of the destruction of the study drug.

Maintain a copy in the regulatory files.
**Attachment A**

**DRUG ACCOUNTABILITY FORM**

Protocol #: __________________________ Protocol title: __________________________

**Investigational article received**

<table>
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<tr>
<th>Bottles</th>
<th>Blister packs</th>
<th>Capsules</th>
<th>Ampules</th>
<th>Patches</th>
<th>Other (describe)</th>
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Date of receipt: __/__/__  Received by: ____________

Amount: __________________________ Lot number: __________________________

Amount: __________________________ Lot number: __________________________

**Investigational article dispensing record:**

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<th>Pt. #</th>
<th>Pt. initials</th>
<th>Number dispensed</th>
<th>Number used</th>
<th>Number returned</th>
<th>OK? Y/N</th>
<th>Comments</th>
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For investigational article not returned or accounted for, complete the following:

<table>
<thead>
<tr>
<th>Pt. #</th>
<th>Pt. initials</th>
<th>Reason</th>
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Date that all investigational articles was returned to sponsor: __/__/__

Signature of person completing this form: ________________ Date __/__/__
4.1

STANDARD OPERATING PROCEDURE FOR INFORMED CONSENT DEVELOPMENT AND IMPLEMENTATION

I. INTRODUCTION AND PURPOSE

The ethical conduct of clinical investigations is based upon the voluntary consent of the subject who has been appropriately informed about a study’s risks and benefits. It is the responsibility of the investigator to ensure that all 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. Documentation of the informed consent process is required to establish that the subject was accurately and adequately informed and that no study-related procedures were initiated prior to obtaining informed consent.

This standard operating procedure (SOP) describes the steps for fulfilling the regulatory and ethical requirements for developing the informed consent document and for appropriately obtaining the subject’s informed consent.

2. SCOPE

This SOP applies to the activities involved in preparing the informed consent form, submitting it for IRB approval, and for obtaining informed consent from research subjects who participate in all clinical studies conducted at this investigative site. It applies to obtaining consent under general requirements or routine circumstances as well as identifies the specialized procedures for obtaining informed consent from subjects who do not speak English and from children. This SOP also specifies the conditions for exceptions from the general requirements for obtaining informed consent and for emergency research.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 50.25 Elements of informed consent
21 CFR 56.109 IRB review of research
21 CFR 56.111 Criteria for IRB approval of research
21 CFR 312.54 Emergency research
21 CFR 312.60 General responsibilities of investigators
21 CFR 312.62 Investigator recordkeeping and record retention
4. ATTACHMENTS

A. Informed Consent Checklist  
B. Informed Consent Template  
C. Guidelines for Obtaining Informed Consent  
D. Assent of Children Form  
E. Clarification of the Short Form of Informed Consent

5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in drafting the informed consent form, submitting it to the IRB for approval, and for obtaining informed consent from research subjects. This includes the following:

1. Principal investigator  
2. Sub-investigator  
3. Research nurse/coordinator

6. PROCESS OVERVIEW

A. Drafting or adapting the written informed consent form  
B. Obtaining written consent from the subject (or the legal representative)  
C. Documenting the informed consent process  
D. Revisions to the informed consent form  
E. Exceptions from general requirements for informed consent  
   1) Verbal consent using a short form and summary sheet  
   2) Consent of children  
   3) Waiver of informed consent in emergency situations  
   4) Exception from informed consent for emergency research
7. PROCEDURES

A. Drafting or adapting the written informed consent form

• PI
• Research manager
• Research nurse/coordinator

Based upon the protocol and investigator’s brochure, prepare a draft informed consent form (Attachment A, Informed Consent Checklist and Attachment B, Informed Consent Template) and/or use a template provided by the IRB.

• PI
• Research manager
• Research nurse/coordinator

OR

Adapt an informed consent document provided by the sponsor/CRO for use at this clinical site. Verify that all required and additional elements of the informed consent form are incorporated by using the Informed Consent Checklist (Attachment A) and inserting the appropriate language as required by the IRB. Ensure the document also meets all state and local requirements.

• PI
• Research manager
• Research nurse/coordinator

Submit the draft informed consent form to the IRB for review and approval along with the other IRB-required documents. In consultation with the sponsor/CRO, make modifications requested by the IRB. After the informed consent form document has been approved by the IRB, file the original IRB approval letter and informed consent form document appropriately and send copies of both documents to the sponsor.
B. Obtaining written consent from the subject (or the legal representative)

- PI
  - Ensure that the most recent version of the IRB-approved consent form is used.

- Sub-investigator
  - In a location that provides privacy, review the informed consent form with the subject by discussing all of the elements: provide an overview of the study, explain its purpose, procedures, risks and benefits, drug and comparative agent (if applicable), alternatives, research-related procedures, etc. (Attachment C, Guidelines for Obtaining Informed Consent).

- Research nurse/coordinator
  - Allow the subject time to read the document and ask questions.
  - Encourage input from family members and other care providers, if appropriate.

- Interpreter
  - If the subject does not speak English, ensure that the above procedure is implemented in the subject’s language, using a qualified interpreter. Ensure that both the subject and an impartial witness sign and date the informed consent document that has been translated into the language of the subject and approved by the IRB.
C. Documenting the informed consent process

- PI
  - After consenting to participate in the clinical study, ensure that the subject signs and dates the document.
- Sub-investigator
- Research nurse/coordinator

- PI
  - Provide a copy of the informed consent form document to the subject (or the legal representative).
- Sub-investigator
- Research nurse/coordinator

D. Revisions to the informed consent form

- PI
  - Review changes to the protocol and investigator’s brochure as well as IND safety reports, to assess the need for revising the informed consent form.
- Sub-investigator
  - Submit the revised informed consent form with changes requested by the sponsor and/or investigator to the IRB for approval.
- Research nurse/coordinator
  - If appropriate, contact all subjects enrolled in the study to request that they sign the revised informed consent form.

- PI
- Sub-investigator
- Research nurse/coordinator

Follow all procedures for obtaining and documenting the original informed consent process as outlined above.
E. Exceptions from general requirements for informed consent

1) Verbal informed consent using a short form and summary sheet

- PI
- Sub-investigator
- Research nurse/coordinator

If the IRB has waived the requirement for written informed consent from the subject (or the legal representative), develop two documents: a “short form” that captures the elements of informed consent (Attachment A, Informed Consent Checklist) and a summary sheet of the information that is to be presented verbally to the subject or the legal representative (Attachment E, Clarification of the Short Form of Informed Consent).

- PI
- Sub-investigator
- Research nurse/coordinator

Using the IRB-approved short form, read the document to the subject or the legally authorized representative. If the subject (or the legal representative) does not speak English, ensure that the information presented verbally in the subject’s native language has been translated and that the translation has been approved by the IRB.

Ensure that the person obtaining consent signs and dates the short form and request that an impartial witness sign both the summary sheet and the short form to document that the informed consent process was properly implemented.

Ensure that the subject (or the legal representative) signs the short form.

- PI
- Sub-investigator
- Research nurse/coordinator

Provide the subject (or the legal representative) with a copy of both the short form and the summary sheet.
2) Consent of children

- PI
  Consult with the IRB regarding state and local laws for the consent of minors.

- Sub-investigator
  If the subject is considered to be a legal minor, obtain consent from one or both parents, or legal guardian.

- Research nurse/coordinator
  Follow all procedures for obtaining and documenting the informed consent process as outlined above.

- PI
  Provide a copy of the informed consent form to the parent(s) or legal guardian(s).

- Sub-investigator

- Research nurse/coordinator
  Consult with the IRB regarding their requirements for the assent of minors.

- PI
  Develop a form to be used by children for their verbal or written consent for their participation in the study that describes the risks and benefits in age-appropriate language (Attachment D, Assent of Children Form).

- Sub-investigator

- Research nurse/coordinator
  Follow all procedures for obtaining and documenting the informed consent process outlined above.

- PI
  Provide a copy of the informed consent form to the child and parent(s) or legal guardian(s).
3) Waiver of informed consent in emergency situations

- **PI**
- **Sub-investigator**
  - or
  - **Second physician**

Establish that informed consent cannot be obtained from the subject for *all* the following reasons:

a. The subject is in a life-threatening situation requiring the use of the test article,

b. Informed consent cannot be obtained from the study subject,

c. There is insufficient time to seek consent from the subject’s legal representative,

d. No appropriate alternative therapy is available or recognized as being effective.

If time does not permit the independent judgment of a second physician and the life of the subject is at stake, administer the test article.

Submit documentation of the above action to a second physician not involved with the study for review and evaluation.

Within 5 working days of the emergency use of the test article, provide the IRB with documentation from the investigator and the second physician.

Notify the sponsor as soon as possible of the above actions.
4) Exception from informed consent for emergency research

- **PI**

Establish that a licensed physician not participating in this study, who is an IRB member or a consultant to it, determines that the clinical investigation cannot be conducted with prior informed consent from subjects for *all* the following reasons:

a. The subjects are in a life-threatening situation, where available treatments are unproven or unsatisfactory, and scientific knowledge gained from the study will be used to determine the efficacy and safety of the test article,

b. Informed consent cannot be obtained from the study subjects or legal representatives prior to initiating the experimental treatment,

c. The clinical investigation could not be carried out without waiver of consent.

- **PI**

In addition, the investigator must:

a. Assure that risks to the study subjects are reasonable and subjects may directly benefit from the research study,

b. Document all attempts to obtain consent from the subject as soon as possible, or to contact the subjects’ legal representatives to obtain informed consent (pre-approved by the IRB) within the pre-established protocol duration,

c. Ensure that family members have been afforded the opportunity to object to the subject’s participation,

d. Comply with all other mandates for the waiver of consent as required by the IRB and federal regulations, including requirements for:

4. Community input prior to initiating the study,

5. Independent data monitoring committee to oversee the study,

6. Public disclosure to the community at the completion of the study.
(a) The following information from 21 CFR 50.25 lists the **basic elements** of the informed consent which are **required** to be included in the informed consent form document:

<table>
<thead>
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<th>Yes</th>
<th>No</th>
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1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

2. A description of any reasonably foreseeable risks or discomforts to the subject.

3. A description of any benefits to the subject or to others which may reasonably be expected from the research.

4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.

6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
(8) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) **Additional elements of informed consent.** When appropriate, one or more of the following elements of information shall also be provided to each subject:

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
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</table>

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

| ![ ] | ![ ] |

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

| ![ ] | ![ ] |

(3) Any additional costs to the subject that may result from participation in the research.

| ![ ] | ![ ] |

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

| ![ ] | ![ ] |

(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.

| ![ ] | ![ ] |

(6) The approximate number of subjects involved in the study.

| ![ ] | ![ ] |
INFORMED CONSENT TO PARTICIPATE IN A RESEARCH STUDY

1. Introduction
You are being asked to volunteer for a research study. This study is being conducted at:

The investigator in charge of this study is:

The sponsor of the study is:

2. Purpose of This Research Study
The purpose of this research study is:

3. Length of Your Participation:
Your participation in the study will last ___________________. You will take the study medication / use the study device for about ________ and be followed up for ________. You will need to visit the doctor’s office _____ times.

4. Where the Study is Being Done and Number of People Participating
This study is taking place in ________________________, and about _____ people are expected to take part.

5. Study Procedures
Before you take part in this research study, the study must be explained to you and you must be given the chance to ask questions. You must read and sign this informed consent form. You will be given a copy of this consent form to take home with you.
If you agree to take part in this study, the following will happen

Visit 1:

Visit 2, 3 (Weeks ____, ____ etc).

Final Visit (Week ___)

Follow-up

6. What Will Happen When You Complete the Study

When your participation in the study ends, you will no longer have access to (the study article).

7. Procedures that are Not Standard Care for Your Condition or are Experimental

Use of a placebo (inactive agent), blinding (one or more parties unaware of the treatment assignment), and randomization (study drug selection by chance) are only done for research studies. Although _________ and ____________ are often part of standard medical care, these procedures are only being done for the purposes of the study and are not part of your routine care.

8. Possible Risks or Side Effects of Taking Part in this Study

__________ may cause the following side effects:

Allergic reactions can occur with any drug. Common symptoms may include: rash, itching etc.

Rarely, a severe and possibly life-threatening allergic reaction can occur. Symptoms of a severe reaction include: swelling of the face, difficulty breathing, a sudden drop in blood pressure that may cause dizziness. If you have any of these symptoms, call your doctor at once.

___________ is still being tested; therefore, you may experience other side effects that have not yet been reported. However, you will be kept informed of any significant new findings which may relate to your willingness to continue to take part in this study.

In addition, since you cannot (take any other medication) to treat your ________ while you are (receiving the study medicine), your condition may worsen.
9. Important Information for Women

The effect of the study article on a baby's development is not known. Therefore, pregnant and breastfeeding women may not take part in this study. Women who have a chance of becoming pregnant must have a negative pregnancy test at study entry and use birth control during the study. Acceptable methods include birth control pills, Depo Provera, diaphragm, intrauterine device (IUD), cervical cap, condom with sponge or foam. If you become pregnant during this study, you must stop taking the study drug and call your doctor immediately.

10. Other Important Information

If you experience any new symptoms, contact your doctor.

Obtaining blood can cause pain, bleeding, bruising, or swelling at the site of the needle stick. Fainting sometimes occurs and infection rarely occurs.

11. Costs for Taking Part in this Study

___________________________ will be free to you during the study. You or your insurance company will have to pay for ______________________________.

12. Payment for Taking Part in this Study

You will be paid as follows: If you complete the study, you will be paid ________. If you do not complete the study for any reason, you will be paid _______ for each visit you complete.

13. Possible Benefits to You for Taking Part in the Study

There are no direct benefits to you for participating in this study. However, your participation in this study may add to the medical knowledge about the use of this medication.

14. Other Treatments Available

Other treatments for _________________ are:

15. About Participating in this Study

Your participation in this study is voluntary. You may stop participating in this study at any time. Your decision not to take part in this study or to discontinue participation will not affect your medical care or any benefits to which you are entitled. If you decide to stop taking part in this study, you should tell the investigator.

Your doctor, the investigator and/or the sponsor may stop your participation in the study at any time if they decide that it is in your best interest. They may also do this if you do not follow instructions. If you have other medical problems or side effects, the doctor and/or nurse will decide if you may continue in the research study.

16. Compensation for Injury
By signing this consent form, you will not waive any of your legal rights or release the parties involved in this study from liability for negligence.

17. Confidentiality of Study Records and Medical Records

Information collected for this study is confidential. However, the sponsor company, ____________, and the Food and Drug Administration (FDA) of the U.S. Government will receive copies of the study records. Employees of ____________, the FDA, and the Institutional Review Board may see parts of your medical records related to this study. Data collected and entered into the Case Report Forms are the property of ____________. In the event of any publication regarding this study, your identity will not be disclosed.

18. Release of Personal Information

19. Names of Contacts for Questions About the Study

If you have any questions about taking part in this study, or if you think you may have been injured because of the study, call ____________ at ____________. If you have any questions about your rights as a research subject, you can call the Institutional Review Board at <phone>.
VOLUNTEER'S STATEMENT

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about taking part in this study or research-related injury, I may contact ______________ at ________________.

I understand that my participation in this research project is voluntary. I know that I may quit the study at any time without harming my future medical care or losing any benefits to which I might be otherwise entitled. I also understand that the investigator in charge of this study may decide at any time that I should no longer participate in this study.

If I have any questions about my rights as a research subject in this study I may contact:

IRB Chairperson Name
Address
Telephone (collect calls will be accepted)

By signing this consent form, I have not waived any of my legal rights or released the parties involved in this study from liability for negligence.

I have read and understand the above information. I agree to participate in this study. I have been given a copy of this form for my own records.

__________________________________                  __________________________________
Study participant (signature)                                   Date

__________________________________
Print participant’s name
                  Date

__________________________________                  __________________________________
Signature of person who explained the study                       Date
GUIDELINES for OBTAINING INFORMED CONSENT

- Informed consent must be obtained from each subject (or the subject's legally authorized representative) before the subject can take part in any research study, including post-marketing studies of approved drugs.

- Informed consent must be obtained from each subject (or the subject's legally authorized representative) before the subject can take part in any research study, including post-marketing studies of approved drugs and devices.

- Informed consent must be obtained from each subject prior to initiating any requirements of the study protocol, including pre-enrollment washout periods.

- The investigator must give the subject sufficient opportunity to consider whether or not to participate in the study. The investigator cannot coerce or use undue influence to get a subject to participate.

- Non-English speaking subjects must have the information presented in a language that they understand. If non-English speaking subjects will be enrolled, the informed consent should be translated into the appropriate language.

- Each subject must be given a copy of the consent document for his or her reference.

- In a private practice setting, the original signed informed consent should be kept in the patient's chart. In a hospital setting, the original should be in a file maintained by the investigator and a copy should be in the subject's medical record. The informed consent document should not be kept in with the case report forms.
What is a research study?

A research study is something like a science project you do in school. The people running the study want to learn something new. So they see what happens to people (like you) when they do things which are part of the study. When the study is over, they will write a paper about what happened.

What if I don’t want to be in the research study?

You do not have to be in the study if you do not want to be. If you do not want to be in the study, even if you said you would, you do not have to be in it.

What do I have to do in the research study?

The people in charge of the study must tell you what will happen to you during the study. You can ask questions about what you have to do and they will be answered.

I have been told what this research study is all about. I understand what I am being asked to do and what may happen while I am taking part in this research project.

I know I may ask questions at any time and get them answered.

No one has told me I have to take part in this study if I do not want to. I want to be in this research study.

Signature of Child (printing is OK) ___________________________ Date ___________________________
Based upon 21 CFR 50.27, there must be a witness to each oral presentation of the short form of the informed consent. The subject receives a copy of both forms.

**SUMMARY**

IRB must approve the text of oral presentation.

Summary contains all the required elements of IC to be presented orally.

____________________________________

Person obtaining consent

____________________________________

Witness

**SHORT FORM OF INFORMED CONSENT**

The study had been explained to me.

My questions have been answered.

I choose to participate in this study.

______________________________

Subject

______________________________

Witness
I. INTRODUCTION AND PURPOSE

The recruitment phase of a clinical study is frequently difficult and challenging. Successfully recruiting subjects involves the development and implementation of a well-coordinated plan that may require the efforts of the entire research team. Once in place, subject recruitment efforts must be constantly assessed, with new strategies implemented as necessary. After potential subjects have been identified through recruitment efforts, the process of subject selection begins.

This standard operating procedure (SOP) describes the steps for fulfilling the regulatory and clinical requirements involved in subject recruitment and selection.

2. SCOPE

This SOP applies to the activities involved in recruiting and screening subjects for clinical studies conducted at this investigative site subject to investigational new drug (IND) regulations for drugs and biologics during all phases of development, investigator initiated research and observational studies.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 50.20 General requirements for informed consent
21 CFR 56.109 IRB review of research
21 CFR 312.60 General responsibilities of investigators
21 CFR 312.62 Investigator recordkeeping and record retention
FDA Information Screening Tests Prior to Study Enrollment and Recruiting Study
Sheets, October 1998 Subjects
May 1997 International Conference on Harmonization; Good Clinical Practice:
Consolidated Guideline

4. ATTACHMENTS

A. Screening and Enrollment Log
5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in conducting clinical trials/research studies at this research site. This includes the following:

1. Principal investigator
2. Sub-investigator
3. Research nurse/coordinator
4. Support staff

6. PROCESS OVERVIEW

A. Develop and implement an overall recruitment plan
B. Assess the effectiveness of the recruitment plan
C. Initiate screening procedures

7. PROCEDURES

A. Develop and implement an overall recruitment plan

- Research manager
  - Research nurse/coordinator
  Based upon the specific inclusion/exclusion criteria for a study, identify the target population for potential study subjects.
  - Establish a recruitment timeline.
  - Identify sources of potential participants.

- Research nurse/coordinator
- Support staff
  - Determine recruitment methods (e.g., space/radio ads, letters, community talks, newspaper articles, patient support groups, Internet).
  - Develop recruitment materials and submit to the IRB as appropriate.

- Research manager
- Research nurse/coordinator
  - Project costs associated with each recruitment strategy.
  - Hire additional staff if necessary and provide training.
B. Assess the effectiveness of the recruitment plan

- Research manager
  - Monitor progress and assess results of the recruitment strategy. Develop appropriate alternative strategies, if necessary.
- Research nurse/coordinator
  - Institute alternative strategies if enrollment projections lag.
  - Evaluate final results.

C. Initiate screening procedures

- Research nurse/coordinator
  - Develop a screening log based upon the study inclusion/exclusion criteria to collect screening information on all potential subjects (Attachment A, Screening and Enrollment Log).
  
  - Note if individuals went on to enroll in the study; if they were not enrolled, document the reason.
- PI
- Research nurse/coordinator
  - Obtain informed consent. Maintain a log of when informed consent was obtained from each subject.
  - Retain all signed informed consent forms from subjects who terminate their participation in the study during the screening process.
## SCREENING and ENROLLMENT LOG

<table>
<thead>
<tr>
<th>Screening</th>
<th>Enrollment</th>
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<tbody>
<tr>
<td>Screen Date</td>
<td>Enroll Date</td>
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<td>ID #</td>
<td>ID #</td>
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<td>ICF Signed</td>
<td>If not enrolled, explain</td>
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<td>Consent ed by</td>
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<td>Staff Initials</td>
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STANDARD OPERATING PROCEDURE FOR SUBJECT MANAGEMENT WHILE ON STUDY

I. INTRODUCTION AND PURPOSE

The safety and well-being of subjects is of paramount concern to the research team. This standard operating procedure (SOP) describes the steps for fulfilling the regulatory and clinical requirements to ensure adherence to study procedures for the evaluation of a subject’s response. Through close monitoring and careful assessment of subjects, adverse events can be detected early and treated appropriately. By following these procedures, close attention is paid to subject well-being and to integrity of the data.

2. SCOPE

This SOP applies to the activities involved in managing subjects on clinical studies conducted at this investigative site subject to investigational new drug (IND) regulations for drugs and biologics during all phases of development, investigator initiated research and observational studies.

3. APPLICABLE REGULATIONS AND GUIDELINES

<table>
<thead>
<tr>
<th>CFR Section</th>
<th>Description</th>
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<tbody>
<tr>
<td>21 CFR 50.20</td>
<td>General requirements for informed consent</td>
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<tr>
<td>May 1997</td>
<td>International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline</td>
</tr>
</tbody>
</table>

4. ATTACHMENTS

A. Medical History
B. Physical Examination
C. Concomitant Medication Log
D. Adverse Event/Inter-current Illness Log
E. Patient Summary
5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in ensuring the appropriate clinical management of all clinical research activity. This includes the following:

1. Principal investigator
2. Sub-investigator
3. Research nurse/coordinator

6. PROCESS OVERVIEW

A. Enrollment assessments and management
B. Follow-up, completion and early termination from the study
C. Communication with primary or referring medical providers
D. Management of ineligible subjects

7. PROCEDURES

A. Enrollment assessments and management

• PI Elicit and document the subject’s medical history (Attachment A, Medical History).
• PI Perform a complete or directed physical examination (Attachment B, Physical Examination).
• PI Establish the subject’s baseline signs and symptoms.
• PI Review with the subject the use of any current medication (Attachment C, Concomitant Medication Log).
• PI Inform the subject about the required study procedures and visits.
• PI Collect specimens as directed by the protocol
• PI Order tests/procedures as directed by the protocol.
• PI Provide contact information to the subject.
• PI Schedule the follow-up visit.

• PI Randomize and dispense the test article.
• Study pharmacist Review with the subject the use of any study aids, such as a diary.
• Research nurse/coordinator
B. Follow-up, completion and early termination from the study

- **PI**  
  Perform a complete or directed physical examination.

- **Research nurse/coordinator**  
  Assess the subject for signs and symptoms of any inter-current illness and document adverse events appropriately (Attachment D, Adverse Event/Inter-current Illness Log).  
  Collect specimens as directed by the protocol.  
  Order diagnostic tests and procedures as necessary.  
  Institute appropriate therapy if required by the subject’s condition.  
  Review any use of concomitant medication.  
  Schedule follow-up visits per protocol.

- **PI**  
  Assess the subject’s compliance with the test article.

- **Study pharmacist**  
  Collect unused test article, if appropriate.

- **Research nurse/coordinator**  
  Dispense additional test article, as required.

- **PI**  
  Diagnose and document any inter-current illness and endpoints.

- **Sub-investigator**  
  Review the subject’s laboratory and other test results.

C. Communication with primary or referring medical providers

- **Research nurse/coordinator**  
  Inform the subject’s primary care provider about the subject’s progress while on study, if the subject agrees.
  
  Ensure that the primary care provider receives copies of the subject’s laboratory test results and reports of procedures, etc. if the subject agrees.
  
  Confer with the primary care provider, as appropriate.
D. Management of ineligible subjects

- PI
- Research nurse/coordinator

Document the reason for ineligibility. Retain any supporting data available.

Complete any clinical and laboratory assessments required by the protocol.

Collect any unused test article and any used test article containers, and record data in the investigational drug log.

Discuss treatment alternatives with the subject. Follow the subject as required by the protocol.

Notify the sponsor as required.
**MEDICAL HISTORY**

Patient Name: ______________________________ Date: ___/___/___

Please check the appropriate box and, if abnormal, describe.

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<tr>
<th>Normal</th>
<th>Abnormal</th>
<th>Describe the abnormality</th>
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<td>Ears, nose and throat ____________________________</td>
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<td>Ophthalmic _________________________________</td>
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<td>Respiratory _________________________________</td>
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<td>Smoker Yes ___ No ___ # packs/week ________</td>
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<td>Cardiovascular ________________________________</td>
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<td>Urogenital ________________________________</td>
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<td>Psychiatric ________________________________</td>
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<td>Drug allergies ______________________________</td>
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Signature ______________________________ Date: ______________________________
**Attachment B**

## PHYSICAL EXAMINATION

Patient Name: _________________________________  Date: __/__/__

*Please check the appropriate box and, if abnormal, describe.*

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<th>Normal</th>
<th>Abnormal</th>
<th>Describe if abnormal</th>
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<td>Neurological</td>
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Height ___________ [ ] ins [ ] cms  
Weight ___________ [ ] kg [ ] lb

Vital Signs: Temp _______ [ ] F [ ] C  
B/P _______  P _______

**Comments:**

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

Signature _______________________________  Date: ____________
Attachment C

Patient #: ______
Patient initials: ______

CONCOMITANT MEDICATIONS LOG

<table>
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</table>
## ADVERSE EVENT and INTERCURRENT ILLNESS LOG

<table>
<thead>
<tr>
<th>Adverse Event/Inter-current Illness</th>
<th>Severity</th>
<th>Start Date</th>
<th>Stop Date</th>
<th>Treatment or Procedure</th>
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## PATIENT SUMMARY

### Protocol Information

- **Protocol #:**
- **Protocol Title:**

### Baseline Information

- **Pt. initials:**
- **Wt. at baseline:** ________ (kg)

### Enrollment Details

- **Date enrolled:** ___/___/___
- **Date completed:** ___/___/___
- **Total time on study:** ______

### Dose Changes

<table>
<thead>
<tr>
<th>Date</th>
<th>Rationale</th>
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### Adverse Events

<table>
<thead>
<tr>
<th>Date</th>
<th>SAE?</th>
<th>Description</th>
<th>IRB report?</th>
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</thead>
<tbody>
<tr>
<td><em><strong>/</strong></em>/___</td>
<td>Y ☑</td>
<td>N ☐</td>
<td>Y ☑ N ☐</td>
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<td>Y ☑ N ☐</td>
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<td>Y ☑ N ☐</td>
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</table>

### Protocol Deviations

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<th>Date</th>
<th>Description</th>
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</tbody>
</table>

### ICF Amendments

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### Comments:

- _______________________________________________________________________
- _______________________________________________________________________
- _______________________________________________________________________
- _______________________________________________________________________
4.4

STANDARD OPERATING PROCEDURE
FOR ADVERSE EVENT REPORTING

1. INTRODUCTION

Subject safety is of the greatest importance for both the individual subject and the goals of the clinical study. Investigators are required to report to the sponsor all adverse events occurring during a study. If the event is serious and unexpected, prompt reporting to the sponsor and to the IRB is mandatory. This standard operating procedure (SOP) describes the steps this clinical research team follows to fulfill the regulatory and clinical requirements for adverse event reporting.

2. SCOPE

This standard operating procedure (SOP) describes the responsibilities of the research team for managing, reporting and documenting adverse events from the time an adverse event is identified until all follow-up activities associated with its resolution have been completed. This SOP also describes the mechanisms used to provide the information necessary for sponsors to prepare Investigational New Drug (IND) safety reports. Finally, the procedures for processing and transmitting IND safety reports received from the sponsor to the IRB are defined.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.32 IND safety reports
21 CFR 312.33 Annual reports
21 CFR 312.44 Termination
21 CFR 50.25 Elements of informed consent
21 CFR 56.108 IRB functions and operations
21 CFR 56.109 IRB review of research
21 CFR 56.115 IRB records
45 CFR 46.103 Assuring compliance with this policy-research conducted or supported by any Federal Department or Agency
45 CFR 46.109 IRB review of research
45 CFR 46.115 IRB records
45 CFR 46.116 General requirements for informed consent
FDA Information
Sheets, October 1998
Continuing Review After Study Approval
May 1997
International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline

4. ATTACHMENTS

A. MedWatch Form 3500
B. MedWatch Form 3500A
C. Procedures for Managing Adverse Events

5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in ensuring the appropriate management of adverse events. This includes the following:

- Principal investigator
- Sub-investigator
- Research manager
- Research nurse/coordinator
- Data manager
- Support staff

6. PROCESS OVERVIEW

A. Managing adverse events
B. Handling IND safety reports from sponsors
C. Reporting to the IRB
7. PROCEDURES

A. Managing adverse events

- PI
- Sub-investigator
- Research nurse/coord
- Study pharmacist

Follow up appropriately when a research subject experiences any adverse change from baseline or pretreatment condition, ensuring that all appropriate resources are directed toward subject safety and well-being. Follow the subject until the event is resolved.

- PI
- Sub-investigator
- Research nurse/coord
- Study pharmacist

If necessary for the immediate medical care of the subject only, break the drug blind after consultation (if possible) with the sponsor.

- PI
- Research nurse/coord
- Support staff

If the adverse event is serious and/or unexpected, inform the sponsor as soon as possible after the subject is stabilized. Provide as much information as is available.

- PI
- Research nurse/coord

Record the details of the adverse event in the source documentation and complete the appropriate CRFs.

- Research nurse/coord
- Support staff

Keep originals or photocopies of all relevant documentation, including facsimile confirmations, and file in the study binder with appropriate documents.
B. Handling IND safety reports from sponsors

- PI
- Sub-investigator
- Research nurse/coordinator
- All research staff involved in subject assessment and care
- Research nurse/coordinator
- Support staff

Promptly review IND safety reports received from sponsors.

File IND safety reports in the study regulatory file.

C. Reporting to the IRB

- PI
- Research nurse/coordinator
- Support staff

Ensure that the IRB is notified of all serious or alarming events occurring at this site during the approval period for the ongoing study.

Ensure that all IND safety reports received from sponsors are promptly submitted to the IRB.

Ensure that the clinical site reports to the IRB all routine adverse events as part of the periodic or annual reporting requirements.
Attachment A
FORM FDA 3500

To retrieve (PDF) format of the above forms go to web site:


Download this form, or xerox a copy of the form provided as an attachment in the SOP printed document.
Attachment B
FORM FDA 3500A

To retrieve (PDF) format of the above forms go to web site:


Download this form, or xerox a copy of the form provided as an attachment in the
SOP printed document.
## PROCEDURES for MANAGING ADVERSE EVENTS

### 1. Identification, assessment and management of an adverse event

<table>
<thead>
<tr>
<th>REGULATIONS</th>
<th>PROCEDURES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition of an adverse event (AE):</strong></td>
<td>Ensure that the following are appropriately investigated:</td>
</tr>
<tr>
<td>• Any adverse change from baseline (pretreatment) intercurrent illness which</td>
<td>• Spontaneous reports by subjects</td>
</tr>
<tr>
<td>occurs during the course of a clinical study after treatment has started,</td>
<td>• Observations by clinical research staff</td>
</tr>
<tr>
<td>whether considered related to treatment or not</td>
<td>• Reports to research staff by family or medical care providers</td>
</tr>
<tr>
<td>• Any effect that is unintended and unfavorable, such as a sign, a symptom,</td>
<td>• Possible AEs documented in medical records, progress notes, etc.</td>
</tr>
<tr>
<td>a laboratory abnormality or a disease or condition</td>
<td>• Reports of a subject death within four weeks after stopping treatment or</td>
</tr>
<tr>
<td></td>
<td>during the protocol-defined follow-up period, whichever is longer,</td>
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<td></td>
<td>whether considered treatment-related or not</td>
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<tr>
<td><strong>Serious adverse events (SAEs) include:</strong></td>
<td>Manage the adverse event to ensure that all appropriate resources are</td>
</tr>
<tr>
<td>• Death</td>
<td>directed toward subject safety and well-being. Institute therapeutic</td>
</tr>
<tr>
<td>• Life-threatening experience</td>
<td>intervention/support measures. If applicable:</td>
</tr>
<tr>
<td>• Inpatient hospitalization or prolongation</td>
<td>• Discontinue the investigational product, comparator, or placebo</td>
</tr>
<tr>
<td>• Persistent or significant disability/incapacity</td>
<td>• Reduce dosage (as per protocol)</td>
</tr>
<tr>
<td>• Congenital anomaly/birth defect</td>
<td>• Interrupt drug (as per protocol)</td>
</tr>
<tr>
<td>• Events that would require medical or surgical intervention to prevent</td>
<td>• Challenge (as per protocol)</td>
</tr>
<tr>
<td>any of the above</td>
<td>Follow the subject and assess the adverse event until stabilized/resolved.</td>
</tr>
</tbody>
</table>

Ensure that the following are appropriately investigated:

- Spontaneous reports by subjects
- Observations by clinical research staff
- Reports to research staff by family or medical care providers
- Possible AEs documented in medical records, progress notes, etc.
- Reports of a subject death within four weeks after stopping treatment or during the protocol-defined follow-up period, whichever is longer, whether considered treatment-related or not

Manage the adverse event to ensure that all appropriate resources are directed toward subject safety and well-being. Institute therapeutic intervention/support measures. If applicable:

- Discontinue the investigational product, comparator, or placebo
- Reduce dosage (as per protocol)
- Interrupt drug (as per protocol)
- Challenge (as per protocol)

Follow the subject and assess the adverse event until stabilized/resolved.
2. Reporting SAEs to the sponsor

- Report **serious and unexpected** adverse experiences, whether considered drug-related or not, to the sponsor as soon as possible.
- Provide details to the sponsor as they become available. If additional information cannot be obtained for whatever reason, document this.
- Inform the sponsor when no other information is expected.

### SPONSOR RESPONSIBILITIES

| Sponsors are required to notify the FDA by IND safety reports of **any serious adverse experience associated with use of the drug** in the clinical studies conducted under an IND as soon as possible but no later than **15 calendar days** after initial receipt of the information. |

### SITE RESPONSIBILITIES

| To meet expedited reporting requirements, inform the sponsor as soon as possible after the subject is stabilized. |

If the event is **fatal or life-threatening and associated with use of the drug**, sponsors are required to notify the FDA by telephone or fax within **7 calendar days** of initial receipt of the information.

<table>
<thead>
<tr>
<th>Provide as much of the following information as is available:</th>
</tr>
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<tbody>
<tr>
<td>• Protocol name and number</td>
</tr>
<tr>
<td>• The possible test articles: investigational product, comparator, or placebo</td>
</tr>
<tr>
<td>• Lot number and expiration date</td>
</tr>
<tr>
<td>• Subject identifiers</td>
</tr>
<tr>
<td>• Demographic data</td>
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<tr>
<td>• The nature of the event</td>
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<tr>
<td>• The severity of the event</td>
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<tr>
<td>• The probable relationship of the AE to the investigational product</td>
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<tr>
<td>• The date (and time) of AE onset</td>
</tr>
<tr>
<td>• The date (and time) of AE resolution, if available</td>
</tr>
<tr>
<td>• The dose, frequency, and route of administration</td>
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<tr>
<td>• The start and stop dates of test article administration</td>
</tr>
<tr>
<td>• Concomitant medications and therapies</td>
</tr>
<tr>
<td>• Clinical assessment of the subject at this time</td>
</tr>
<tr>
<td>• The results of any laboratory and/or diagnostic procedures, treatment, autopsy findings</td>
</tr>
<tr>
<td>• The follow-up plan</td>
</tr>
<tr>
<td>• The outcome</td>
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</tbody>
</table>
3. Research documentation

<table>
<thead>
<tr>
<th><strong>SOURCE DOCUMENTATION</strong></th>
<th><strong>CASE REPORT FORM COMPLETION</strong></th>
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<tbody>
<tr>
<td>Record in the source documentation, noting</td>
<td>Complete the appropriate case report form(s)</td>
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<tr>
<td>• The nature of the event</td>
<td>• The site-prepared data collection form for SAEs or</td>
</tr>
<tr>
<td>• The severity of the event</td>
<td>• The sponsor-generated CRF for routine AEs</td>
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<tr>
<td>• The probable relationship of the AE to the investigational product</td>
<td></td>
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<tr>
<td>• The date (and time) of AE onset</td>
<td></td>
</tr>
<tr>
<td>• The date (and time) of AE resolution, if available</td>
<td></td>
</tr>
<tr>
<td>• The possible test articles: investigational product, comparator, or placebo, the dose, frequency, and route of administration</td>
<td></td>
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<tr>
<td>• The start and stop dates of test article administration</td>
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<tr>
<td>• Concomitant medications and therapies</td>
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<tr>
<td>• Clinical assessment of the subject at this time</td>
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<tr>
<td>• The results of any laboratory tests and/or diagnostic procedures</td>
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<tr>
<td>• The follow-up plan</td>
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<tr>
<td>• The outcome</td>
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4. Sponsor-generated IND safety reports

<table>
<thead>
<tr>
<th><strong>RESPONSIBILITIES TO IRB</strong></th>
<th><strong>RESPONSIBILITIES TO SPONSOR</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Submit all IND safety reports to the IRB and retain a copy of the transmittal memo in the study regulatory binder.</td>
<td>• Acknowledge receipt of expedited safety report to sponsor with letter/facsimile.</td>
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<td>• Copy sponsor on the transmittal memo to the IRB, if required.</td>
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<td></td>
<td>• Inform sponsor of action required by the IRB, such as revisions to the informed consent form.</td>
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<td>• Follow up with the sponsor as required.</td>
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</tbody>
</table>
1. INTRODUCTION AND PURPOSE

The proper collection and processing of specimens obtained from study subjects are part of the data collected in a clinical study. The specimens provide important information about the drug’s action within the body and the subject’s biologic and clinical response. To ensure accurate data, specimens must be collected at the specified time points, processed, possibly preserved, and then shipped appropriately. Additionally, research or ancillary staff must adhere to good laboratory practices when collecting, processing, and arranging for shipment of the specimens to the testing laboratory. This standard operating procedure (SOP) describes the steps for fulfilling the regulatory and clinical requirements involved in specimen collection and handling.

2. SCOPE

This SOP applies to the activities involved in collecting and handling specimens from subjects enrolled in clinical studies conducted at this investigative site subject to investigational new drug (IND) regulations for drugs and biologics during all phases of development, investigator initiated research and observational studies.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.62 Investigator recordkeeping and record retention
May 1997 International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline

4. ATTACHMENTS

A. Specimen Shipping Log

5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in ensuring appropriate specimen collection and handling at this research site. This includes the following:
1. Principal investigator
2. Sub-investigator
3. Research nurse/coordinator
4. Technician

6. PROCESS OVERVIEW

A. Collecting the specimens
B. Processing the specimens
C. Preparing the specimens for shipping to the testing laboratory

7. PROCEDURES

A. Collecting the specimens

- Research nurse/coordinator
- Technician

Observing appropriate precautions based upon OSHA guidelines, infection control manual, and/or the institutional procedure manual for the handling of bodily fluids, collect the appropriate specimens identified in the study protocol.

In the subject’s medical record and/or on the case report form, note the date and time of the collection as well as any relevant information pertaining to the subject’s status at the time of the procedure.

Label the test tubes or other containers with subject identifiers, date, time, and any other information required.

B. Processing the specimens

- Research nurse/coordinator
- Technician

Process the specimen according to the specifics defined in the protocol (for example, centrifuge speed, duration, temperature requirements).

Spin, separate and transfer the specimen to the appropriate transport tube(s), as required.

Label the study-specific test tubes or other containers with subject identifiers, date, time, and any other information required to prepare for storage or shipment.
Complete the laboratory requisition slip. Include one copy with the specimens when shipped. Retain one copy and file with the other study-related subject records.

C. Preparing the specimens for shipping to the testing laboratory

- Research nurse/coordinator
- Technician

Prepare and package the specimens according to the shipping instructions specified in the protocol and/or central laboratory procedure manual.

Complete the specimen shipping log (Attachment A).

Retain a copy of the shipping receipt and file with the other study-related subject records.
<table>
<thead>
<tr>
<th>STUDY #</th>
<th>INITIALS</th>
<th>SAMPLE DATE</th>
<th>SPECIMEN TYPE</th>
<th>VISIT #</th>
<th>VISIT #</th>
<th>VISIT #</th>
<th>NO. OF SAMPLES SHIPPED</th>
<th>DATE SHIPPED</th>
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STANDARD OPERATING PROCEDURE
FOR DATA MANAGEMENT

I. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) describes the processes followed at this investigative site for the collection of clinical research data, transcription of the data to case report forms (CRFs), and the management of the data, including procedures for:

- Quality control
- Data query resolution
- Record retention and archiving

2. SCOPE

This SOP applies to data management for all clinical studies subject to investigational new drug (IND) regulations for drugs and biologics during all investigational phases of development, investigator initiated research and observational studies.

3. APPLICABLE REGULATIONS AND GUIDELINES

- 21 CFR 312.50 General responsibilities of sponsors
- 21 CFR 312.56 Review of ongoing investigations
- 21 CFR 312.60 General responsibilities of investigators
- 21 CFR 312.62 Investigator recordkeeping and record retention
- 21 CFR 312.64 Investigator reports
- 21 CFR 312.68 Inspection of investigator's records and reports
- 21 CFR 312.70 Disqualification of a clinical investigator
- FDA Information Sheets, October 1995
- January 1988 Guidelines for the Monitoring of Clinical Investigations
- May 1997 International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline
4. ATTACHMENTS

A. List of Logs Kept for Each Study
B. Source Documentation Requirements
C. Data Clarification Form

5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in data collection, transcription to CRFs, and the management of the data.

This includes the following:

1. Principal investigator
2. Sub-investigator
3. Research manager
4. Research nurse/coordinator
5. Study pharmacist
6. Support staff

6. PROCESS OVERVIEW

A. Collection of clinical research data
B. Transcription of the data to case report forms (CRFs), including remote data entry
C. Management of the data, including procedures for:
   • Quality control
   • Data query resolution
   • Record retention and archiving

7. PROCEDURES

A. Collection of clinical research data

• Research nurse/coordinator: Ensure that copies of the most recent IRB-approved consent form are available for subject enrollment.

Based upon the protocol and case report forms, develop study-specific source documentation, checklists and logs (Attachments A and B).
B. Transcription of the data to case report forms (CRFs), including remote data entry

- **Research nurse/coordinator**
- **Support staff**

Record all documentation in black ball point pen. Complete all fields in the CRFs according to sponsor specifications. Correct errors by striking through the error, dating and initialing it, and making the correction. Ensure the original entry is not obliterated. If necessary, note an explanation in the right margin.

Ensure that data for the CRFs are transcribed promptly from the source documentation.

- **Research nurse/coordinator**
- **Support staff**

If the sponsor requires remote data entry, ensure that data are entered by computer according to sponsor specifications promptly from the source documentation.

C. Management of the data

- **Research manager**
- **Research nurse/coordinator**

Ensure that the first sets of completed CRFs are reviewed for completeness and accuracy by another member of the research team or by another designated individual.

- **Research nurse/coordinator**

Request a copy of the sponsor’s SOPs for making changes or corrections to the CRFs.

Collect any discrepancies noted at the sponsor’s monitoring visit on a data clarification form to ensure a trail of clarifications and corrections. If a sponsor-specific form is not available, ensure that any discrepancies are noted on a generic data clarification form (Attachment C, Data clarification Form).

Ensure that the data clarification forms are kept with the other study records in the regulatory files for this study.

Correct errors to the CRFs noted at the monitoring visit by using the procedures described above.

- **Research nurse**
- **Research manager**
- **Support staff**

At the conclusion of the study, ensure that data are retained according to regulatory and sponsor requirements. Inform the sponsor of the study in writing and obtain approval prior to destroying any study-related data.
Attachment A

<table>
<thead>
<tr>
<th>LIST OF LOGS KEPT FOR EACH STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Subject screening/enrollment log</td>
</tr>
<tr>
<td>□ Subject identification code list</td>
</tr>
<tr>
<td>□ Signature sheet</td>
</tr>
<tr>
<td>□ Record of retained body fluids/tissue samples (if appropriate)</td>
</tr>
</tbody>
</table>
SOURCE DOCUMENTATION REQUIREMENTS

For each study, source documentation to support case report form data should include the following:

1. Date of entry into the study, sponsor’s protocol number, and subject number.

2. Note that written informed consent was obtained; consent form dated and signed by subject (or subject’s representative).

3. Record any current medications and medications discontinued within the last month (or longer, as specified by the protocol).

4. Record subject’s diagnosis and status prior to treatment, including documentation of medical history, particularly that relevant for the disease or condition being treated.

5. Record names of possible study drugs and dosing times.

6. Document the dates and the results, evaluations and procedures required by the study; note any deviations from the protocol and provide an explanation.

7. Record any reported complaints or adverse events that occurred during the treatment period and for a period specified by the sponsor following the last dose of study drug. Record any treatment administered and/or recommended.

8. Record subject’s condition during and/or after treatment.

9. Document final disposition of the subject and subject status at time of study termination.
**DATA CLARIFICATION FORM**

Study Number: ____________  
Sponsor: ____________________________

Study Title: _________________________________________________________________
_____________________________________________________________________

<table>
<thead>
<tr>
<th>Pt. #</th>
<th>Initials</th>
<th>CRF</th>
<th>Clarifications</th>
<th>✔</th>
<th>Initials</th>
<th>Date</th>
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Signature of person completing the form

____________________________________________________________________

Investigator’s Signature

____________________________________________________________________

Date
I. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) serves as a companion to SOP 5.1, Standard Operating Procedure for Data Management. This investigative site follows SOP 5.1 for general management of all clinical research data. We refer to this SOP for additional guidance concomitantly required when all or portions of the data that are required by an FDA predicate rule for a submission or inspection, are collected, managed and/or transmitted electronically, or include the use of electronic signatures in required records.

II. SCOPE

This SOP applies to electronic data management for all clinical studies subject to investigational new drug (IND) regulations for drugs and biologics, and investigational device (IDE) regulations for medical devices, during all investigational phases of development, investigator initiated research and observational studies. This SOP does not apply to computerized medical devices, diagnostic laboratory devices or analytical laboratory devices that are used during a clinical trial. Nor does it apply to paper records that are transmitted electronically.

III. APPLICABLE REGULATIONS AND GUIDELINES

- 21 CFR 812 Subpart E: Responsibilities of Investigators
- 21 CFR 812 Subpart G: Records and Reports
- 21 CFR 11: Electronic Records; Electronic Signatures
- April 1999: FDA Guidance for Industry: Computerized Systems Used in Clinical Trials
4. ATTACHMENTS

A. Electronic Data Management Log

5. RESPONSIBILITY

This SOP applies to those members of the clinical research team and others involved in computerized system setup and use, and electronic data capture and management.

This includes the following:

- Sponsor
- Site Information Systems manager
- Principal investigator
- Sub-investigator
- Research manager
- Research nurse/coordinator
- Study pharmacist
- Support staff

6. PROCESS OVERVIEW

A. System setup, training, security and maintenance
B. Collection of clinical research data
C. Transcription of the data to case report forms (CRFs), including remote data entry
D. Management of the data

7. PROCEDURES

A. System setup, training, security and maintenance

1. Sponsor responsibilities

   - Sponsor and/or primary institution
     Retain primary responsibility for ensuring computerized systems used in clinical studies data management at this facility are in compliance with applicable regulations, as regards to design and validation.
• Sponsor and/or primary institution

Train all clinical research team members on the proper use of all sponsor/institutional-provided electronic systems used to capture study data (electronic patient diary, e-CRF), and on the relevant regulatory requirements.

Train the research manager and/or research nurse/coordinator to conduct appropriate reviews of electronic data and audit trails at designated time periods.

2. Research site responsibilities

• Information Systems (IS) Manager

Work with sponsor/investigators to facilitate setup, implementation and maintenance of an FDA-compliant computerized system.

Work with sponsor/investigators to ensure that computerized systems used in clinical studies have a logoff or comparable security function after a designated period of inactivity.

Assign unique and secure User ID/password combination for each clinical research team member who has access to the computerized system(s).

Establish and maintain a schedule for changing each team member’s User ID/password combination at appropriate intervals.

Invalidate stolen, lost or otherwise compromised User ID/password combinations and replace with a new combination.

Ensure that proper computer system function is routinely monitored.

Ensure that sponsor-provided computerized systems are used only for the purposes for which they were intended and validated.

• Information Systems (IS) Manager

If the sponsor/investigator requires a cryptographic digital signature or a biometric-based electronic signature rather than a handwritten signature, work with the sponsor/investigator to establish and securely maintain that
identifier.

Ensure that computerized systems are securely stored when not in use.

- Principal Investigator (PI); Research manager; IS manager
  Login using his or her unique User ID/password combination or other electronic signature when preparing to perform computer data entry or management functions.

- All team members
  Do not divulge unique User ID/password combinations to anyone else for any purpose.

  Do not use anyone else’s unique User ID/password combination or perform any required computer functions under anyone else’s User ID/password combination.

  Log off when computer data entry/management activities are completed.

B. Collection of clinical research data

- PI; Nurse manager
  Ensure protocol identifies at which steps a computerized system will be used.

- Nurse manager
  Maintain a record listing the hardware and software that will be used for each clinical study.

C. Transcription of the data to case report forms (CRFs), including remote data entry

- Research nurse/coordinator
  Ensure that sponsor-provided computerized systems are used only for the purposes for which they were intended and validated.

  Ensure the audit trail documents all changes to electronic records (who, when, why) and that the original entries are not overwritten.

  Ensure that all annotations to electronic records are attributable as to who and when (date, time) the annotations
<table>
<thead>
<tr>
<th>Department of OB/GYN</th>
<th>Approved By:</th>
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</thead>
<tbody>
<tr>
<td>Standard Operating Procedures For Management of Electronic Medical Records</td>
<td>SOP No. 5.2</td>
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<td>Original Version Date:</td>
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<td>Effective Date:</td>
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<tr>
<td>Revisions:</td>
<td>Page 1 of 5</td>
</tr>
</tbody>
</table>

- Data manager
  - Enter all required data into the appropriate fields of e-CRFs.
  - Check and correct (or annotate) all data before transmitting the e-CRF to the sponsor.

**D. Management of the data**

- PI; Nurse manager
  - Ensure that an original or certified copy of all electronic source documents and audit trail records are retained on file.
  - With respect to an FDA audit, treat electronic records as you would paper records.

- Nurse manager
  - Ensure that changed CRFs and eCRFs also display all prior information.
  - Work with sponsor to ensure that audit trail reviews are performed and documented at defined intervals.
  - Retain audit trail records according to regulatory and sponsor requirements.
**ATTACHMENT A**

**ELECTRONIC DATA MANAGEMENT LOG**

<table>
<thead>
<tr>
<th>Study Number: ______________________</th>
<th>Sponsor:_________________________________</th>
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<tbody>
<tr>
<td>Study Title: __________________________________________</td>
<td>Site:__________________________</td>
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</table>

### Hardware Used for Data Capture/Input

<table>
<thead>
<tr>
<th>Item</th>
<th>ID#</th>
<th>Sponsor-Dedicated to Provided (Y/N)</th>
<th>Study (Y/N)*</th>
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Examples: Computer station, laptop computer

### Accessory Items Used for Data Transmission

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<tr>
<th>Item</th>
<th>ID#</th>
<th>Sponsor-Dedicated to Provided (Y/N)</th>
<th>Study (Y/N)*</th>
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Examples: Facsimile machine, Palm Pilot

### Software

<table>
<thead>
<tr>
<th>Item</th>
<th>Version</th>
<th>Sponsor</th>
<th>Off-the-Shelf Provided (Y/N)</th>
<th>Shelf (Y/N)</th>
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*Note: For computerized systems that are NOT dedicated to this study, provide explanation of how control is maintained over access to the system and its software.

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6.1

STANDARD OPERATING PROCEDURE FOR AUDITS

1. INTRODUCTION
   This standard operating procedure (SOP) describes the operations followed at this investigative site when an audit (internal, sponsor/CRO and FDA), occurs to assess this site’s extent of compliance with regulatory requirements/guidelines and SOPs for conducting clinical research.

2. SCOPE
   This SOP applies to the procedures to prepare for an audit of all clinical studies conducted at this site. It describes the steps followed by the site from the time the audit is scheduled until all follow-up activities associated with the audit have been completed.

3. APPLICABLE REGULATIONS AND GUIDELINES
   21 CFR 312.60  General responsibilities of investigators
   21 CFR 312.62  Investigator recordkeeping and record retention
   21 CFR 312.64  Investigator reports
   21 CFR 312.66  Assurance of IRB review
   September 1993  FDA Internal Compliance Program Guidance Manual, 17348: 811 Clinical Investigators
   FDA Information Sheets, October 1998  FDA Clinical Investigator Inspections
   May 9, 1997  International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline
   January 1988  Guidelines for the Monitoring of Clinical Investigations

4. ATTACHMENTS
   A. Preparing for an Audit Checklist

5. RESPONSIBILITY
   This SOP applies to those members of the clinical research team involved in arranging, managing, or participating in the audit at this research site. This includes the following:
   • Principal investigator
   • Sub-investigator
   • Research manager
   • Research nurse/coordinator
• Data manager
• Study pharmacist
• Support staff

6. PROCESS OVERVIEW

A. Preparing for the audit
B. During the audit
C. Following up after the audit

7. PROCEDURES

A. Preparing for the audit

• PI
• Research nurse/coordinator
• Support staff

If notified of an FDA audit, notify the sponsor as soon as possible.

Ensure that all documentation, including informed consent forms, source documents, CRFs, and the regulatory binder for the study identified as the focus of the audit are accurate, complete and available for review by the auditor (Attachment A, Preparing for an Audit Checklist).

• Research nurse/coordinator

Ensure that the study drug dispensing records are accurate, complete and available for review. If there were any instances in which emergency breaking of the blind was required, have that documentation available.

• Study pharmacist

Ensure that drug accountability records are accurate, complete and available for review.

• Research manager
• Research nurse/coordinator
• Support staff

Ensure that records of staff qualifications and training are available for review by the auditor.
B. During the audit

- PI
- Research manager
- Research nurse/coordinate

Meet with the auditor or inspector. Request to see identification, and if this is an FDA audit, request Form FDA 482.

Provide orientation and access to the study records and files.

Provide copies of requested study-related documents.

Ensure that questions posed by the auditor or inspector are answered by appropriate study personnel.

C. Following up after the audit

- PI
- Research nurse/coordinate
- Investigator

Participate in the exit interview with the auditor or inspector. If this was an FDA audit, request Form FDA 483, if available.

Respond to the audit report as soon as possible after its receipt. Reply to each item in the report, providing clarification or steps that will be taken to institute corrective action.
## PREPARING FOR AN AUDIT CHECKLIST

<table>
<thead>
<tr>
<th>I. ORGANIZATION</th>
<th>YES</th>
<th>N/A</th>
<th>COMMENTS</th>
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<tbody>
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<td>Sponsor (if an FDA audit)</td>
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<td>IRB</td>
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<td>Sub-investigators</td>
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<td>Pharmacy</td>
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<td>Laboratories</td>
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<td>Medical records</td>
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<td>Administration</td>
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<td>Legal counsel</td>
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<tr>
<td>Reserve work space for the auditor</td>
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<tr>
<td>Prepare a general overview of the study</td>
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<tr>
<td>List all personnel and responsibilities delegated</td>
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<tr>
<td>List all subjects enrolled including name, address, and/or phone number, date enrolled and completed, medical record number (to be kept as a reference for site research staff)</td>
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<td>List all subjects screened</td>
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<td>2. FILES MANAGEMENT</td>
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<td><strong>Organize all regulatory files by general heading arranged in chronological order</strong></td>
<td>Protocol (all versions)</td>
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<td>Investigator's Brochure (all versions)</td>
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<td>Protocol amendments</td>
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<td>Form FDA 1572 (all versions)</td>
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<td>CVs for PI and sub-investigators listed on all versions of Form FDA 1572</td>
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<td><strong>IRB files</strong></td>
<td>Approval letter (initial) for initial protocol with original informed consent</td>
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<td>Amendment approval(s) with approved informed consent (if applicable)</td>
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<td>Informed consent forms (originals) for enrolled subjects</td>
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<td>Informed consents for screened subjects</td>
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<td>• Yearly renewal(s)</td>
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<td>• Adverse events</td>
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<td>• Study termination</td>
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<td>• Final summary</td>
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<td>Monitoring log</td>
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<td><strong>Laboratory</strong></td>
<td>Laboratory certification and normal ranges</td>
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<td>Drug log to include:</td>
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<td>• Receipt of drug</td>
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<td>• Dispensing</td>
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<td>• Return</td>
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<td><strong>Subject documents</strong></td>
<td>Completed CRFs for each subject enrolled</td>
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<td>Source documents for each subject enrolled</td>
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<td><strong>Collect and review for each subject enrolled</strong></td>
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<td>CRFs completed for each subject enrolled</td>
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<td>Data correction forms for CRFs</td>
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<td>Source documents for each subject enrolled that document the following:</td>
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<td>• Condition of subject at time of entry into the study (i.e., all inclusion/exclusion criteria are met)</td>
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<td>• Exposure to test article</td>
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<td>• Concomitant medications</td>
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<td>• Clinical assessments of the subject during the course of the study</td>
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<td>• Laboratory reports</td>
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<td>• Diagnostic tests</td>
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<td>• Dose modifications</td>
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<td>• Adverse events/death</td>
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<td>• Protocol exemptions</td>
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<td>• Early termination</td>
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## Fax Log

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7.1

STANDARD OPERATING PROCEDURE FOR SAFEGUARDING PERSONAL HEALTH INFORMATION

I. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) describes the steps taken to ensure that subject personal health information (PHI) is kept confidential and access to such information is limited to authorized research staff for approved purposes only. Access to confidential information should only be permitted for direct subject management, administrative oversight, or with Institutional Board approval. Maintaining high standards of conduct with respect for the privacy of individuals and the confidentiality of information is essential for all personnel involved with the conduct of clinical research.

2. SCOPE

This SOP applies to all staff, employees, students, consultants, monitors and others at this research site to maintain high standards of conduct with respect for the privacy of individuals and the confidentiality of information both during the hours they are performing their professional and work-related activities and outside their work-related activities.

3. APPLICABLE REGULATIONS AND GUIDELINES

None

4. ATTACHMENTS

A. Guidelines for Safeguarding Personal Health Information
B. Fax and E-mail Transmission Procedure
C. Fax Log

5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in conducting or overseeing clinical studies at this research site. This includes the following:
1. Principal investigator
2. Sub-investigator
3. Research nurse/coordinator
4. Data manager
5. Information systems manager
6. Study pharmacist
7. Monitor
8. Support staff

6. PROCESS OVERVIEW

A. Oral and phone communication
B. Computer access and security
C. Electronic communication
D. Documents and written communication
E. Transporting of confidential information

7. PROCEDURES

A. Oral and phone communication

- All research team members

Oral communications between investigators and research staff and other health care providers, whether in person or by phone, are essential to effectively manage subjects while on study. (Attachment A, Guidelines for Safeguarding Personal Health Information.)

Ensure that discussions regarding the treatment of individuals take place in areas that are not public and where others cannot overhear confidential information and identifiers.

Ensure that staff and employees do not discuss subjects in public areas, such as elevators, waiting rooms, cafeterias, and hallways.

Names and unique descriptions of individuals should not be discussed except in areas where privacy is maintained, such as a private office or treatment room.

- PI
- Research nurse/coordinator
- Support staff

When a PI/research coordinator talks with a subject in a semi-private area, such as a hospital or clinic room, emergency room, or other areas where absolute privacy cannot occur, conversations should take place behind
curtains, or in a partitioned area. When it is impossible to ensure absolute privacy, staff and employees must make every effort to remove themselves from the area, when possible, and to keep anything over heard confidential.

Ensure that PHI is not discussed on a cell phone except in an emergency. If subjects' PHI must be discussed via cell phone, it will be done in a private area (parked car, office, etc.).

### B. Computer access and security

- **Information systems (IS) manager**
  - Limit and control direct access to the PHI that resides on the site's computer system(s).
  - Locate workstations in areas of limited public access, except when necessary to provide care.
- **PI**
- **Research manager**
  - Maintain access lists and password assignments.
- **Research nurse/coordinator**
  - Determine access level prior to allowing individual access to PHI. Base these determinations on minimum necessary access.
  - Instruct users regarding passwords, logging on and off.

### C. Electronic communication

- **PI**
- **Research nurse/coordinator**
  - Ensure that each member of the research team is aware of and adheres to requirements for safeguarding PHI via:
    - **e-mail** – Do not transmit PHI unless individuals request such transmission in writing, or such information is protected via encryption software.
    - Make copies whenever e-mail that includes PHI is sent.
  - **Fax** – Care shall be taken when documents containing PHI are transmitted via fax. (Attachment B, Fax and E-mail Transmission Procedure.)
• Research nurse/Coordinator
• Support staff
• Information systems (IS) Manager

Intranet, internet – Transmit PHI on secure servers only.

Install and monitor encryption procedures or other security software and update regularly.

• Research nurse/Coordinator
• Support staff

Monitor the fax logs and e-mail transmissions regularly.
(Attachment C, Fax Log.)

D. Documents and written communication

• PI
• Research nurse/Coordinator

Handle all PHI in written form in a manner that respects the privacy of the individual and the confidentiality of information.

Ensure that staff do not carry, transport, use, or share written information in a careless manner.

Share case report forms, documents, test results, notes, and any other written information about a subject only with other staff members who have a need to see such information as part of their duties.

Ensure that written information is not held in public areas, not taken off premises and not handled in a manner that allows unauthorized access.

E. Transporting of confidential data

• PI
• Research nurse/Coordinator

Transport confidential documents by authorized staff only, using secure methods.

Remind individuals transporting confidential information of their responsibility for the security of such information until it arrives at another secure location.
Attachment A

Guidelines for Safeguarding Personal Health Information

Subject information is never discussed in public areas.

Conversations with the subject/family regarding confidential information is not held in public areas, particularly waiting rooms.

Phone conversations are held in areas where confidential information cannot be overheard.

Except for the subject's name, confidential information is not called out into the waiting room or discussed in transit to the examination room.

Lists, including scheduled procedures and appointment types and notes, with information beyond room assignments are not readily visible by others.

Records are filed in storage cabinets and rooms are locked.

Dictation is completed in an area where confidential information cannot be overheard.

At the front desk or examination rooms, documents with subject information are kept face down or concealed to avoid observation by patients or visitors. Only authorized site personal have access to confidential information.

Paper records and medical charts are stored or filed to avoid observation by others.

Physical access to fax machines and printers is limited to authorized personnel.

Confidential information is not left on an unattended printer, photocopier or fax machine, unless these devices are in a secure area.

Release of confidential information is done by staff specifically authorized to do so.

Answering machines are turned down so information being left cannot be overhead by other staff or visitors.

Confidential information is discarded by shredding and placing in an appropriate container.

Confidential information should remain in the medical/research record. Original records should never be removed from the site.

Confidential information should not be copied or removed in any form from the site without appropriate approval.

Computer monitors are positioned away from common areas.

The screens on unattended computers are returned to a logon screen. IDs and passwords are never shared.

Subjects are appropriately escorted to ensure they do not access staff areas, chart storage etc.
Attachment B

Facsimile and E-mail Transmission Procedures

General Policies

Only fax machines in non-public areas are to be used to send and receive faxes that contain PHI; or

Only fax machines in areas that require security keys, badges, or similar mechanisms in order to gain access shall be used to send and receive PHI.

Double check the recipient’s fax number before transmittal and to confirm delivery via telephone or review of the appropriate confirmation of fax transmittal.

_______ shall check fax machines every ____ hours for faxes that contain PHI. Documents found shall be immediately secured in the appropriate location or given to ____________.

Fax machines should be pre-programmed to destination numbers whenever possible to eliminate errors in transmission from misdialing.

Fax and e-mail senders of individually identifiable health information should routinely check and re-check fax numbers and e-mail addresses of recipients before transmission.

Destination numbers and e-mail addresses should be checked and confirmed at least quarterly. Frequent recipients of individually identifiable health information should be encouraged to notify you if their fax number or e-mail address is to change.

Each user is to complete an entry in the Fax log for every item sent (this may be revised if the fax machine is able to provide fax transmittal summaries and confirmation sheets) The logs shall be reviewed periodically for unauthorized access or use by ____________.

Mitigation

The fax cover sheet and e-mail transmissions must have a confidentiality statement at the bottom:

The documents accompanying this transmission contain confidential health information that is legally privileged. This information is intended only for the use of the individual or entity named above. The authorized recipient of this information is prohibited from disclosing this information to any other party unless required to do so by law or regulation and is required to destroy the information after its stated need has been fulfilled.

If you are not the intended recipient, you are hereby notified that any disclosure, copying, distribution, or action taken in reliance on the contents of these documents is strictly prohibited. If you have received this information in error, please notify the sender immediately and arrange for the return or destruction of these documents.

If the sender becomes aware that a fax or e-mail was misdirected, contact the receiver and ask that the material be returned or destroyed.
STANDARD OPERATING PROCEDURE FOR INFORMATION ACCESS CONTROL

I. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) describes the steps taken to ensure that subject personal health information (PHI) is controlled and access to such information is limited to authorized research staff for approved purposes only. Adequate password protection is vital to safeguarding PHI and must be limited to research staff who require access to this information. Therefore, each user of PHI will be identified and allowed access to information based on his/her assigned password.

2. SCOPE

This SOP applies to all research staff with access to private health information.

3. APPLICABLE REGULATIONS AND GUIDELINES

None

4. ATTACHMENTS

None

5. RESPONSIBILITY

This SOP applies to those members of the clinical research team involved in conducting clinical studies at this research site. This includes the following:

1. Principal investigator
2. Sub-investigator
3. Research nurse/coordinator
4. Data manager
5. Support staff
6. PROCESS OVERVIEW

A. Access of PHI via computer
B. Assignment of passwords
C. Password oversight

7. PROCEDURES

A. Access of PHI via computer

- PI
- Research Manager

Control access through individual identification and authentication.
Assign users a unique identification code.
Change passwords every _____ days (90 days, 180 days, etc.).

- PI
- Research Manager

Ensure that each individual who has been assigned a password is responsible for its safekeeping.
Stress that divulging a password may result in a disciplinary action.

B. Assignment of passwords

- Information systems (IS) manager
- Research Manager

Assign a password and maintain a log of assigned passwords.
Require that all individuals, prior to being issued a password, sign a confidentiality statement.

- IS manager
- Research Manager

Deactivate passwords when:
- Users are no longer associated with this research site, or
- Responsibilities change and minimum necessary level changes
C. Password oversight

- PI
- Research nurse/ coordinator

Control issuing and use of passwords centrally.
Ensure passwords are changed every _____ days.
Remind users that they are responsible for proper password use.
Instruct users that passwords must be protected by the user and not shared with or divulged to others.